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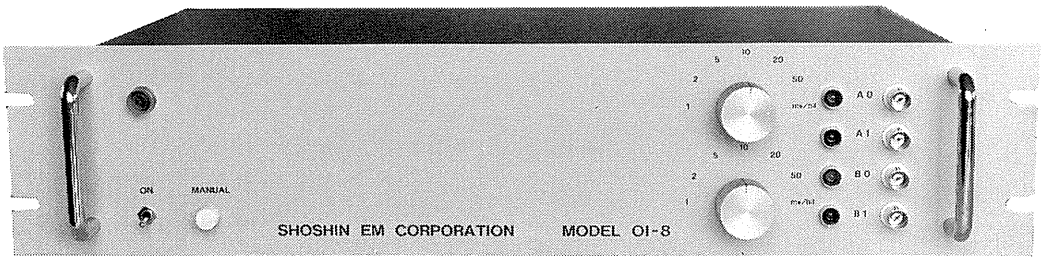
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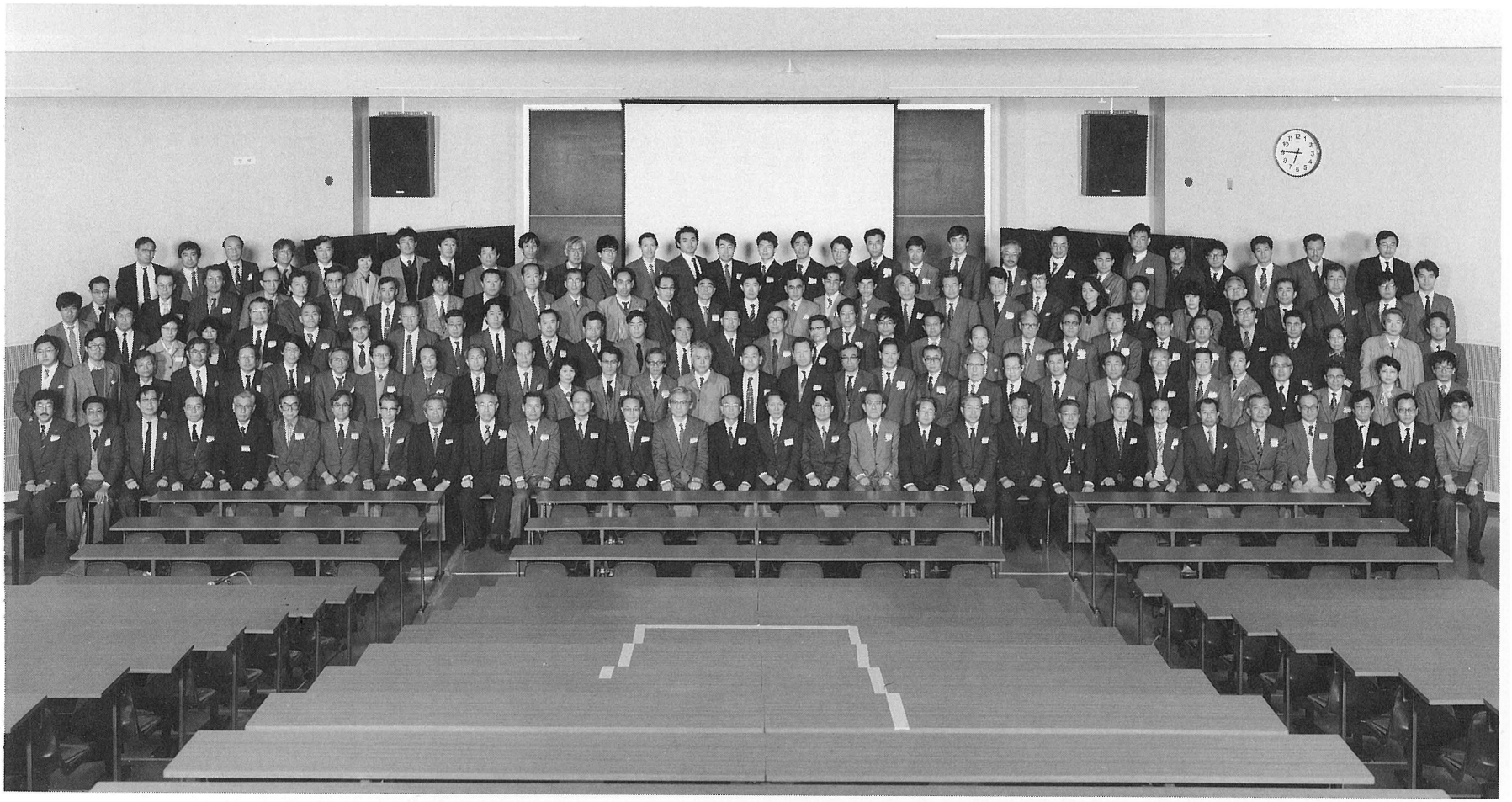
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第65回　日本生理学会大会　　昭和63年４月４日～６日　於 和歌山大学キャンパス

第65回日本生理学会大会を省みて

第65回日本生理学会大会
当番幹事　松下　宏・辻本　毅・辻　繁勝

第65回日本生理学会大会は昭和63年4月2日(土)の市民公開講演会を皮切りに，翌日曜日の各種委員会と常任幹事会を経て，4日(月)から6日(水)の3日間にわたる大会をまがりなりにも滞りなく終えることができました．

第63回山形大会で和歌山を正式にお決めいただいて以来の数多の不安が終えてみると全く嘘のように，また，夢のように思われます．偏えに参加会員各位の御協力の賜物であり，心から感謝致しております．

さて，今回の大会について会員諸兄はどのような御感想を抱かれたでありましょうか，もちろん，貧弱な当市の交通，宿泊事情等は一応横に置いていただいた上でございます．私共は及第点を頂くことはもとよりまずはないものと覚悟いたしております．と申しますのは，御覧いただいた如く今大会の開催について，当番幹事の自主性という名分を良いことにして，私共は従来の生理学会の伝統をまるきり弁まえなかったからであります．否，意図的に敢えて大胆な試みをさせていただいたからであります．

功罪の対象となるその最たるものは17課題にも及ぶシンポジウムを羅列したことでありましょう．このようなことはマンモス学会の一つとされる日本生化学会でも且て見られたことでしょうか，ましてや伝統を誇る生理学会の大多数の方々にとっては眼を回さんばかりのプログラムであったと思います．

事実，私共も当初はこれ程のテーマを予期していなかったのでありますが，恒例のグループディナーセクションの御希望を伺っているうちにこのような結果になってしまったのでありまして，いま少し選択の余地はあったかとも思います．しかし，永年各セクションが内々に育てて来られた成果なり将来への研究構想をこの際些かなりとも他の分野の人々にも知って置いてもらいたいという御意向は私共にも理解されむげに割愛するに偲びなかった事も御諒察願いたいのであります．

生理学大会は従来にもまして内容的にコンパクトにすべしとの御意見はよく承知しておりますが，今回のように対照的に巾広いプログラムを提供し，この中から各自の糧を収穫してお帰りいただくという一つのあり方を大胆にも試行させていただいたのであります．けれどもこの問題は大会の基本理念にもかかわることでもありますし，また今回のやり方にメリットがあるとしても，こんごいろいろと修正し補っていただかねばならないと考えます．

大袈裟にいって結果的に学会のあり方について不謹慎ながら一石を投じさせていただいたことになりましたが，御叱正の程は甘受しなければならないと思います．

なお，今回の名取・渡辺両先生の特別講演については各位から多大の御高評を頂いたように承っておりますが，これについては後日日生誌に掲載いただく御計画がありますので，大へん嬉しく存じております．また，運動制御に関する本間・浅沼両先生の2日間の早朝講演も私共の科学する心を強く刺激させて下さいました．教育シンポジウムは時間の関係と内容の豊富さから若干不消化に終ったように感じましたが明年もひきつづき御計画下さることと存じます．

また，最終日に配置されていたために出席者は誠に少のうございましたが，塚田先生の名司会のもと，慶応義塾大学実験動物センターの前島一淑教授の「動物実験の倫理と実験動物の福祉」と題するお話は多くの医学分科会の中でも逸早くとりあげたものだけに大きな意義があったと自負すると共に前島先生と動物実験に関する委員会に厚くお礼申しあげます．なお，動物実験のあり方については上記委員会からその基本的指針が提案されると共に J. J. P. 編集委員会からも，これと並行して投稿規程に Ethical Approval をつけ加える事が総会で決議されたことは国内専門誌の嚆矢として誇り得るものと思います．総会ではこの他，明年より大会英文抄録が日生誌から J. J. P. に移行掲載されることが決定されたことも特筆されると存じます．

大会運営に当り到らなかったのみではなく盛り沢山に過ぎた計画が，あるいは不消化に終りさらには各方面で多大の御不満や御迷惑のあったと危惧する点等宜しく御寛怒下さればと思います．

明年の岡山大会は多分今回を参考にされ爽やかなものとなりましょうが楽しみに参加させていただきたいと存じております．

THE 65th ANNUAL MEETING
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April 4 — 6, 1988

Wakayama Medical College

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SYMPOSIA(S-1—S-17)

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S-1 How Far Explain of Cell Function with Molecular Terms

S1-1

^{1}H-NMR STUDIES ON THE WATER STRUCTURE IN LIVING SYSTEMS. ERA, S.
Dept. Physiol., Sch. Med., Gifu Univ., Gifu 500

It was reported by several groups that water is structurally modified by ions or by proximity to surfaces of solid, membrane and cytoskeletal components. So, the present author studied the water structure in protein sol(solution), protein gel, normal rat liver, heptocellular tumor and regenerating rat liver, using spin-lattice relaxaiton times(T_1), spin-spin relaxation times(T_2) and cross-relaxation times(T_{IS}) from irradiated protein protons to water protons. Plots of $1/T_1$, $1/T_2$ or $1/T_{IS}$ of water protons in protein gel vs protein concentration were far steeper than those of protein solution, indicating the large amount of hydration and rapid exchange between bound and bulk water in protein gel. Plots of $1/T_1$ or $1/T_{IS}$ of normal rat liver vs dry weight(W(%)) were steeper than those of hepatocellular tumor and regenerating rat liver, indicating that the water structure of normal rat liver is gel-like state. Thus, various physiological states of tissues might be characterized by water molecules existing in different physical states.

S1-2

MOVEMENT OF INTRACELLULAR ELECTROLYTES DURING SECRETION AS MEASURED BY NMR.
Masataka Murakami, Dept. Molecular Physiology, National Institute for Physiological Sciencess, Okazaki 444.

^{23}Na and ^{39}K NMR (nuclear magnetic resonance) spectroscopy was applied to measure intracellular Na and K contents of the isolated perfused mandibular salivary gland. The intra- and extra-cellular electrolytes were discriminated using Dy(TTHA) as a chemical shift reagent; Na_{in} and K_{in} were estimated as 10 and 135 mmol/l ICF, respectively. The relaxation time of the intracellular K was measured very short (2 msec) rather than the extracellular K (40 msec), suggesting the presence of some interaction between the K ions and large molecules in cytosol. Without added chemical shift reagent, the time course of intracellular K was measured by a modified inversion recovery sequence during secretion with acetylcholine and during inhibition with ouabain, which well agreed with a accumulative value of K net-flux (measured from K content of effluent and saliva).

S1-3

TRANSPORT OF ENERGY IN MUSCLE: EVALUATION OF THE PHOSPHOCREATINE SHUTTLE HYPOTHESIS BASED ON DIFFUSIVITIES OF PHOSPHOCREATINE AND ATP.

YOSHIZAKI, K. Dept. Physiol., Kyoto Pref. Univ. Med., Kyoto 602

The flux of creatine kinase (CPK) reaction and the diffusivities of ATP and phosphocreatine (CPK) in muscle were studied to evaluate the energy transport role of PCr and CPK system. Diffusion coefficient of PCr was 1.4 times larger than that of ATP measured by ^{31}P pulsed gradient NMR, indicating the advantage of PCr molecule for the intracellular energy transport. The life time of free ADP molecule could be estimated from the CPK flux obtained by ^{31}P saturation transfer NMR and ADP concentration calculated from the CPK equilibrium constant. The mean square length of diffusion of ADP molecule, calculated from the diffusion coefficient of ATP, was larger than the diameter of the myofibril. Therefore in heart muscle having the alternate arrangement of mitochondria and myofibril, ADP molecule can move from myofibril to mitochondria without CPK reaction. The role of CPK reaction would be the spatial buffering for energy transport and/or the adjustment of metabolic regulators such as ADP and inorganic phosphate.

S1-4

INTRACELLULAR SIGNAL TRANSMISSION; THE ROLE OF THE CALCIUM ION IN CELL REGULATION

Hideki Matsui
Dept. of Physiology, Kagawa Med. Sch. Kagawa, 761-07

Calcium ion (Ca^{2+}) is one of the most important clues for intracellular second messenger system. Calmodulin, a main Ca^{2+} receptor protein in cell, transmit Ca information to a wide variety of enzymes through its calcium-dependent interaction with target proteins. Calcineurin (CaN), a calmodulin dependent phosphatase, is one of the most important and abundant calmodulin regulating enzymes in brain. We developed monoclonal antibodies against each subunit of CaN A (60K) and B (20K) and performed an immunohistochemical study.

Calcineurin A was abundant in striatum, hippocampus and thalams, but was very little in rat brain cortex. This distribution well agreed with that of adenylate cyclase, and suggested close relationship between c-AMP regulating system and calcineurin. In contrast to CaN A, B subunit was most abundant in brain cortex. The purified CaN contained free B subunit, and the dissociation and reassociation of free B to CaN were controlled by Ca-calmodulin.

The isolated B subunit, but not intact CaN (A+B), had the ability to inhibit calmodulin dependent protein kinase II in brain. These suggest that free B subunit is present in brain and may have independent physiological activity itself.

S1-5

MEMBRANE FLUIDITY AND PHOSPHOLIPID MOTION.

ARAISO, T., Research Institute of Applied Electricity, Hokkaido University, Sappooro, 060

Viscosity (η) in the phospholipid bilayer and the wobbling angle (θ_w) for the hydrocarbon chain of phospholipid could be measured by the time-resolved fluorescence anisotropy technique. In mixed lipid bilayers of DPPC (dipalmitoylphosphatidylcholine) and DMPC (dimyristoylphosphatidylcholine), both η and θ_w were changed by the alteration of molecular ratio of DPPC to DMPC. The value of η was mainly governed by the "free volume" of the hydrocarbon chains which depend on the θ_w and chain length. From the photobleaching recovery technique, the lateral diffusibility of the band 3 protein in rat erythrocyte membrane was found to be $4.5 \times 10^{-11} cm^2/s$ for normal membrane and $2.5 \times 10^{-9} cm^2/s$ for spectrin dysfunctional membrane at 25℃. By the use of $\eta = 3$ poise at 25 ℃ for rat erythrocyte membrane from fluorescent method, the lateral diffusibility of the band 3 protein was calculated to be $9.8 \times 10^{-9} cm^2/s$. This value is four times larger than the value for the spectrin dysfunctional membrane in which the band 3 protien is free from the spectrin network. It appeared that the caluclated value of the diffusibility may indicate the rate of free diffusion, and the rate is controlled by the range of wobbling motion of phospholipid molecule.

S1-6

MOLECULAR MECHANISMS OF CELL VOLUME REGULATION UNDER HYPOTONIC CONDITIONS. OKADA, Y. AND HAZAMA, A. Dept. Physiol., Kyoto Univ. Sch. Med., Kyoto 606

Under anisotonic conditions, a variety of cell species can readjust their volume after initial osmotic swelling or shrinkage. The cells exhibit a regulatory volume decrease (RVD) upon hypotonic stress due to induction of the KCl effluxes. Different transport pathways, including K^+ and Cl^- channels, K^+-Cl^- symporters, as well as K^+-H^+ and Cl^--HCO_3^- antiporters, have been suggested to be involved in the RVD. Direct evidence of separate activation of K^+ and Cl^- channels during the RVD process has recently provided in cultured human epithelial Intestine 407 cells (Hazama & Okada, 1988, J. Physiol. in press). Intracellular recordings of the K^+, Na^+ and Cl^- concentrations with ion-selective microelectrodes showed that operation of these channels can actually drive water effluxes during the RVD process. Cytosolic Ca^{2+} measurements with Ca^{2+}-selective microelectrodes or fura-2 showed that the cells respond to hypotonic stress with biphasic Ca^{2+} increases interposed by a transient decrease. The Ca^{2+} response and the RVD were abolished by deprivation of extracellular Ca^{2+} ions and by administration of a Ca^{2+} channel blocker, nifedipine. The K^+ channel activation was found to be associated with the Ca^{2+} increase, whereas the Cl^- channel activation was with the Ca^{2+} decrease. It is concluded that activation of Ca^{2+}, K^+ and Cl^- channels is prerequisite to the volume regulation of hypotonically swollen epithelial cells.

S-2 Physiological Studies in Tissue Culture

S2-1

DIFFERENTIATION OF THREE DIMENSIONAL MICROSTRUCTURES BY GROWTH CONES AND NERVE FIBERS. FUKUDA, J. Dept. Physiol., Fac. Med., Univ. Tokyo, Bunkyo-ku, Tokyo 113.

Dorsal root ganglion cells of adult mice were grown on a pure quartz glass surface on which grating-associated microstructures (MS) were fabricated by the lithographic and ionetching techniques. The MS was comprised of a repetition of rectangular microgrooves (mGV, 0.1-10 um wide and 0.1-2 um deep) and microsteps (mST, 0.1-10 um wide). Nerve fibers grown on the MS exhibited an oriented growth in the axial direction of the MS within a small angle ($\leq$ 20 degrees). This orientation of the nerve fibers was considered to be a result of mechanical guidance from the MS due to purely physical properties of the glass substrate, since no coating was made on the MS surface with any extracellular matrix materials, and since growth of nonneuronal, guide-post cells was rare on the MS surface. The orientation of the nerve fibers was enhanced by deepening the mGV and by shortening the width of the mGV and mST. Phase contrast microscopical observation revealed that 2/3 of nerve fibers grew on the mGV surface of the double-etched MS, on which the ultrafine surface configuration was identical between the mGV and mST. Growth cones, by contrast, represented an even distribution between the mST and the mGV of the double-etched MS. These observations suggest that the mechanisms underlying the recognition of the ultrafine configuration of the glass surface were different between the nerve fiber membranes and the growth cone membranes.

S2-2

MONOLAYER PARIETAL CELLS IN PRIMARY CULTURES OF NEONATAL RAT GASTRIC FUNDUS: NEW MATERIALS FOR STUDY ON THE ACID SECRETION. Okada Y. and Ueda, S. Dept. Physiol., Kyoto Univ. Fac. Med., Kyoto 606

Since the parietal cells reside deep in the pits of gastric epithelia together with chief cells and mucous neck cells, it was difficult to study on acid secretion at the single cell level. Recently, methods of isolation of gastric glands or parietal cells have been established. These experimental systems, however, have an inherent limitation concerning accessibility to the luminal membrane. We have established another system consisting of monolayer parietal cells adhered on the substrate in primary cultures of neonatal rat gastric fundus (Okada & Ueda, 1984, J. Physiol. 354, 109). The cells were found to have separate receptors for acetylcholine, gastrin and histamine, and to retain the ability of acid production at least for several days in culture. The monolayer cells were found to be very feasible for fluorescence-microscopical observations. Thus, the acid production was easily monitored by acridine orange uptake. The cytosolic free Ca^{2+} concentration could be measured in single fura-2-loaded cells. Locations of the tight junction and microvilli indicated that the upper free surface represents the luminal membrane. Therefore, this monolayer culture system appears to be useful for the study on the luminal membrane in intact cells. In fact, our recent patch-clamp studies on this membrane provided, for the first time, direct evidence for the induction of Cl^- channel activities by stimulation with acid secretagogues on the apical memebrane.

S2-3

PATCH-CLAMP STUDIES OF ION CHANNELS IN HIPPOCAMPAL NEURONS IN DISPERSED CELL CULTURES. OZAWA, S. Dept. Physiol., Sch. Med., Gunma Univ., Maebashi 371

Detailed analyses of the channel events of the neuronal membrane in the mammalian central nervous system (CNS) have not been carried out, since neurons in the CNS are not easily accessible to the patch-clamp technique. This difficulty can be overcome by adopting tissue culture techniques which allow development and maintenance of CNS neurons in monolayer cultures. Using the patch-clamp technique we have studied the properties of ion channels activated by N-methyl-D-aspartate (NMDA) in cultured hippocampal neurons prepared from 18-day-old fetal rats. Mg^{2+} at the physiological concentration markedly reduced the NMDA-induced currents recorded in the potential range more negative than -40 mV. In Mg^{2+}-free solution the application of NMDA elicited discrete pulse-like current flows through the cell-free outside-out membrane patch. The single channel conductance of the main open state was 40-50 pS at -84 mV, although several open states with lower conductances were detected. Quinolinate, an excitotoxic brain metabolite, caused membrane currents which were blocked by the selective NMDA receptor antagonist 2-amino-5-phosphonovalerate. This excitotoxin exclusively activated 40-50 pS conducting state.

S2-4

TWO CALCIUM CHANNEL CURRENTS IN SPHERICAL CHICK SKELETAL MUSCLE CELLS IN CULTURE.
KANO, M. AND SATOH, R. Dept. Physiol., Sch. Med., Kitasato Univ., Sagamihara, Kanagawa 228

Spherical muscle cells were grown under tissue culture conditions from embryonic chick skeletal muscle. Currents through Ca channels were recorded under voltage clamp with a suction pipette which was used to pass current and perfuse internally. To suppress Na, K and Cl channel currents, the pipette contained Cs aspartate and EGTA, and the external solution included Ba, TEA, Cs and acetate in place of Na, K, Ca and Cl. A suction pipette with an inner diameter at the tip of 10-15 μm was used. A microelectrode was used to record membrane potential. Under these conditions, depolarizations from a holding potential of -80 mV elicited clear inward current. The inward current was separated into two components. The first one was activated at a low-threshold potential (-50 mV), inactivated within tens of milliseconds, and was insensitive to an organic Ca channel blocker. The second inward current has a higher threshold potential of activation (-20 mV), inactivated much more slowly, and was blocked by the organic Ca channel blocker. Both currents were dependent on the external Ba concentration and both were blocked by Co. The results reveal that the two types of Ca channels coexist in the developing skeletal muscle cells. This may suggest that these Ca channels play roles in the early process of the development.

S2-5

AXOPLASMIC TRANSPORT IN TISSUE CULTURED NERVE CELLS
KAWAKAMI,T.,AND TAKENAKA,T. Dept. of Physiol.,Yokohama City Univ.,Sch. of Med., Fukuura,Kanazawaku,Yokohama,236.

Movement of transported particles in neurites was observe with AVEC-differential interference contrast video microscope and fluorescence optics with SIT camera. Dorsal root ganglia from 3-5 month old mice were cultured. After 3 days in culture the movement of particles in neurites was observed with this system. The mean velocities of anterograde and retrograde directions were 1.14 ± 0.40 μm/sec and 1.25 ± 0.48 μm/sec respectively. The movement of mitochondria was observed by specific fluorescent labeling of rhodamine 123. Mitochondria move in both directions. The velocities are 0.46 ± 0.20 μm/sec in the anterograde direction and 0.51 ± 0.24 μm/sec in the retrograde direction. Some mitochondria suddenly reversed their directions while moving toward the terminal. The retrogradely moving mitochondria become dominant at locations more proximal to the cell body. The direction of movement has no correlation with the central or peripheral routes.

S-3 Progress of Epithelial Transport Physiology

S3-1

PROGRESS OF EPITHELIAL TRANSPORT PHYSIOLOGY

FUJIMOTO,M.
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Epithelial membranes separate fluids with different compositions, through which molecules can be moved to individual cells to maintain the constant internal environment. During the past 10 years, collaboration of physiologists of many fields led to a general scheme of transporting epithelia. The function of epithelia can be classified into two major categories: secretion and absorption, depending upon the direction of the net movement of molecule outward and inward, respectively. This feature originates from the site and direction of pump-leak system in the epithelial borders. The coupled transport is comprised of two or three different kinds of moving solutes are linked together in traversing the membrane. Biophysical and biochemical approaches are necessary to explore these mechanisms. This symposium was designed to overview the recent progress of epithelial transport physiology. Prof. Hoshi will present some topics in the field of small intestine and kidney tubule as absorbing epithelia, whereas Prof. Takeguchi will introduce his extensive work on the physiology of gastric acid secretion. Prof. Y. Imai will explain how to apply the basic idea of network thermodynamics to the study of transport as an investigation tool.

S3-2

TERTIARY ACTIVE TRANSPORT IN RENAL AND SMALL INTESTINAL EPITHELIA.

HOSHI,T., Physiol. Lab., Sch. of Food & Nutr. Sci., Univ. of Shizuoka, Yada, Shizuoka 422

Our recent studies on Na^+-independent H^+-dependent transport of di- and tripeptides across intestinal and renal brush border membranes have shown that the transport is a typical example of the tertiary active transport in view of its energy utilization. Uptake of these peptides by brush border membrane vesicles (BBMV) was shown to be absolutely Na^+-independent, strongly dependent on an inward-directed H^+ gradient and electrogenic. Marked overshoot uptake was demonstrated in the presence of a pH gradient and inside negative membrane potential. The stoichiometry of the H^+:peptide cotransport was estimated to be 2:1. Both acidic microclimate pH and intracellular pH are dependent on the Na^+/H^+ antiport which is inhibitable by amiloride. Normally, a pH gradient more than one pH unit is maintained by this antiport which is dependent on the Na^+/K^+ ATPase. Coexistence of the Na^+-dependent mechanisms for free amino acids (secondary active) and H^+-dependent one for peptide (tertiary active) seems to have an important physiological meaning since each has unique properties which may compensate the properties of the other and such a compensation seems important for efficient absorption of protein hydrolysates.

S3-3

GASTRIC ACID SECRETORY MECHANISM.

TAKEGUCHI, N., Fac. Pharmaceu. Sci., Toyama Med. & Pharmaceu. Univ., Toyama 930-01

Parietal cell secretes HCl. H,K-ATPase is an active H pump in the apical membrane of the cell. We found that tubulovesicles of the cell in the resting state has closed Cl channel in addition to H,K-ATPase and that the Cl channel can be opened by S-S cross-linking. We raised several monoclonal antibodies against tubulovesicles. One of them named HK2032 partially inhibited H,K-ATPase and completely inhibited the Cl channel. The inhibition of both H,K-ATPase activity and the Cl channel was direct evidence that the Cl channel was a function of H,K-ATPase. Since Na,K-ATPase and Ca-ATPase do not contain anion channel, the channel in H,K-ATPase is very specific. The C-terminal regions of the amino acid sequence of the enzyme is rich in cystein residues, that may engage in S-S $\leftrightarrow$ 2SH (open $\leftrightarrow$ close) transformation of the Cl channel. The property of tubulovesicles, in which Cl channel was opened by cross-linking, was the same as that of apical membrane vesicles, indicating that the fusion of tubulovesicles with the apical membrane occurs in the process of stimulation and it accompanies increase in Cl conductance. Both H,K-ATPase in tubulovesicles and the apical membrane were immunologically the same. Another antibody HK4001 completely inhibited the enzyme activity and partially inhibited the Cl channel.

S3-4

SYSTEM DYNAMIC APPROACH OF SALIVARY SECRETION

IMAI,Y. Department of Physiology, Osaka Medical College
2-7 DAIGAKUMACHI, TAKATSUKI, OSAKA 569

Mechanism of primary acinar secretion is still not established, although several hypothetical models are proposed. In order to clarify the action of acinar model, system dynamic approach is carried out. The acinar epithelia was first subdivided into the structural subsystems: barrier-subsystems and solution-compartment -subsystems, and then was reconstituted as a whole model of acinus. Since thermodynamic processes are proceeding with thier interaction in each subsystem, subsystems were again subdivided into elemental thermodynamic processes: dissipative processes, power converting processes and free-energy increasing or decreasing processes. Each subsystem was reconstituted as module of bond graphs, which represented the resistive-barrier-module and the capacitive-compartment -module. As the respective bond-graph-module has the power balance thermodynamically, whole model with modules balances also in their power process. Using the model, some computer simulation were demonstrated.

S-4 Development and Differentiation of the Nervous System

S4-1

INDUCTIVE NEURAL-TYPE DIFFERENTIATION IN TWO INTERACTING CLEAVAGE-ARRESTED BLASTOMERES SEPARATED FROM THE 8-CELL Halocynthia EMBRYO. OKADO, H., OKAMURA, Y. AND TAKAHASHI, K. Dept. Neurobiol., Institute of Brain Res., Sch. Med., Univ. of Tokyo, Tokyo 113

As previously reported, when the Halocynthia embryo is cleavage-arrested at early developmental stages, 1- to 4-cell, and cultured further until the normal hatching time, the membrane of the large blastomeres expresses exclusively the epidermal-type excitability, while, when cleavage-arrested after 8-cell stage, some of blastomeres show neural-type excitability. The difference can be caused by further segregation of egg cytoplasmic factors and/or cell-cell interaction after 8-cell stage. In the present experiment, a single anterior-animal blastomere which includes the presumptive neural region in the 8-cell embryo, when dissociated, cleavage-arrested and cultured in isolation, differentiated exclusively to epidermal type judging from membrane excitability and immunoreactivity. However, when the same blastomere was cultured in contact with a single anterior-vegetal blastomere which includes the presumptive notochordal region, it displayed Na spikes and showed no expression of the epidermal antigen, suggesting "neural induction" resulted in a single cell during the interaction with a single neighboring cell. This simple two-cell system can be used for further studies on the induction mechanism at the cellular and molecular level, eliminating a complexity of the multicellular interaction.

S4-2

TRANSDIFFERENTIATION OF ADRENAL CHROMAFFIN CELLS INTO NEURONS IN VITRO
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Adrenal chromaffin cells, even after terminally differentiated as endocrine cells, are capable to differentiate into neurons both in vivo and in vitro, when exposed to nerve growth factor (NGF). We observed that chromaffin cells isolated from neonatal rats acquire morphological and electrophysiological characteristics of neurons in vitro. And by analogy to diversity of neurochemical phenotype in sympathetic neurons in culture, the transdifferentiated chromaffin cells formed cholinergic and adrenergic synapses depending on culture conditions. We also examined whether the proliferative activity of chromaffin cells is preserved or lost along with their transdifferentiation, since it has been speculated that neural characteristics emerge only after passing through the critical mitosis of their progenitors. Chromaffin cells required a new synthesis of RNA and proteins for onset of transdifferentiation, but not DNA replication. Using monoclonal antibodies against bromodeoxyuridine, we observed that once chromaffin cells were committed to conversion into neurons, they tended to irreversibly lose their mitotic potential.

S4-3

DEVELOPMENT, GROWTH AND DIFFERENTIATION OF THE NERVOUS SYSTEM OF MAMMALS. KATSUHIKO MIKOSHIBA, Division of Regulation of Macromolecular Function, Institute for Protein Research, Osaka Univ. 3-2 Yamadaoka, Suita, Osaka 565

There are many neuropathological mutants which have abnormalities at various steps of neurogenesis. Analysis of the mutants compared with respective control animals gives us great information on the differentiation of the nervous system. Neuron-glia, and neuron-neuron interrelationship are very important for maintaining the brain activity. Myelin formation is a result of neuron-glia relationship. Shiverer, myelin deficient (mld), jimpy and quaking are the typical examples of mutants which have abnormality in myelin formation resulting symptoms of intentional tremor, tonic convulsion and ataxic movement. Cerebellum is a very good model to study neuronal interrelationship. There are many mutants which have abnormality in the cerebellum. They show typical cerebellar symptoms. I described the results of the analysis of these mutants at the level of gene, protein and morphology.

S-5 Recent Advances in Synaptic Transmission and Modulation

S5-1

RECENT PROGRESS IN STUDIES OF SYNAPTIC TRANSMISSION. KUBA, K., Dept. Physiol., Saga Med. Sch., Saga 840-01.

New findings and concepts recently achieved for the mechanisms of synaptic transmission were reviewed briefly. Many new substances and putatitive transmitters have been identified as a true transmitter in both central and peripheral synapses. New subtypes of transmitter receptors have been classified by newly-synthesized antagonists or newly-found toxins, and their primary and secondry structures have been clarified. The structure and function of the nicotinic acetylcholine receptor channel have been clarified to a large extent by the use of a patch clamp technique, gene cloning, its mutation and expression, electron microscopic image analysis and monoclonal antibody. Modulatory effects of transmitter has become a concrete and important field of neuroscience. Explosive accumulation of knowledges and concepts of intracellular transduction mechanisms has been extended to synaptic physiology. This has led to new understandings of several types of the mechanisms involved in regulation of ion channels by transmitters, which are found to operate in the mechanisms of slow postsynaptic potentials and modulation. It was suggested that specification (in individual neurones) and generalization of various synaptic mechanisms are expected to grow in future.

S5-2

MULTIPLE MUSCARINIC REGULATION OF SYNAPTIC TRANSMISSION IN THE SYMPATHETIC GANGLIA. Mochida, S., Kobayashi, H. and Tosaka, T. Department of Physiology, Tokyo Medical College, Shinjuku-ku, Tokyo 160.

Functionally different muscarinic receptors associated with the post synaptic potentials (PSPs) appear to exist in the superior cervical ganglion of rabbits. These are (1) postsynaptic receptors mediating s-IPSP and s-EPSP, (2) heteroreceptors in SIF interneurones modulating s-IPSP and (3) autoreceptors in the preganglionic nerve terminal regulating transmitter release. These receptors can be classified to be M_1 or M_2-muscarinic receptor subtype based on their affinity to the selective antagonist, pirenzepine (M_1) or AF-DX 116 (M_2), and selective agonist, McN-A-343 (M_1) or AF102B (M_1): The heteroreceptor and postganglionic receptor mediating s-EPSP appear to be M_1-type but the autoreceptor and postganglionic receptor mediating s-IPSP may be M_2-type. Furthermore, the muscarinic acceleration of the repolarizing phases in the action potential in the postganglionic neurones is mediated by the M_2-receptors. G protein and PI metabolites may be intermediators of the M_2-receptor activated responses. The M_1 muscarinic responses seem to be more complicated; cGMP in addition to G protein and PI metabolites appears to be the intracellular messenger. These metabotropic muscarinic actions regulate integrately the synaptic transmission by regulating the firing rate of postganglionic neurones.

S5-3

SLOW SYNAPTIC RESPONSES IN THE ENTERIC NERVOUS SYSTEM. MIHARA, S.[2], HIRAI, K.[1] AND KATAYAMA, Y.[1] 1) Dept. Autonomic Physiology, Medical Research Institute, Tokyo Medical and Dental University, Tokyo 101, and 2) Dept. Physiology, Kurume University School of Medicine, Kurume 830.

The enteric nervous system controls gastrointestinal motility, gastric acid secretion, intestinal transport of water and electrolytes, and other functions. Many endogenous neuroactive substances including peptides have been found in the alimentary tract. Four classes of synaptic events were recorded from guinea-pig enteric neurons: fast EPSP's; slow EPSP's; IPSP's and presynaptic inhibition of neural transmission. Some of the bioactive substances were localized in particular groups of enteric neurons with characteristic shape and electrical properties, and were assumed to be putative substances mediating as well as modulating these synaptic events. GTP-binding protein, cyclic AMP and/or calcium ions might be involved either directly or indirectly both in the actions of several endogenous substances and in generating the slow synaptic responses. Intrinsic nerve fibers responsible for all of the postsynaptic potentials travelled up to about 15 mm (average, 8 mm) in the myenteric plexus along the intestine and for shorter distances circumferentially.

S5-4

NORADRENERGIC MODULATION IN SYMPATHETIC PREGANGLIONIC NEURONS. YOSHIMURA, M., INOKUCHI, H., CHIBA*, T. and NISHI, S. Dept. Physiol., Kurume Univ. Sch. Med., Kurume 830 and *Dept. Anatomy, Saga Med. Sch., Saga 840-01

Recent investigations on the effect of noradrenaline (NA) on the sympathetic preganglionic neurons (SPN) in tissue slices of cat spinal cord revealed the possibilities of various modulatory roles of the endogenous NA. NA produces a prominent spike afterdepolarization (ADP) which is absent in normal Krebs solution. The ADP is due to generation of a tetrodotoxin (TTX)-insensitive inward current which is most likely a Ca-activated Na influx. Despite the formation of typical synapses between the adrenergic nerve terminals and the SPN, NA does not mediate the fast EPSP nor the fast IPSP. Instead, NA mediates the slow EPSP and the slow IPSP via alpha-1 and alpha-2 receptors, respectively. The slow EPSP is associated with a decrease in the Ca-dependent K conductance, while the slow IPSP is accompanied by an increase in the voltage-independent K conductance. The most recent studies point to that the former is likely to result from the activation of proteinkinase C as well as the accumulation of cAMP and that the latter is mediated by a GTP binding protein which probably raises the open probability of the K channels.

S5-5

RECENT PROGRESS IN STUDIES ON THE MECHANISM OF LONG-TERM POTENTIATION. YAMAMOTO, C. Department of Physiology, Faculty of Medicine, Kanazawa University, Takaramachi Kanazawa, 920

After a brief tetanic stimulation of an excitatory pathway in the hippocampus, synaptic transmission through the tetanized pathway is potentiated for a long period. This phenomenon is called long-term potentiation, and has been considered to be a reasonable analog of the synaptic plasticity underlying memory storage. It reamins undetermined whether long-term potentiation results from an increase in the amount of transmitter released from presynaptic terminals or from an increase in responsiveness of postsynaptic neurons to transmitter. There are several lines of evidence supporting both presynaptic and postsynaptic origin. We devised a method to apply quantal analysis to the hippocampus. We analyzed potentiation of synaptic transmission between mossy fibers and CA3 neurons by phorbol diacetate as a model of long-term potentiation, and found that the potentiation was accompanied by increases in quantal contents with no detectable changes in quantal amplitude. We concluded, therefore, that the potentiation results from an increase in the release of transmitter.

S-6 Motor Function of Brain Stem and Spinal Cord

S6-1

MORPHOLOGICAL FEATURES OF MUSCLE-UNIT PORTION OF TYPE-IDENTIFIED MOTOR-UNITS AND CORRELATION TO THEIR PHYSIOLOGICAL CHARACTERISTICS. KANDA, K. Dept. of Physiol., Tokyo Metropolitan Institute of Gerontology, 35-2, Sakaecho, Itabashi-ku, Tokyo 173, Japan.

Motor units in the rat medial gastrocnemius (MG) muscle were classified into four major types: FF (32.3%), FI (3.1%), FR (47.9%), and S (17.6%). Estimated aggregate tetanic force for the different motor-unit types were 58.6 % for type FF+FI, 39.4 % for type FR, and 2.0 % for type S. In 26 MG muscles, a single motor-unit was characterized physiologically and subsequently depleted of its glycogen through repetitive stimulation of an isolated ventral root filament under pentobarbital anesthesia. Serial muscle cross-sections were stained for glycogen using PAS reaction. Fibers belonging to the stimulated motor-unit were identified visually, and whole muscle-unit portion was reconstructed, and their cross-sectional areas were measured with an image processing computer. Density of unit fibers within the territory for type S motor-unit was significantly less than those for types FF and FR. The tetanic tension was correlated to innervation ratio ($r=0.95$), mean cross-sectional area of unit fibers ($r=0.87$), and total cross-sectional area ($r=0.99$). Specific tensions, derived from total cross-sectional area of unit fibers and the tetanic tension, were 15.5 N/cm^2 for type S, 21.4 N/cm^2 for type FR, and 23.9 N/cm^2 for type FF motor-unit. Difference between types S and FF was significant (0.001 level, Scheffe multiple range test). Calculated mean innervation ratios were 58 for type S, 169 for type FR, and 273 for type FF motor-units.

S6-3

BRAINSTEM-SPINAL CORD MECHANISMS INVOLVED IN GENERALIZED POSTURAL SUPPRESSION IN CATS.

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Studies in both acute decerebrate and concious cats have demonstrated that electrical stimulation of the dorsal portion of the caudal tegmental field (DTF) in the pons resulted in suppression of extensor muscle tone and as a consequence inhibition of upright standing posture. Our immunohistochemical studies demonstrated that small-to-medium sized cells in the nucleus reticularis pontis oralis give off descending axons coursing through the midline DTF area, and that the descending axons terminate on large cells on the nucleus reticulris gigantocellularis. These cells, in turn, projected their descending axons as far caudally as the lumbar spinal cord. Rescently, we have obtained evidence that the above described descending system is one of the excuting systems mediating generalized inhibitory effects upon hindlimb alpha-motoneurons from the brainstem to the spinal cord. The brainstem neuronal mechanisms will be discussed in relation to the previously raised "stage setter hypothesis".

S6-4

PATTERN GENERATION OF RHYTHMICAL JAW MOVEMENTS IN THE BRAIN STEM. NAKAMURA, Y., NOZAKI, S. and IRIKI, A. Dept. Physiol., Fac. Dent., Tokyo Med. Dent. Univ., Bunkyo-ku, Tokyo 113

A central pattern generator of the cortically-induced rhytmical masticatory jaw movement (RMJM) of the guinea pig is located in the bulbar reticular formation (BRF), which is activated by the corticobulbar fibers projecting mainly contralaterally to the dorsal portion of the paragigantocellular nucleus (dPGC). The dPGC neurons monosynaptically excite the neurons in the oral portion of the gigantocellular nucleus (GCo), which in turn directly excite the trigeminal premotor neurons in the BRF dorsolateral to the caudal portion of the gigantocellular nucleus (GCc). In this paper our recent studies are reviewed on the central generation of the RMJM induced by repetitive stimulation of the cortical masticatory area (CMA) of the guinea pig. 1) All the dPGC neurons responded with a spike to each repetitive CMA stimulus pulse, while most GCo neurons showed a rhythmical burst during repetitive CMA stimulation, which was sustained in GCo after a coronal section between GCo and GCc. 2) A spike of GCo neurons evoked by an intracellular depolarizing pulse was followed by an IPSP that was blocked by systemic bicuculline injection. Microinjection of bicuculline into GCo changed a CMA-induced rhythmical digastric EMG burst into a tonic activity. We conclude that 1) the CMA-induced RMJM is generated in the GCo without feedback from the BRF premotor neurons, and 2) a GABAergic recurrent inhibition is essential for the rhythm generation in GCo.

S-7 Control Mechanism of Voluntary Movement in the Central Nervous System

S7-1

CONTROL MECHANISM OF VOLUNTARY MOVEMENTS IN THE CENTRAL NERVOUS SYSTEM. SASAKI, K. Dept. Physiol., Inst. for Brain Res., Fac. Med., Kyoto Univ., 606 Kyoto

Movements of our skeletal muscles may be classified into many grades between two extremes, reflex and ideal voluntary movement. The intermediates can be called 'automatic movements', and appear to include both components of the reflex and voluntary movement in various ratios. Therefore it is impossible to dichotomize all movements either to be reflex or voluntary movement. The reflex is usually thought to be manifested by an innate, definite (although modifiable) neuronal circuit, reflex arc, whereas the voluntary movement is assumed to be mediated by complicated neuronal networks that are more or less nurtured by an environmental history of individual. We take here voluntary movements to be the movements, of which the grades are nearer to the ideal voluntary movement than reflex. All structures in the central nervous system can deal with such voluntary movements. In this symposium, we discuss mainly about physiological events in the basal ganglia and related structures, which are recently thought to be confused in the concept regarding motor control mechanisms. Understanding of the neuronal events in the basal ganglia is urgently important, since their chemical, pharmacological and clinical data recently accumulated should be interpreted on the basis of dynamic activities of the neuronal circuits in the basal ganglia. It appears also to be a key to the cererbal cortex and so to the voluntary movement.

S7-2

PATHOPHYSIOLOGICAL STUDIES IN THE BASAL GANGLIA DISEASES. KATO M., Dept. of Neurophysiol., Neurol. Instit., Kyushu Univ. 60, Fukuoka 812

Recent advances in the pathophysiological studies of the basal ganglia diseases were reviewed. Somatotopic relation of the dorsal part of the striatum to the neocortical functions, and of the putamen to the motor function were demonstrated also in humans by histochemical method and positron emission tomography. Two subunits, the matrix and striosome, were distinguished histochemically in the striatum, and preferential involvement of projection neurons originated from the striosome was found in Huntington's disease, with preserved somatostatin and neuropeptide Y contents. These findings indicate necessity of future investigation of striatal subunits. Functional analyses of the basal ganglia with glucose metabolism also led to the same conclusion. Kinesie paradoxale, a peculiar feature of hypokinesia showing sudden regain of the ability to initiate particular voluntary movement in the presence of specific sensory and/or emotional stimulations, seems to suggest an interaction between sensory and motor functions in the basal ganglia to initiate voluntary movements. Motor analyses of patients with Parkinson's disease suggested a difficulty in executing learned motor plan although programming itself remained intact. Possibility of involvement of the basal ganglia in cognitive function should be studied in the future.

S7-3

THE BASAL GANGLIA CONTRIBUTE TO THE INITIATION OF MOVEMENT BY DISINHIBITION. HIKOSAKA,O. Dept. Physiol. Toho University School of Medicine, 5-21-16 Omori-Nishi, Ota-ku, Tokyo 143.

Saccadic eye movement, among a variety of movements, is controlled by the basal ganglia. This is accomplished by a powerful inhibitory connection from the substantia nigra pars reticulata (SNr) to the superior colliculus (SC). Neurons in the SNr are characterized by their high, tonic spike discharges. If a monkey attempts to make a saccade to a visual target or a remembered target, SNr neurons stop discharging. Cells in the intermediate layer of the SC, which receive inhibitory afferents from the SNr, are then released from the tonic inhibition. This disinhibition, probably in conjunction with excitatory inputs notably from the frontal eye field, allow the SC cells to fire in a burst, leading to a saccade. A similar mechanism may at work for the initiation of skeletal movements.

S7-4

THALAMIC NEURON WITH PALLIDAL INPUT AND PROJECTION ON THE MOTOR CORTEX, AND ITS ROLL IN CONTROL OF MOVEMENT. JINNAI, K. Dept. of Physiol., Shiga Univ. of Med. Sciences, Seta, Ohtsu, Shiga 520-21

Thalamic neurons with input from the internal segment of globus pallidus (GPi) and with projection on the arm area in the motor cortex (Mcx) were identified by their inhibitory response to stimulation of GPi and antidromic response to that of the area in Mcx in awake monkeys. About half (8/14) of the GPi-inhibited thalamic neurons projecting on Mcx (PTM-neurons) changed their discharge rate whenever a monkey moved its hand to lift a lever on all different tasks, i. e., reaction-time task with visual cue, delayed GO/NOGO discrimination task and self-paced movement. Such a discharge pattern of PTM-neurons was quite similar to that of neurons recorded in arm region in the globus pallidus of the same monkey. This indicates that the movement-related activities of pallidal neurons are conveyed through the thalamocortical pathways directly to Mcx. Small number (3/8) of PTM-neurons changed their firing rate prior to onset of the earliest EMG by more than 30 ms. It is suggested that PTM-neurons can contribute not only to ongoing and feed back control of movement but also to initiation of movement.

S7-5

ROLE OF BASAL GANGLIA IN THE SELECTION AND EXECUTION OF VOLUNTARY MOVEMENT. KIMURA. M Dept. Physiol., Jichi Med. Sch. Minamikawachi, Tochigi, 329-04

In order to study how the putaminopallidal system engages in the voluntary movement, neuronal activity was recorded in the putamen and globus pallidus (GP) of monkeys performing visually triggered arm movement task. The putamen neurons showed: 1) responses to visual or auditory stimulus (356 cells) as a trigger for learned movement and the strongly enhanced responses when the presentation of the triggering stimulus was anticipated. 2) tonic activity during preparation of movement with or even without warning stimulus before the trigger (62 cells). 3) movement related activity (273 cells). Thirty-five cells were identified electrophysiologically as projection cells to GP. Most of their activity were related to movement execution or preparation for movement. Task-related activity of 36 cells in the internal segment of GP showed depression of their high frequency discharges (50-100 Hz) during preparation for movement, while they showed not only depression but also further increase of their high frequency discharges during movement excecution. These observations lead to propose a hypothesis that the putaminopallidal system is involved in the process of, first, preparation or selection of movement by disinhibition, and second, movement excecution by not only disinhibition but also active inhibition through the pallidofugal system.

S7-6

MOTOR AND BEHAVIOR CONTROL BY THE DORSAL AND VENTROMEDIAL BASAL GANGLIA SYSTEMS IN THE MONKEY AND RAT. NISHINO,H., Dept.Physiol.,Nagoya City Univ.Med.Sch.,Nagoya 467

1, Single neuron activities were recorded in the monkey caudate (CD), globus pallidus (GP), substantia nigra (SN) and ventral tegmental area (VTA) during bar press feeding task composed of recognition of food, motivated bar press and ingestion reward. Neurons in the dorsolateral part of CD , GP and SN responded to motor events of the feeding,i.e. extention/flexion of the arm, bar pressing, chewing or gaze. Neurons in the ventromedial CD and rostoventral GP showed different responses for food and nonfood during recognition and bar press phases. Neurons in the VTA responded only in the first part of bar press phase.

2, Unilateral nigrostrial dopamine (DA) depletion in the rat made the animal turn to lesioned side. The turning recovered by the graft of fetal rat nigral cells in DA depleted CD. Bilateral DA depletion in the nucleus accumbens decreased open field activity, especially exploratory behaviors, Results suggest the dorsal and ventral systems of the basal ganglia have different roles in behavior output.

S-8 Neuronal and Endogenous Chemical Factors for Emotional Behavior

S8-1

ROLE OF MONKEY AMYGDALA AND HYPOTHALAMIC NEURONS IN EMOTIONAL BEHAVIOR. ONO, T., Dept. Physiol., Fac. Med., Toyama Med. and Pharmaceu. Univ., Sugitani, Toyama 930-01.

Lesion and stimulation suggest importance of sequential sensory information processing through association cortex-limbic system, amygdala (AM) or hippocampus (HI) and lateral hypothalamus (LHA), in stimulus-affective association and emotional behavior. Neuronal activity from alert monkey, AM, HI and LHA was recorded during discrimination learning of reward or aversion cues. AM neurons responded primarily to novel stimuli (vision, audition, gustation and multimodal); they habituated to repeated stimuli with no affective significance, but not to stimuli with affective significance. Few AM cells were highly selective, responding specifically to one biologically significant object or sound. HI neuron responses depended on environmental conditions such as position and direction. Some LHA neurons responded to any food or reward-related object. Inferotemporal cortex cooling modulated AM visual responses, and AM cooling modulated visual and gustatory responses of LHA neurons. Results suggest relations of the AM to stimulus-affective association based on learning and memory, HI to stimulus-situation association, and LHA to initiation of positive reinforcement responses. Emotional behavior is thought to depend on association cortex and limbic system (AM, HI, and LHA) dynamic information processing.

S8-2

NEURONAL HISTAMINE IN THE HYPOTHALAMUS MODULATES INGESTIVE BEHAVIOR. SAKATA, T. Dept. Intern. Med. I, Faculty med., Kyushu Univ., Fukuoka 812

Histamine H_1-receptors are relatively dense in the hypothalamus. Infusion of α-fluoromethylhistidine (αFMH), a suicide' inhibitor of histidine decarboxylase (HDC), into the third cerebroventricle (icv) during the early light induced feeding potently. No periprandial drinking decreased, but exploration increased, concomitantly with feeding after the infusion. Neuronal histamine in the hypothalamus was almost completely inhibited by infusion of αFMH. When the effect on H_1- or H_2-receptors was differentiated, H_1-antagonists induced feeding dose dependently, but H_2-antagonists did not affect ingestive behavior or exploration. Feeding induced by H_1-antagonists was attenuated when rats were further evaluated during decrease of hypothalamic histamine content and HDC activity in the early dark. Bilateral microinfusion identified that the VMH, but not the LHA or the PVN, was a main locus for the induction of feeding due to αFMH and H_1-antagonists. Hypothalamic neuronal histamine may suppress food intake, at least in part, through H_1-receptors in the VMH, and diurnal fluctuations of food intake may mirror neuronal histamine levels.

S8-3

REGULATION OF FEEDING THROUGH THE NEURONAL AND CHEMICAL FACTORS. SHIMIZU, N. AND OOMURA, Y. Dept. Physiol., Fac. Med., Kyushu Univ. 60, Fukuoka 812

Feeding behavior is affected by several neural centers and peripheral organs. These include hypothalamus, medullary sites, liver, gut and pancreas. They respond to endogenous chemical substances, whose levels are affected by the state of hunger and satiety, and which in turn affect feeding behavior. Some recently identified metabolites have potent effects on food intake. The sugar acid 2,4,5-trihydroxypentanoic acid γ-lactone induces feeding, and 3,4-dihydroxybutanoic acid γ-lactone and 2-buten-4-olide suppress feeding. Further, a phasic increase in acidic fibroblast growth factor (aFGF) was detected in the cerebrospinal fluid of rats after feeding. The microinfusion of aFGF into the third cerebral ventricle (ICV) suppressed food intake in rats. ICV injection of cytokines (IL-1ß and tumor necrosis factor; approximately the same structure as FGF) suppressed food intake dose-dependently. The central infusion of inactivated aFGF, or the peripheral administration of aFGF in doses equivalent to or higher than those administered centrally were without effect. The action of all of these substances is mediated by glucose-sensitive and/or glucoreceptor neurons in the hypothalamus. The neural networks involved in the integration of the signals from the chemosensitive neurons open new possibilities for understanding the central mechanism of hunger and satiety.

S8-4

NEURAL AND CHEMICAL MECHANISMS OF THERMOREGULATORY BEHAVIORS.

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The behavioral thermoregulation is phylogenetically older than autonomic thermoregulation which newly has evolved in birds and mammals. Playing a central role for manifestation of thermoregulatory behavior are the thermosensitive neurons in the rostral hypothalamus, which have been found in the poikilothermic vertebrates as well as in the homeothermic animals. Hypothalamic thermosensitive neurons work not only as thermosensors but also as integrators of thermal signals of whole body. Among thermosensitive neurons in the brain and spinal cord, hypothalamic thermosensitive neurons are unique in their abundance of information, based on the massive neural connections with periphery and also with limbic forebrain and association cortices. Our observation on the unit activity of hypothalamic thermosensitive neurons in the alert monkey during thermoregulatory operant behavior has revealed that these neurons are involved also in the processes of motivation and reward recognition in the behavior. In addition, multiple chemical sensitivity of these neurons, together with the facts that hypothalamus is readily accessible for blood-borne substances and is the site where many endogenous neuroactive substances are synthesized and/or released, may provide the chemical basis of complex forms of processing of interoceptive and exteroceptive signals.

S8-5

CHEMICAL AND NEURAL MECHANISMS IN THE CONTROL OF DRINKING BEHAVIOR.

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The homeostatic drinking is controlled by chemical and neural factors. As the chemical factors, angiotensin II (AII) and atrial natriuretic polypetide (ANP) which are known to exist in the drinking related hypothalamic areas and to induce a strong drinking and inhibition of drinking respectively were studied in the rat hypothalamic slice preparations. AII predominantly excited the neurons in these areas while ANP inhibited. Interesting finding is that ANP antagonized the AII-induced excitation in the subfornical organ. The osmotic stimulus is a most important factor to control drinking. The hyper- and hypotonic solutions of NaCl or mannitol were applied to neurons in the basal forebrain of the anesthetized rats by a pressure ejection system. The physiological range of osmotic stimuli could excite or inhibit the neurons of these areas. The neural pathways to affect drinking behavior were studied by activation of gastric and cardiovascular receptors. It was possible to trace the effects to the neurosecretory neurons in the PVN through the solitary tract nucleus, observing an inhibition by atrial stretch and gastric distention. We conclude that plasma AII, ANP and osmotic level are detected in the hypothalamus and the information is integrated with that coming from the visceral afferents to control drinking behavior.

S-9 Effects of Gonadal Hormones on the Central Nervous System

S9-1

GONADAL STEROID CONTROL OF CIRCUIT FORMATION AND NEURONAL PLASTICITY IN THE NEUROENDOCRINE BRAIN.

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Gonadal steroids exert complex effects on neuroendocrine brain. Whether the effect is organizational or activational, and whether neurotropic or neurotoxic, the morphological responses to sex steroids are primarily specific to the steroid receptor-containing neuron system. The circuitries involved in neuroendocrine and behavioral functions are under the direct control of gonadal steroids throughout life. In perinatal animals aromatizable androgen or estrogen affects brain sexual differentiation by regulating the number of target neurons, stimulating axonal and dendritic growth, and modifying synaptic connectivity. The onset of puberty is dependent on a complex process of neuroendocrinological events which involve the maturation of the hypothalamic pituitary gonadal axis. This may be correlated with a sex steroid facilitation of synaptogenesis in the neuroendocrine brain. In adult animals sex steroids can affect synaptic remodelling in ceratin neural substerates which possess considerable plasticity and where vacated synaptic sites are made available by spontaneous degeneration during aging or surgical deafferentaion. So morphologiccal response of the neuroendocrine brain to gonadal steroids is detectable at the different sequences of the developmental process and after aging.

S9-2

ORGANIZATION OF THE FEMININE OR MASCULINE DEVELOPMENT OF THE RAT HYPOTHALAMUS AND PREOPTIC AREA BY SEX STEROID HORMONES.

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The ventromedial hypothalamic nucleus (VMN) and the medial preoptic area (POA) are both associated with estrogen-dependent neural regulation of neuroendocrine and behavioral functions. In the female rat, these structures control lordosis reflex, the major component of female reproductive behavior in this and other rodent species. Efferent neurons in these areas of the female rat, with axons projecting to the midbrain, are sensitive to estrogen such that their antidromic activation thresholds and absolute refractory periods were altered by treatment with this hormone. We have shown in the ovariectomized female rats that treatment with estrogen 48 hrs prior to the recording caused reciprocal changes in the excitability between those neurons in the VMN and POA. Estrogen increased the excitability of the VMN neurons while inhibited those in the POA. In the males and neonatally testosterone treated (TP) females, estrogen had no effect on the neuronal excitability either in the VMN or the POA. These results suggest that the inability of estrogen to disinhibit the POA action contribute to the lack of lordosis in the males and TP females, together with the absence of the estrogen-induced activation of the VMN in these animals.

S9-3

RAPID EFFECT OF 17β-ESTRADIOL ON AMYGDALA AND HYPOTHALAMIC NEURONS.

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The mechanism by which sex steroids rapidly modulate the excitability of neurons was investigated by intracellular recording of neurons in the amygdala (AMY) and the ventromedial hypothalamus (VMH) using brain slice preparations. Brief hyperpolarization and increased potassium conductance were produced by 17β-estradiol in the centromedial AMY. In the VMH, 17β-estradiol produced two types of responses, depolarization and hyperpolarization with decrease and increase in potassuium conductance, respectively. These effects persisted after elimination of synaptic input and after suppression of protein syntheses. Thus, 17β-estradiol directly changes the ionic conductance of the membrane. In addition, a greater proportion of the neurons from estrogen treated females than from males or ovariectomised, estrogen untreated females, responded to 17β-estradiol. The effects of 17β-estradiol were enhanced by the phosphodiesterase inhibitor, isobutylmethylxanthine (IBMX). The specific adenylate cyclase activator, forskolin, enhanced only the depolarization. The phosphodiesterase-resistant analogue of cyclic AMP, 8-bromo cyclic AMP, mimicked the depolarizing responses.

S9-4

ESTRADIOL ACTIONS ON DOPAMINE SYNTHESIS IN TUBEROINFUNDIBULAR DOPAMINERGIC NEURONS.

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When estradiol is administered for a long term or at high doses, enormous prolactin-secreting pituitary tumors can be induced in rats. On the other hand, tuberoinfundibular dopaminergic (TIDA) neurons of the hypothalamus synthesize dopamine, a prolactin release inhibitory factor, and secrete it into hypophysial portal blood. Therefore, we determined dopamine synthesis in vitro in TIDA neurons of rats bearing estradiol-induced pituitary tumors, using hypothalamic slices. The results suggest that (1) chronically administered estradiol inhibits dopamine synthesis in TIDA neurons via a direct action on the hypothalamus and overcomes the facilitatory action of prolactin on dopamine synthesis; and (2) estradiol inhibits all three distinct systems that regulate basal, Ca^{2+}-dependent, and cAMP-dependent dopamine synthesis.

S-10 Brain Mechanisms of Sleep and Wakefulness

S10-1

TRIPLE CONTROL SYSTEMS OF THALAMIC ACTIVITY ARISING FROM MESENCEPHALON-PONS, WITH SPECIAL REFERENCE TO ASCENDING RETICULAR ACTIVATING SYSTEM.
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There are triple diffuse projection systems to the forebrain arising from the mesencephalon-pons; noradrenergic projection from the locus coeruleus, serotonergic projection from the dorsal raphe nucleus, and cholinergic projection from the laterodorsal and pedunculopontine tegmental nucleus. Influences of these projections on thalamic neuronal activity were examined by repetitive electrical stimulation of each nucleus from which they arose. It was found that action of serotonergic projection was inhibitory and that of the other two was excitatory. Among the latter, influences of cholinergic system appeared quickly but subsided in spite of on-going stimulation, while those of noradrenergic system appeared gradually and outlasted the stimulation. These findings suggest that "the ascending reticular activating system" comprises of two systems; the phasic cholinergic system to produce attention, and the tonic noradrenergic system to produce arousal. Observations of behaviors of neurons in the locus coeruleus and laterodorsal tegmental nucleus in response to sensory stimulation support this idea.

S10-2

COMPLEX CORTICAL AROUSAL PROCESSES.
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Behavioral arousal involves initial arrest of ongoing activity and following investigatory movements. Likewise, EEG arousal can be divided into phasic and tonic phases. In carefully maintained encéphale isolé cat preparation with spontaneous sleep-waking cycles, the intracellular responses to EEG arousal in motor cortical neurons were excitation (E), inhibition (I), disfacilitation (DF) or disinhibition (DI). During phasic arousal, lamina I-II neurons all exhibited E, upper-half lamina III neurons E or I, and lower-half lamina III and V-VI neurons E, I, DF or DI. Transmission would thus be cascaded through neuronal relays from superficial to deep layers. This postulate was verified by the same response patterns elicited by stimulating the cortical surface. Large pyramidal neurons were found in a state of readiness by DF, being perhaps relevant to the behavioral arrest. During tonic arousal, lamina V-VI neurons showed E, lower-half III neurons E or I, and upper-half III and I-II neurons E, I, DF, DI or no response. The cascade transmission would then be directed from deep to superficial layers. E in all the deep layer projection neurons may be relevant to the investigatory behavior. The subcortical structures involved in the "reticular activating system" were reviewed as complex sources to yield phasic and tonic functional units composed of dynamic ensemble of cortical activities.

S10-3

SLEEP-INDUCING SUBSTANCES AND HYPOTHALAMIC SYSTEM REGULATING SLEEP.
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The effects of electrophoretically applied sleep-inducing substances were studied in the preoptic area (POA) in the hypothalamus and the posterior hypothalamus (PH) in rats. The substances examined were prostaglandin D_2 (PGD_2), sleep-inducing substance (SPS), uridine and delta sleep-inducing peptide (DSIP). Their interactions with several neurotransmitters are as follows: the inhibitory response of noradrenaline (NA) frequently changed to no effect or excitation during simultaneous PGD_2 or SPS application in the POA. The excitatory effect of acetylcholine (ACh) was sometimes attenuated, blocked or reversed by concurrent PGD_2 or SPS application. Furthermore, neurotransmission in the POA following ventral noradrenergic bundle stimulation was modified in one-third by PGD_2. Uridine had similar effects with those of SPS, but DSIP had no modulatory effects against NA and ACh responses in the POA. Modulations of NA and ACh responses by sleep-inducing substances were rarely seen in the PH. The interactions with NA and ACh of these substances may play a role in sleep-awake cycle formation mechanism in the hypothalamus.

S-11 Neural Information Processing in the Sensory System: Movement Perception

S11-1

A MOTION DETECTION MECHANISM IN THE VERTEBRATE RETINA. Masaki Tauchi, Research Institute, National Rehabilitation Center for the Disabled, 4-1 Namiki, Tokorozawa 359

There are several types of retinal ganglion cell that respond vigorously to the moving targets. Of these cells, direction selective ones(DS) have been most intensively studied. The DS respond best to movement in one direction but only weakly or nothing to movement in the opposite direction. The DS receives a direct excitatory inputs via cholinergic synapses and the direction selectivity is modulated by a inhibitory transmitter,GABA. Since the direction selectivity appears at the level of ganglion cells, this property might be created by cell interactions occurring in the inner retina. We have identified the cholinergic cells as a type of amacrine cells and found that the dendritic plexus of them is very dense as is anticipated by their high cell density and the dendrites brunching profusely. Since the extent of dendritic field of single cholinergic cells is much larger than the resolution of movement detection observed in DS, it is speculated that transient acetylcholine release occurs locally from the restricted region(illuminated area) of the plexus rather than a whole dendritic field of individual cells. So far, the understanding of the GABA-ergic neurons is rather poor compared with that of the cholinergic neurons. It is intriguing to note our recent finding that the cholinergic cell itself is equipped with a machinery(GABA synthesizing enzyme) that is a characteristic of GABA-ergic neurons.

S11-2

VISUAL INFORMATION OF MOVEMENTS OF ISOLATED OBJECTS AND THAT OF COHERENT MOVEMENTS OF A WIDE FIELD ARE SEPARATED FROM EACH OTHER IN THE MACAQUE PRESTRIATE CORTEX.
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The anatomical chain of areas, V1→MT→MST→7a in the macaque cerebral cortex is thought to be responsible for the perception of motion, because directionally selective cells predominate in the latter three areas. We have explored responses of cells in MT and MST in immobilized monkeys anesthetized with N_2O. A half of MT cells have directionally selective surround-inhibition. They do not respond when stimuli in the center and surround parts of the receptive field move in the same direction, but respond if the surround stimulus is stationary or moves in different direction from that of the center stimulus. The other MT cells respond equally well to isolated movements and coherent movements of a wide field. MST is divided into two parts. In the dorsal half, there are Direction, Size-change and Rotation cells which respond to straight movements, expansion or contraction, and clockwise or counterclockwise rotation, respectively. They have large receptive fields and show the selectivity to movements of a wide field. In the ventral half of MST, only Direction cells exist. They prefer movements of a small field, although many of them have receptive fields as large as those of cells in the dorsal MST. The separation between information of object movements and that of field movements is yet incomplete in MT but complete in MST.

S11-3

PROCESSING OF MOVEMENT IN THE MONKEY SOMATOSENSORY CORTEX. IWAMURA, Y. Dept. Physiol., Toho Univ. Sch. Med., Omori-Nishi, Otaku, Tokyo 143

Movement of the palpating hand as well as reaction of objects to the moving hand activate somatosensory receptors. These somesthetic signals may be transmitted to the somatosensory cortex as two separate channels: one from the object-skin interacting system and the other as so-called kinesthetic information. A class of neurons exist in SI which signal the direction of stimulus movement over the skin, and were called as direction-sensitive (D-S) neurons. In our own studies in the awake monkey, D-S neurons were most frequently found in area 2: about 20 % of neurons responding to superficial stimuli. Various examples of receptive field organizations of D-S neurons were described. Among those with discontinuous receptive field, preferred direction differed among different portions of a receptive field. The apparently opposite directions fell in the same direction when the hand assumed a peculier posture of making a fist. For some D-S neurons stationary stimulus of the receptive field was inhibitory. SI neurons coding kinesthetic information were described next, and the functional relationship between the two classes of neurons was discussed in regard to active touch.

S11-4

INFORMATION PROCESSING MECHANISMS FOR FLUCTUATION OF SOUNDS IN THE AUDITORY CORTEX.

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About 25% of the auditory cortical units in cats were non-selective neurons which responded to almost all sorts of sounds. About 10% of the units were highly selective which responded only to the particular and unique stimulus. About 45% were poorly selective neurons. Most of them responded best to the band of noise. These neurons were more or less selective for bandwidth but not selective for center frequency of the stimulus bands.

Recently, we found an evidence that the responses of these neurons to the band of noise were caused by fluctuation of stimulus sounds in amplitude and/or in frequency.

Moreover, some of these neurons were responsive only to amplitude-fluctuation. Therefore, the timbre of sound may depend not only on the structure of spectrum but also on the fluctuating nature in time domain.

S-12 Sensory Transduction

S12-1

TRANSDUCTION MECHANISM IN VERTEBRATE PHOTORECEPTORS

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According to the recent research, absorption of photons by visual pigments initiates a series of activation of the proteins and finally induces reduction in the intracellular cGMP concentration. The cGMP reduction leads to the decrease in the sodium inward current, thereby causes a hyperpolarization. Though the generation mechanism of the photoreceptor potential is now well understood, the control mechanism during light-adaptation is not studied yet. Using a truncated frog rod outer segment, we manipulated the concentration of various chemical substances including GTP and Ca inside of the outer segments. The experiment showed that rod outer segment synthesizes cGMP and that lowering Ca greatly enhances cGMP synthesis. If Ca concentration decreases during light response in intact photoreceptors as suggested by others, our result indicates that Ca possibly participates in the light-adaptation.

S12-2

A PROPOSAL MODEL IN THE PHOTOTRANSDUCTION MECHANISM

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According to the experimental results using Drosophila visual mutant, it was found that the photo-receptor potential is generated via the hydrolysis process of phosphatidyl inositol 4,5-bisphosphate (PIP2) by phospholipase C (PLC). And it is also demostrated with immuno- cytochemical method that PIP2 level in the rod outer segmnt of the rat retina was decreased markedly after the light illumination. The conclusion derived from these observations tells us that inositol trisphosphate (IP3) may play a important role (probably second messengers) in the visual transduction. Excitation and adaptation of limulus ventral photoreceptors induced by IP3 injection was found to be suppressed by EGTA but EGTA can not block the light response. Therefore another intracellular messengers or signalling mechanism should be postulated to mediate the visual excitation. Since PIP2 has 6 negative charges in the physiological conditions, surface charge of the inner membrane is changed dramatically when the molecules are hydrolysed. These kind of state change will cause a cruccial effect to voltage sensitive cation channel, which will lead to produce the visual excitation.

S12-3

TRANSDUCTION MECHANISMS IN CHEMORECEPTION.

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1) Sweet substances and amino acids are recognized by specific receptor proteins on taste receptor membranes, while basic structure of the membranes is concerned with reception of salts, acids, bitter substances and deionized water. 2) Adaptation of the tongue to solutions of salts including salts of impermeable cations suppresses desensitization of taste responses, suggesting that the desensitization does not occur inside the cells but occurs on the receptor membrane. 3) Taste receptor potentials are explained in terms of the phase boundary potential changes. 4) The lipid bilayer membranes exhibit the membrane potential changes in response to various odorants similarly to olfactory cells. Changes in lipid composition of the membranes lead to changes in specificity of the membranes to odorants. 5) Odor discrimination can be explained by postulating that membrane composition of each olfactory cell is different from cell to cell. 6) Ion dependence of the carp olfactory responses suggest that ionic permeability changes at the apical membrane of olfactory cells including ciliary membranes do not contribute the olfactory receptor potentials. Ion dependence of responses to odorants in the olfactory systems is quite similar to that in the lipid membranes, which suggests that the mechanism of depolarization of olfactory cells by odorants closely resembles that of the lipid membranes. 7) A large olfactory response in the carp appears after complete elimination of olfactory cilia, suggesting that olfactory cilia are not concerned with odorant reception.

S12-4

MECHANO-ELECTRICAL TRANSDUCTION IN THE HAIR CELL.

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The hair cell transduces mechanical energy applied to the hair bundle into the electrical signal, and transmits it through the synapse to the primary afferent neuron. The properties of the mechano-electrical transduction (m-e.t.) have been studied in the dissociated hair cells of the chick. (1) The m-e.t. is accomplished through gatings of the mechanically gated ion channels of 50 pS conductance with a relatively broad cationic selectivity. (2) The gating kinetics is faster than 3.5 kHz at 37° C and is faster than 2.5 kHz at 15° C. The Q_{10} of the conductance is 2.5 between 16° C and 33° C. These fast gating properties and the relatively small temperature dependence in the gating kinetics and the current amplitude might eliminate a possibility of metabolic intervention in the m-e.t. (3) The site of the m-e.t. is estimated by the fura-2 fluorescence imaging technique. The influx of Ca^{2+} increased the ratio intensity and the influx of Mn^{2+} depressed it exactly at the insertion of the hair bundle into the cuticular plate where is most likely the site of the m-e.t.

S-13 Physiology of Pain

S13-1

FUNCTIONS OF PRIMARY AFFERENT NEURONS OF PAIN. Kumazawa, T. & Mizumura, K. Dept. Nervous & Sensory Functions, Research Inst. Environ. Med., Nagoya Univ., Nagoya.

Characteristics of three types of primary afferent neurons of pain, the high threshold mechanoreceptor (HTM), the cold nociceptor and the polymodal receptor (PM), were reviewed: HTM is characterized by its exclusive sensitivity to strong mechanical stimulation, is found only in the skin, and considered to be transmitting the first pain. PM responds to all kinds of noxious stimulation, and is found in the skin, the skeletal muscle and many visceral organs. PM is considered to be transmitting the second pain and inflammatory pain. Recent results obtained using canine testis superior spermatic nerve preparations as a model system studying PM, were reviewed: chemical mediators (PG-E_2, -I_2, 5-HT) of inflammation and the temperature increase subthreshold for its activation augmented responses of the testicular PM to algesic substances; sensitizations of PM responses to heat and bradykinin by strong heat were observed in the in vitro preparation without blood supply; ineffectiveness of PG-E_2 in augmenting the thermal response and also of aspirin in suppressing the development of heat sensitization was shown. Possible contributions of sympathetic nervous system in pathologic pain such as causalgia were discussed. Additional new functions of nociceptors releasing neuropeptides to induce vascular changes and immunological changes were briefly introduced.

S13-2

CENTRAL MECHANISM OF PAIN. YOKOTA, T., Dept. Physiol., Medical College of Shiga, Seta, Otsu 520-21

There are nociceptive specific (NS) and wide dynamic range (WDR) neurons in the dorsal horn of the spinal cord and in the caudal medulla oblongata. NS projection neurons are located in the lamina I of the spinal dorsal horn and in the marginal layer of the trigeminal subnucleus caudalis. WDR projection neurons are located in the laminae I and IV-VI of the spinal dorsal horn and in the lateral part of the subnucleus reticularis dorsalis ventromedially adjacent to the trigeminal subnucleus caudalis. Both NS and WDR neurons project to the shell region of the caudal ventrobasal (VB) complex of the thalamus. Both NS and WDR neurons in the shell region of the VB complex show a somatotopic organization, and project to the somatosensory cortex SI. There are also nociceptive neurons in the intralaminar nuclei and in the nucleus submedius of the thalamus. NS and WDR neurons in the VB complex may be concerned with sensory discriminative aspect of pain, whereas nociceptive neurons in the intralaminar nuclei and in the nucleus submedius may be related to emotional motivational aspect of pain.

S13-3

CURRENT NEUROSURGICAL PROCEDURES FOR THE TREATMENT OF INTRACTABLE PAIN. OHYE, C., Dept. of Neurosurg., Gunma Univ. Sch. of Med., Maebashi, Gunma 371.

Neurosurgical procedures for the treatment of intractable (drug resistant) pain was reviewed. Now, various surgical techniques based on different principles were available. I. Desructive procedures: 1) Percutaneous cordotomy-spinothalamic tractotomy for the cancer pain, 2) Dorsal root entry zone lesion-variation of tractotomy for root avulsion, deafferentation pain, 3) Thalamotomy-spinothalamic terminal coagulation for central pain, 4) Neuroadenolysis-alcohol block of anterior hypophysis mainly for hormon dependent cancer pain, 5) Neurovascular decompression -a new treatment of trigeminal neuralgia at root exit zone, 6) Intrathecal opiate administration-continuous infusion for cancer pain. II. Non destructive procedures: 1) Deep brain stimulation-activation of endogenous opiate system for cancer pain, central pain and low back pain, 2) Dorsal column stimulation-originally based on gate control theory for cancer pain. If these procedures are properly selected, most of the pain can be controlled, together with drug therapy. The last and the most difficult problem may be the central pain, the cause of which is still mysterious. We are trying to elucidate the neural mechanism in the central pain, using XCT, PET scan and depth recording.

S13-4

PAIN AND ANALGESIA FROM THE VIEW POINT OF MATERIAL BASIS.
INOKI, R., Dept. of Pharmacol., Faculty of Dentistry, Osaka University, Suita, 565

Pain is a chemoceptive sensation and is mostly evoked by various pain producing substances which are locally produced by noxious stimuli. Nonpainful sensation which is evoked by subthreshold strength of the stimuli is usually sensitized by prostaglandin E_2 to the painful sensation at the polymodal receptor. In the subcutaneous perfusion experiment of the rat paw, Aspirin and morphine showed to inhibit the release of bradykinin from the blood vessels and of substance P from the afferent nerve terminals, respectively. Contribution of bradykinin and substance P upon pain sensation was also discussed. On the other hand, actions of antiinflammatory analgesics were summarized and that of opioids was reviewed in reference to opioid receptor subtype and the descending inhibitory systems from the periaqueductal central gray, nucleus raphe magnus and nucleus reticularis paragigantocellularis. Moreover, the releases of different transmitters, substance P and somatostatin, from the primary afferent at the dorsal horn due to mechanical and chemical stimuli were controled correspondingly with different transmitters, 5-HT and noradrenaline, of different descending inhibitory systems.

S-14 Muscular Contraction Mechanism and Calcium Ion

S14-1

INTRACELLULAR CALCIUM MOBILIZATION MECHANISMS IN SKELETAL AND SMOOTH MUSCLES.

Iino, M. Dept. Pharmacol., Faculty of Medicine, University of Tokyo, Tokyo 113

Ryanodine receptors have been proposed to function as Ca release channels in E-C coupling of skeletal muscle. In skinned fibers from Xenopus laevis, ryanodine treatment reduced the Ca uptake capacity of the sarcoplasmic reticulum. Such effect was observed only when the drug was applied under conditions in which Ca-induced Ca release (CICR) mechanism was activated. These results suggest that ryanodine binds to the open CICR channels and locks them open, and that the ryanodine receptors function as the CICR channels. However, the CICR mechanism has been suggested to be different from the physiological Ca release mechanism because inhibitors of CICR do not block K-contractures of intact fibers. The apparent discrepancy may be resolved if it is postulated that the ryanodine receptors operate in two different modes.

Properties of Ca store of smooth muscles was studied using saponin-skinned fiber bundles. The Ca store seems to consist of two compartments, one ($S\alpha$) has both CICR and inositol 1,4,5-trisphosphate-induced Ca release mechanisms, and the other ($S\beta$) only the latter. Ryanodine locks open the CICR channels, thus removing the function of $S\alpha$. Comparison of the agonist-induced contraction of intact smooth muscle bundles before and after functional removal of $S\alpha$ by ryanodine has revealed that Ca release from $S\alpha$ contributes greatly in the initial phase of the contractions.

S14-2

STRUCTURAL CHANGES OF THE THIN FILAMENT OF FROG SKELETAL MUSCLES ON ACTIVATION

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+Photon Factory, Natl. Lab. High Energy Phys, Tsukuba 203

We studied the time courses of the intensity changes of X-ray reflections from the thin filaments of frog skeletal muscles during activation. In overstretched semitendinosus muscles, the intensity of the second actin layer-line began to increase within 10msec after an electrical stimulation and attained the maximal change at 30-40msec. The intensity began to decrease after reaching the maximum without a noticeable plateau. A similar time course of the intensity increase was also observed in sartorius muscles at a rest length although the return to the resting intensity was slower. In overstretched semitendinosus muscles, an intensity decrease with a similar time course was observed on the equator at a radial spacing of 20-10nm. These intensity changes are faster than those of myosin-related layer-lines and therefore interpreted as due to the structural changes in the thin filament induced by binding of calcium to troponin.

S14-3

MYOTHERMIC MEASUREMENTS ON SINGLE MUSCLE FIBERS FROM FROG.

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Observations of heat production in muscle have usually been made with whole muscles. It is well known that a whole muscle is made up of different types of fibers. Thus, records of heat production from whole muscles give the average of the heat produced from different types of fibers. The time course of heat production may be distorted by the nonuniform distribution and also by possible differences in energetic properties of different types of fibers. Immediately after the start of stimulation, or after any sudden mechanical change, the heat record will be dominated by the response of fibers which lie adjacent to the surface of the thermopile, whereas the mechanical record will be dominated by the behavior of fibers that can respond most quickly to the stimulation or the mechanical change. This distortion in the records from whole muscle can be avoided by using single muscle fibers. Observations of heat production in single fibers will allow a more detailed comparison of energetic with mechanical properties and may contribute to an overall understanding of muscle function.

S14-4

CROSSBRIDGE ENERGETICS IN SHORTENING MUSCLE.
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Muscle shortening takes place by relative sliding of thin and thick filaments. A part of the chemical energy of ATP is transformed to the mechanical energy of shortening by cyclic interaction of crossbridges with thin filament and the remaining part of it dissipated as heat. Important information of the energetics of muscle contraction can be obtained by the energy balance studies; i.e., the comparison between the amount of energy output (heat plus work) and that of energy input (ATP splitting plus other high energy phosphate metabolism). Only recently detailed experimental data of the energy balance of shortening muscle became accessible by wisely separating it from other energetic processes such as Ca binding to troponin and parvalbumin. And it was found that the unexplained enthalpy is produced during muscle shortening and the amount of it is dependent on the velocity of shortening. We will discuss this and other recent findings in relation with the energetics of ATP splitting cycle of crossbridge in contracting muscle.

S-15 Integrative Aspect of Respiratory and Circulatory Functions with Special Reference to Their Synergistic Activities

S15-1

BASIC REGIONS FOR INTEGRATION OF THE CIRCULATORY AND RESPIRATORY FUNCTIONS IN THE LOWER BRAIN STEM. MIURA,M., Dept. of Physiol., 1st Div., Gunma Univ. Sch. Med. Maebashi 371

Mutual relations between the circulatory and respiratory functions has been proposed, and such a relation has been considered to be produced by integrative activities of the lower-brain-stem neurons. The aim of this paper is to determine histologically and physiologically basic regions of the circulatory and respiratory responses to electrical and chemical (kainic acid) microstimulation. The animal was anesthetized, but natural breathing was maintained. The arterial pressure, heart rate, tidal volume and expired air or blood gas were monitored. Responses obtained from about 500 tracks in 30 cats and about 600 tracks in 60 rats were analyzed. Both the circulatory and respiratory responses were elicited in three regions: (1) regions in and around the parabrachial nucleus; (2) regions in and around the retrofacial and ambiguus nucleus; (3) the region in the solitary tract nucleus. Recently, anatomical evidences were accumulated concerning presence of mutual connections between both side of same regions and among the three regions of the ipsilateral side. Since the three regions are connected intimately, changes occurring in one region may influence more or less all the three regions.

S15-2

THE EFFECT OF CEREBRAL BLOOD FLOW ON CONTROL OF BREATHING IN HUMAN. SUZUKI, A., KAWAKAMI, Y. First Department of Medicine, Hokkaido University School of Medicine, N-15 W-7, Kita-ku, Sapporo 060

The change in cerebral blood flow (CBF) during hypoxia may affect the hypoxic ventilatory response (HVR), via the change in brain tissue PCO_2. This effect has not been sufficiently studied in human. We measured $\dot{V}_E$, arterial and jugular venous blood gases in 15 healthy male volunteers during isocapnic hypoxia and hyperoxic hypercapnia. Jugular venous blood gases were regarded as an index of brain tissue gas tension. $PaCO_2$ fell slightly and jugular venous PCO_2 ($PjCO_2$) decreased further during hypoxia, probably due to the change in CBF, but $PjCO_2$ did not differ among each phase of hypoxia. We multiplied hypercapnic ventilatory response by change in $PjCO_2$ and corrected HVR with the product. Corrected HVR was significantly higher than original HVR. But the product and HVR did not correlate. $\dot{V}_E$ decreased during sustained hypoxia but this finding could not be explained by the change of blood gases. These data suggest that the change in CBF during hypoxia has a significant influense on HVR but does not play a key role in the inter-individual variation of HVR nor the decline in ventilation during sustained hypoxia.

S15-3

RESPIRATORY AND CIRCULATORY RESPONSES TO AIRWAY IRRITATION IN ANESTHETIZED HUMAN SUBJECTS. NISHINO, T. Dept. of Anesthesia, National Cancer Center Hospital, Tsukiji 5-1-1, Chuo-ku, Tokyo 104

Effects of stimulation of the tracheal mucosa on respiration and circulation were investigated in human subjects anesthetized with enflurane. The stimulaiton of the tracheal mucosa was given by injecting a small amount of distilled water into the trachea at different depths of enflurane anesthesia and at different levels of $P_{ET}CO_2$, and changes in breathing pattern, blood pressure and heart rate were recorded. Injecting of distilled water caused various changes in respiration and circulation. However, the type and the magnitude of these changes depended on the depths of anesthesia and the levels of $P_{ET}CO_2$. Our results suggest that respiratory and circulatory responses to airway irritation are greatly modified by the depth of anesthesia and by the background chemical drive of respiration.

S15-4

VENTILATORY AND CIRCULATORY RESPONSES TO BARORECEPTOR STIMULATION
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We stimulated the carotid baroreceptors by a neck suction(N.S.) using a neck colour in 16 healthy men. The test was conducted under four steady state different blood gas conditions as well as during Read's CO_2 rebreathing test. Percent decrease in heart rate at the 2nd breath during neck suction with -60 mmHg was as much as 15 %, which was almost the same with different blood gas conditions. The ventilatory response to N.S. was strongly influenced by blood CO_2 concentration, but not by O_2 level. When PAco2 was normal, N.S. induced hyperpnea mainly due to an increased tidal volume. The magnitude of ventilation was depressed as much as 12 % by N.S. at PAco2 60 mmHg during CO_2 rebreathing. We considered that bradycardic response is fairly independent of blood gas state, and that N.S. elicited two opposite ventilatory effects; nonspecific stimulation and inhibition probably due to baroreceptor stimulation, the former being suppressed by an increased CO_2 concentration.

S15-5

RESPIRATORY AND CARDIOVASCULAR RESPONSES BY MUSCULAR POLYMODAL RECEPTOR INPUTS.
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The polymodal receptor is characterized by its wide-distribution in the whole body; by its responsibility to wide-variety of stimuli; by wide-dynamic range and also a low reproducibility of its response.

Pressor responses and increases in respiratory outputs during stimulation of the receptor were parallelly observed in proportion to magnitudes of the stimulation, while respiratory and cardiovascular changes after cessation of stimulation were not. Post-stimulus respiratory depression was induced by a strong stimulation, that was reversed by naloxone and enhanced by enkephalinase inhibitors, and an increase in enkephalin-like immunoreactivity in CSF was observed after stimulation, indicating an implication of endogenous opioids. Tachy-phylaxis for the post-stimulus depression was prominent, that may be caused by concomitant activation of facilitatory system such as with CCK. Involvement of N. Parabrachialis in this long lasting respiratory depression is suggested by decerebration experiments and by microinjection of morphine and microelectrical stimulation of the region.

S15-6

RESPONSES IN PULMONARY MICROCIRCULATION DURING REGIONAL ALVEOLAR HYPOXIA AND HYPERCAPNIA.
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Using a new X-ray TV system, we analyzed changes in internal diameter (ID), flow velocity (V) and volume flow (F) in small pulmonary vessels (100-600 μm ID) during unilobar hypoxia and hypercapnia in anesthetized cats. In hypoxic and hypercapnic lobes, the ID reduced in proportion to the degree of hypoxia and hypercapnia, respectively. The ID reduction was larger in arteries than in veins for a given stimulus. The maximum reduction occurred in arteries of 200-300 μm ID, in which it was 21, 26, 28, and 36% with 5% O_2, 0% O_2, 5% CO_2, and 10% CO_2 inhalations, respectively. In contralateral normoxic lobes, no ID changes occurred. In both hypoxic and hypercapnic lobes, the V and F of small arteries decreased, with 5% O_2, by 18 and 40%, respectively, and, with 5% CO_2, by 23 and 50%, respectively. In contrast, in normoxic lobes, they increased significantly with 5% O_2 and 5% CO_2. We concluded that regional alveolar hypoxia and hypercapnia induced a local vasoconstriction chiefly in small pulmonary arteries and decreased the V and F in the same lung region.

S-16 The Past and the Future of Circulation Physiology

S16-1

Future strategy of Circulation Physiology. Irisawa, H.
National Institute for Physiological Sciences, 444 Okazaki

Before 1956, it has been thought that the vagal stimulation would cause bradicardia by increaseing K^+ conductance in the SA node cells. This hypothesis was firstly demonstrated by Hutter & Trautwein (1956), shortely after introduction of microelectrode into cardiac physiology. Ach activated K current was found in the small SA node preparation. A Question, whether this current differed from I_{K1} remained. Soejima & Noma (1984) recorded the single channel Ach sensitive K current, which proved that Ach activated K current is the independent K channel. Pfaffinger et al.(1985), Breitweiser & Szabo(1985) reported that the activation of muscarinic Ach receptors requires intracellular GTP. Kurachi et al.(1986) found that the channel activity resumed after the application of GTP or GTP analogue to the inner side of the membrane. Horie & Irisawa (1987) showed the relaxation of Ach activated K current in the single channel recording, which is dependent on the concentration of intracellular magnesium. These are one of the remarkable examples of the future strategy in circulation physiology.

S16-2

BIOFLUIDICS AND REGULATION OF BLOOD CIRCULATION. Hatakeyama, I. Dept. Physiol., Kitasato Univ. Sch. Med., 1 Kitasato, Sagamiohara 228

In 1980 I presented a new scientific field "biofluidics" and showed the movement of fluid or particle is phenomenally investigated in the same way as electronics in electromagnetic theory. Apart from the conventional hydrodynamic concept, various biological phenomena were analysed by introducing phenomenal parameters. We know that amplification of voltage, current or power by electronic circuit with transistor and other active elements is explained by phenomenal parameters such as h-parameters. I indicated an amplifying ability in nonlinear hydrodynamic system including blood circulation, and the behavior of blood in vessel as an elastic tube was described by parameters: self conductance, mutual conductance, amplification coefficient etc. Mechanisms of circulatory regulation to be difficult to investigate with conventional methodology were elucidated on the basis of biofluidics concept. For example, dyanamics of closed circulatory system under nervous and humoral regulation was clearly analysed. Biofluidics indicated that cardiovascular system is really not only a lumped active system but also a distributed active hemodynamic circuit.

S16-3

MECHANISMS OF SYSTEMIC ARTERIAL PRESSURE OSCILLATION. MIYAKAWA, K. 2nd Dept. Physiol. Shinshu Univ. Sch. Med., 3-1-1, Asahi-machi, Matsumoto, 390

Systemic arterial oscillation caused by side pressure exertion procedure can be regarded as an adaptatory phenomenon. It is produced by the reciprocity in autonomic innervation of the cardiovascular system which is coupled with newly developed clock mechanism in the cardiovasculr center or its vicinity. The clock mechanism is conjectured to be made by a serial combination of unit oscillators. On the other hand, the cardiovascular system has potential oscillators in the circuit, namely the smooth muscle of the arteriolear wall and the feedback circuit of central ischemic response and pressoreceptor reflex. The peripheral oscillator which gets hegemony in the cardiovascular system selets the central oscillator whose period is intergers of unit period and is in the neighborhood of resonance period of its own. This phenomenon is related to the function of the central nervous system which is more than mere reflex center. This is only a theory for explanation for the results so far obtained. It remains to be verified with concrete experimental results in future.

S16-4

METHODOLOGY FOR CIRCULATORY PHYSIOLOGY.
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Excellent insights into the present states of a biological system could be gained by careful measurement and control. The present states of a system can be divided into two categories: those determined by past events and those determined by future expectations. To measure the state is to estimate a set of parameters which determines a relationship between variables. To control the state is to force one or more of the parameters. There are four steps in the study of the state of a biological system. The first step is to describe the behavior of the biological system with a qualitative signal-flow diagram. The second step is to quantify it. The third step includes estimating a set of parameters which determines a relationship between variables, estimating a system parameter which determines the response of the system and studying the effect of parametric forcing on the behavior of a model of the system. The last step is to find a technique for parametric forcing in the biological system itself. The representative system parameter is an open-loop gain, which can be estimated by an open-loop method, a closed-loop method or a negative product of the first derivatives of two feedback equations. Present research concentrates on measurement of the form and process of the biological state. In order to forge deeper insights into the meaning of biological states, researchers must try to have active control of the subject.

S16-5

CARDIAC DYNAMICS, ENERGETICS, AND LOAD MATCHING.
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One of the most important fields in circulatory physiology involves problems of cardiac contraction, pump performance, oxygen consumption, efficiency, and load matching. We are the witness of the recent advancement of scientific approaches in these aspects. It includes a wide spectrum of techniques and concepts ranging from microscopic and analytical to macroscopic and integral. To the former belong biophysics of contractile machinery, calcium transient analysis, phosphorus kinetics by NMR, monoclonal identification of myosin isoenzymes, etc. To the latter belong systems approaches to circulatory control and optimality principles. In the middle exist many new approaches and advances including our time-varying elastance model of the ventricle, quantification of the total mechanical energy of ventricular contraction by the systolic pressure-volume area, the assessment of the mechanical efficiencies of the contractile machinery, and the optimality principle for physiological control of contractility. (Partly supported by a MESC grant B61480102 and a MHW grant 60C-3)

S16-6

ELECTRICAL DERANGEMENT AND SALVAGE OF CARDIAC CELLS.
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Recent advance of electrophysiologic technique utilizing isolated cardiac cells and patch membranes disclosed a lot of ionic currents through different ionic channels, i.e., I_{Na}, I_{Ca}, I_{K}, $I_{K,rec}$, $I_{K,Ach}$, $I_{K,ATP}$, $I_{K,Na}$, I_{to}, I_{h} and I_{ti}. The others include currents due to electrogenic Na-K pump and Na-Ca exchange. In case of ischemia or metabolic inhibition, some of these current systems are severely impaired so that electrical and mechanical abnormalities will develop. For instance, increased $I_{K,ATP}$ secondary to decreased $[ATP]_i$ shortens AP duration and refractory period ending up with fatal reentrant tachyarrhythmias. $I_{K,ATP}$ is also controlled by $[Mg]_i$, the decrease of which in case of ischemia facilitates dissipation of $[K]_i$, resulting in decreased resting potentials and loss of excitability. Several attempts have been made to salvage the cells in this chaotic condition. Increases in extracellular glucose concentration antagonized this increase of $I_{K,ATP}$ by enhancing ATP production via facilitated glycolysis. However, more straightforward protection would be the use of specific blocker(s) to $I_{K,ATP}$ channels, effective from outside the cells. Tolbutamide is allegedly an agent for this purpose. Such single cell experiments provide us more insight how to protect the cells from irreversible damage, that is a practical aspect of the state-of-the-art technique and which stimulates future study.

S16-7

"A BLOOD PRESSURE OSCILLATION" BY K. MIYAKAWA AND ITS IMPACT ON THE STUDY OF THE CARDIOVASULAR CENTER. Kumada, M. Institute of Basic Medical Sciences, Univ. of Tsukuba, Tsukuba 305, Japan.

One of the most important issues in the central neural control of the circulation is identification and characterization of the cardiovascular center, the neuronal mechanism to generate tonic sympathetic vasomotor discharges and to control them reflexly. "A Blood Pressure Oscillation", a collection of works by Prof. Miyakawa and colleagues published in 1972, drew attention of investigators at Cornell University, since it described a reliable method to elicit the cerebral ischemic response caused by activation of the cardiovascular center. A series of studies was subsequently conducted by the Cornell group and, together with several other competing groups, eventually led to the discovery that the rostral ventrolateral medulla played a critical role in the tonic and reflex control of sympathetic vasomotor discharges. The works by Miyakawa and colleagues were thus instrumental to deepen our understanding on the central neural mechanism to control the circulation.

S-17 Progress in Thermal Physiology

S17-1

THERMOSENSITIVE NEURONS IN THE BRAIN - ITS ROLE IN HOMEOSTATIC FUNCTIONS.

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Thermosensitive neurons in the preoptic and anterior hypothalamus (PO/AH) have been proposed to play a central role in thermoregulation, based on numerous findings showing good correlations between the activity of these neurons and thermoregulatory responses. Such relationships have been observed during thermal (hypothalamic and peripheral) and pharmacological stimulations, during modulation of neural inputs from extraPO/AH brain regions, and during actual thermoregulatory responses. In vitro studies utilizing hypothalamic tissue slices have demonstrated the existence of 'primary' warm-sensitive and cold-sensitive neurons having inherent thermosensitivity in the PO/AH. Temperature transduction mechanisms of the neurons have been partially revealed by our recent study on the dispersed, isolated single PO/AH neuron. We have also found that 40-70 % of PO/AH thermosensitive neurons respond to non-thermal homeostatic parameters such as blood pressure, local and peripheral osmolality, and non-thermal emotional stimuli. A high degree of convergence of thermal and non-thermal homeostatic signals on the PO/AH neurons, together with abundant neural connections between PO/AH and divergent areas of brain, suggests that these neurons may be involved also in the coordination of thermoregulation and non-thermal homeostatic functions controlled in the hypothalamus.

S17-2

THERMOREGULATORY AND NONTHERMOREGULATORY CONTROLS OF HUMAN SKIN CIRCULATION.

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The arterioles of the human skin are under tonic control of sympathetic vasoconstrictor fibers, and are also regulated by an active vasodilator system in the skin areas other than the glabrous sides of the extremities. They respond principally to thermal demands by vasodilatation, enhancing heat dissipation from the skin. The skin sympathetic nerve fibers also serve regulation of circulating blood volume through arterial and cardiopulmonary baroreflexes, postural reflexes, and reflexes associated with exercise. The competition between skin vasoconstrictor and vasodilator reflexes will take place during exercise at high ambient temperatures. The efferent arms of the nonthermoregulatory reflexes are sympathetic vasoconstrictor fibers to arterioles and AVAs, and the active vasodilator system may not be the case. During exercise at thermoneutral temperatures, however, reduction of blood flow was consistent only in the glabrous side of the hand and not in the forearm skin. In the hand, the extent of this nonthermoregulatory vasoconstriction during exercise was in proportion to exercise intensity, which was again not observed in the forearm skin. Heat loss from the forearm skin appeared to be greatly influenced by blood flow through AVAs in the glabrous side of the hand.

S17-3

WHAT IS THERMAL ACCLIMATION ?

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Thermal acclimation is a physiological adjustment to prolonged exposure to the changes in ambient temperature, resulting in an improvement of thermoregulatory capacity. The present discussion is especially focused on the metabolic acclimation to cold. Metabolic cold acclimation is characterized by an enhanced nonshivering thermogenesis (NST), which occurs mainly in brown adipose tissue (BAT). Major factor regulating this tissue is the sympathetic noradrenaline (NA). However, the experimental evidence from our laboratory suggests that pancreatic hormone, glucagon, is also involved in metabolic cold acclimation through regulating BAT function. Thermogenic actions of these factors are substantially potentiated in cold acclimation. It is inferred that such phenomenon is mediated by an increased activity of mitochorial uncoupling protein in BAT. Overfeeding or repetitive nonthermal stress (immobilization) can induce cross adaptation to cold by means of enhancing NST in BAT through an indentical neuroendocrine mechanism. Intermittent cold exposure can cause the same extent of cold adaptation as that by continuous cold exposure under less stressful state and for shorter period of time. Moreover, NST would appear to regulated by other factors such as insulin, adrenaline, thyroidal and adrenocortical hormones. Accordingly, it may be claimed that the concept of multiple activation of NST function as a fail-safe system in order to ensure a homeothermic organization in cold-exposed organism.

S17-4

RECENT ADVANCES IN FEVER STUDY. MURAKAMI, N. Dept. Physiol., Yamaguchi Univ. School of Med., Ube, Yamaguchi 755

In rabbits, intravenous administration of endogenous pyrogen (EP), known as peptides released from phagocytic mononuclear cells in response to exogenous pyrogen, caused biphasic fever in high concentration. In low concentration, they produced only the first phase of fever. The ventricular injection of EP produced a fever similar to the second phase of the biphasic fever. Indomethacin, a strong cyclooxygenase inhibitor, could induce antipyresis only when indomethacin was administered with the same route to EP injection. From these results, it is concluded that the first phase of biphasic fever is caused by EP acting via structures outside the blood-brain barrier, and the second phase by pyrogen acting via structures within the blood-brain barrier. From the standpoint of view that there is two separate mechanisms inside and outside the blood-brain barrier for producing febrile response, acute phase responses were analyzed, with the consequence that these two mechanisms are also involved in the induction of the acute phase response.

ORAL PRESENTATION AND POSTER EXHIBITION

1

IN SITU ^{31}P-NMR PROBE EQUIPPED WITH SENSORS FOR PHYSIOLOGICAL MEASUREMENTS. NISHIKAWA,H., SHIMAMOTO,N[1]*.,SHINTANI,M[1]*.,OTSUKA,S[2]*.AND YOSIZAKI, K. Dept.Physiol.and Dept.Internal Med[2]., Kyoto Prefectural Univ. Med., Kyoto 602 and Central Research Div[1].,Takeda Chemical Industry, Osaka 532

A superconducting magnet with a wide bore and a high and homogeneous magnetic field made possible to apply a ^{31}P-NMR to the study on in situ energy metabolism of a rat heart and other tissues. More physiological measurements are required to analyze the physiological role of the metabolism in addition to a ^{31}P-NMR spectrum. In this study a homemade ^{31}P-NMR probe to obtain an ECG, a blood pressure of the left femoral artery and a rectal temperature together with a ^{31}P-NMR spectrum was made for an NMR, JEOL SMR200 with a 4.8T, vertical 7cm bore superconducting magnet. The probe had further a homeothermic blanket and a glass tracheal cannula to control the body temperature and the respiration of an experimental animal respectively. The body temperature and blood pressure of an anethetized rat were maintained within their normal ranges during ^{31}P-NMR measurements using the probe, ^{31}P-NMR spectra of the rat heart under these conditions showed the increase of phosphocreatine and the decrease of Pi as the heart rate decreased.

2

THE ROLE OF GLYCOSAMINOGLYCAN ON THE VISCOELASTICITY OF NUCLEUS PULPOSUS ANALYZED BY 1H-NMR RELAXATION TIMES. OHTOMO, S*., KUSAKA, Y*., MIFUNE, T*., YAMASHITA, F*., CHATANI, K*., NISHIKAWA, H., Dept. of Orthop.* and Physiol., Kyoto Pref. Univ. of Med., Kawaramachi Hirokoji, Kyoto 602.

The nucleus pulposus of intervertebral disc (NP) has viscoelasticity owing to its high water content. Glycosaminoglycan (GAG) in the NP, which has properties to retain water and to ristrict its mobility, plays an important role on the viscoelasticity of the NP. In the present study, NP of cow discs containing two different amounts of GAG were prepared: normal NP and GAG digested NP by hyaluronidase. The relationship between the 1H-NMR relaxation times (T1,T2) which indicate the mobility of water, and the dynamic viscoelasticity (|E*|) of those materials were analyzed. The result showed that the T1 and T2 value correlated well with the |E*| value. However, the correlation differed according to the content of GAG in the NP. It was suggested that the |E*| value of the normal NP depended chiefly on the mobility of water which is regulated by GAG. On the other hand, the |E*| value of the GAG digested NP depended not only on the mobility of water but also on the elastic property of the collagen fiber in the NP.

3

MONTE-CARLO ANALYSIS OF FREE FLOW ELECTROPHORESIS. NAGAOKA, M., UYEDA, M.*, TANIFUJI, S.** AND IZUMISAWA. S.*** National Space Development Agency, Tokyo, *Dept. of Physiol., Gifu Univ. Sch. of Med., **Dept. of Technol., Osaka City Univ., Osaka and ***Mitsubishi Haevy Industries, Kobe.

Free flow electrophoresis is a medium-free separation technique. For the estimation of chamber size and condition for the expriments on the ground or in space, we analyzed the system numerically. The analysis includes both the fluid dynamic properties depended on the shape of the chamber, heat production by applied electric field, electro-osmosis, the properties of medium and their combined effects, and electrophoretic behavior of molecule in the field. For the electric and flow field analysis, the finite element method was applied. The analytical solution by Nee and Hu (1979) was applied for electro-osmotic flow calculation. The electrophoretic behavier of the sample molecule was simulated by Monte-Carlo calculation of forced convective diffusion equation. The limit of thickness of medium caused by heat convection and electro-osmosis of the ground experiments were estimated. The interference effect of electro-osmosis in microgravity were also estimated.

4

LIQUID JUNCTION POTENTIAL BY RBCL AND CSCL BRIDGE-ELCTRODE

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LJP is present in the interface that a different electrolyte solution contacts with a different concentration of the liquid. LJP differs only in the values of a diffusion coefficient of a cation and an anion. The diffusion coefficient is different from both of a kind of ion and a concentration. LJP does not exclude completely from electrolyte solution. When LJP is requested with a calculation,LJP is necessary activity counting of each ion. An activity coefficient was unable to calculate by using an electrode. Istly in the experiment, LJP between 3 and 4 component ion from a septum of one hole was measured by the electrode using a salt bridge of Cs^+, Rb^+, K^+ with a saturated concentration and coexistence of Cl^- ion respectively. The standard curves of LJP using the bridge of Cs^+ and Rb^+ were more steady than that of K^+-bridge in all component and they did not show linearity to a different concentration. The standard curves were shown a wave form of concave and convex to 3 and 4 component ion. 2ndly, the ionic component of Cs^+, Rb^+, K^+, Na^+, Li^+ with the same concentration of both bridge and cell was set up. The LJP was shown zero only in the same ion of Rb^+ and Cs^+. When the component is changed to the other ion, LJP did not show zero. From the results with activity was able to be counted of each ion, LJP did not measure a diffusion coefficient by use of electrode.

5

DEVELOPMENT OF CONVENIENT MICROSCOPIC IMAGE PROCESSING SYSTEM BASED ON PERSONAL MICROCOMPUTER AND ITS APPLICATION TO THE WEAK FLUORESCENT IMAGE.

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We developed a convenient color image processing system based on 16 bits personal microcomputer(PC-9801Vm2) equipped with CCD color TV camera(Nakamura Sci.Co.Ltd.,IK-1570N),interface board (Nippon Board Computer Co.Ltd.,NBC-PB9801) to convert color microscopic image into 256 X256 pixels with each RGB 6 bits binary data during 1/60 seconds, simple wide band video amplifier for dim image, color video monitor, mouse and electromagnetic shutter to lower fade-out. Programs were described with N88 DISK BASIC(86) and assembly language. Using this hardware system and program for adding pictures, we suceeded to detect the weak fluorescent image obtained by injection of Lucifer Yellow into the cultured mouse neuroblastoma cells, by histofluorescent methods for dopaminergic cells or by immunofluorescent method for the bipolar cells in the carp retina.

6

VIZUALIZATION OF THE BRAIN ACTIVITY BY LUCIFERIN-LUCIFERASE-ATP LUMINESCENCE. KIMURA, Y. AND TERAKAWA, S. Dept. Cell Physiology, Natl. Inst. Physiol. Sciences, Myodaiji, Okazaki, 444 Japan

Purified brain synaptosomes are known to release ATP when they are stimulated by raising extracellular potassium concentration or by some other chemicals. We could visualize the ATP release in the brain tissue by using the luciferin-luciferase-ATP reaction. Rat brain slices were immersed in luciferin-luciferase reaction mixture and were stimulated by acetylcholine, nicotine and elevated potassium concentration. The very low luminescence from rat brain slices could be successfully observed in real time by single photon counting camera. The most prominent response to acetylcholine and nicotine were obtained at hypothalamus. This method gives information about the input/output of cells in contrast that the methods using microelectrodes and voltage sensitive dyes give information about the state of the cells. However, ATP released from broken or damaged cells left the non-physiological responses. Some instability of both luciferin and luciferase made the measurement in tissues difficult. The possibility of measuring the single synapse activity was discussed.

7

A NOTE ON IMPLEMENTING COMPUTER PROGRAMS OF ACOUSTIC ANALYSIS OF SPEECH SOUNDS. SIMADA, Z. Dept. of Physiol., Sch. of Med., Kitasato Univ., Sagamihara, Kanagawa 228

This paper suggests a preferred program structure for acoustic analysis of speech sounds. Acoustical characteristics of particular sounds are determined by means of a sequence of modules computing output based on input parameters. What kind of modules to use and how to combine them for constructing a particular processing system depend on the goal of analysis. The goal is best achieved if the modules are independent of each other for programming, if only simple computation is required of the modules, and if no more than a single complicated problem is imposed at one time. In this way a wide variety of processing can be selected by combining any of the modules freely. Besides the independence of each module, its output parameters must be manipulated in three directions: (1) the parameters must be saved as a file, (2) checked on a terminal or a printer, and (3) displayed graphically. The problem is how to implement these principles in a common format across all the modules executed in the sequence. FORTRAN has been shown to be incapable of this three-way implementation. Different types of languages, for instance the object-oriented, lend themselves more suitably to the structure suggested in this paper.

8

A TWO-PATCH-PIPETTE VOLTAGE CLAMP SYSTEM FOR RECORDING OF MEMBRANE CURRENT OF LARGE CELLS. NISHIYAMA, A., WAKUI, M., *HOSHIMIYA, N., **MARUYAMA, Y., AND ***OHBA, S. Dept. of Physiol., Tohoku Univ. Sch. of Med., Sendai 980, *Res. Inst. Appl. Elect., Hokkaido Univ., Sapporo 060, **Dept. of Physiol., Facult. Med., Univ. Tokyo, Tokyo 113, ***Facult. Eng., Tohoku Univ., Sendai 980.

A voltage clamp system which allows to record membrane ionic currents of large cells with good signal-to-noise ratio has been designed and built. Two separate tight-seal patch pipettes of low resistances (about 5MΩ) were attached in whole-cell mode: one to measure the intracellular voltage and the second to inject the current into the cell. With these low resistance pipettes and a membrane model of 100MΩ and 50pF the background noise of the clamp system was 10^{-27} - 10^{-26} A^2/Hz at frequencies between 0.1 - 1000Hz which was low enough to allow the detection of the infinitesimal current fluctuations reflecting the opening and closing of the membrane ionic channels. Insertion of a simple low-pass filter in the voltage control amplifier and compensation of the frequency characteristics of the voltage clamp system stabilized the system operation. With this clamp system a voltage-dependent K current (2-3 nA) in the mouse lacrimal gland acinar cells (about 20um diameter) and a voltage-depend transient K current (several tens nA) in the mouse magakaryocytes (about 50um diameter) were recorded.

9

A SIMPLE METHOD FOR CALCULATION OF CONCENTRATIONS OF FREE METAL IONS IN THE PRESENCE OF MULTIPLE METAL IONS AND A CHELATING AGENT. WATANABE, K., HASEGAWA, K., OHTAKE, H. and KOGA, M. Dep. Physiol., Dokkyo Univ. Sch. Med., Mibu, Tochigi 321-02

Calculation of free metal ion concentrations in the presence of a chelating agent (ligand) and multiple metal ions is complicated. We developed a simple method for calculation of free ion concentrations from given total ion concentrations. The outline of this method is as follows: i) Using an arbitrarily chosen provisional value of free ligand concentration (p-Lf), calculate a total ligand concentration (Lt). ii) Divide the p-Lf by the ratio, the calculated Lt (c-Lt)/ the specified Lt (s-Lt). iii) Take the resulting value as the next p-Lf and repeat the calculation until c-Lt is close enough to s-Lt. At this point, p-Lf is supposed to be set to a good approximation of true free ligand concentration. iv) Finally, calculate free metal concentrations from the above approximation.

As an application of this method, we calculated the free zinc concentration in EDTA-treated culture media. In primary culture of hepatocytes, a good correlation between the rate of DNA synthesis and the free zinc concentration was seen. Thus, this method proved to be useful for practical applications.

10

IMPLANTABLE LOW-COST AND MINIATURIZED PRE-AMPLIFIER FOR RECORDING NEURAL SIGNALS IN AWAKE ANIMALS.
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We developed a low cost, small and lightweight (10.5gr) implantable pre-amplifier for recording neural signals in awake animals. To reduce a size and interference, the pre-amplifier is constructed by a few electronics parts; two IC tips (CA3078H), four tip capacitors and eight tip resistors. The pre-amplifier which was constructed by parallel arranged two non-inverting operational amplifiers, have 40 dB gain. The hybrid circuit was fabricated on ceramic plate, and encapsulated by brass metal box. The metal box was further coated by epoxy and then by silicon rubber to protect from liquid and biological reactions. Neural signals recorded by a collagen electrode were amplified by a developed device. If the amplitude of the neural signals are greater than about 10μ Vp-p, our developed device can discriminate the neural signals from noise.

11

DEVELOPMENT OF COMPUTER CONTROLLED DEVICE FOR DETERMINATION OF ODOR PREFERENCE RANKING. MURAMOTO, K., ONO, T., TABUCHI, E., NISHIJO, H., NAKAMURA, K. and INDO, M.*. Dept. Physiol., Fac. Med., Toyama Med. and Pharmaceu. Univ., Sugitani, Toyama 930-01 and *Takasago International Corp., Kamata, Ohta-ku, Tokyo 144

A personal computer controlled system was developed for quantitative determination of odor preference ranking. This system contains three main parts: an input (bar press), a controller (computer) and an output (odor spray). The rat can produce an odor by pressing an appropriate lever. After pressing a bar a certain number of times, according to a preset fixed ratio (FR 1-99), a spray trigger pulse is sent to the driver controlled by that bar. After each spray, the bars are disabled for a predetermined time. In this system, all input-output relations, day-night light control, and recording intervals are computer controlled and established with software. Data can be stored on floppy disks and analyzed off-line.

12

RESONANCE RAMAN STUDY OF THE COMPLEXES BETWEEN ANIONIC SEMIQUINOID FLAVOPROTEIN D-AMINO ACID OXIDASE AND LIGANDS. NISHINA, Y., TOJO, H.,* AND SHIGA, K. Department of Physiology, Kumamoto University Medical School, Honjo, Kumamoto 860, *Department of Biochemistry, Osaka University Medical School, Kita-ku, Osaka 530

Picolinate binds to the anionic semiquinoid form of D-amino acid oxidase (DAO), and the complex formed has a charge transfer absorption band in the long wavelength region extending beyond 800 nm. The binding has a stoichiometry of 1:1 with respect to the enzyme. The dissociation constant at 25 ℃, was 30 μM at pH 7.0. The pH dependence of the dissociation constant indicates that one proton is associated with the complex formation. By adding dithionite to the oxidized DAO solution containing pyruvate and methylamine, a similar anionic semiquinoid DAO complex having a broad long wavelength absorption band, appeared. Resonance Raman spectra of the complex indicate that the complex consists of the anionic semiquinoid DAO and N-methyl-α-iminopropionate produced from pyruvate and methylamine, and that the imino group must be protonated. This supports the proposal that the presence of a positive charged group in the vicinity of flavin is required for the stabilization of the anionic semiquinoid flavin. The results also suggest that the broad absorption band is derived from the charge transfer interaction between the anionic semiquinoid flavin and the imino acid, in which the flavin C(4a)-N(5) locus and the imino acid H-N=C-COO$^-$ locus are important for the interaction.

13

H-NMR BEHAVIOR OF NITROGENOUS COMPOUNDS .IN URINE.
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Dept. of Physiol.2 ., Sch. of Med., Iwate Med. Univ., Morioka 020.

The interactions between water and urinary nitrogenous compounds were studied by means of H-NMR spectrum and relaxation times. In the FT-spectrum of urine, with water suppression by homogated decoupling method, the peaks of many components such as creatinine (CH_3 = 3.0, CH_2 = 4.0 ppm), glycine (CH_2= 3.2 ppm), histidine, hippurate, lactate etc. were observed. But the urea NH_2 peak as well as the NH group of creatinine, uric acid and amino acids could not be recognized due to rapid exchange with water. An urea signal at 5.8 ppm appeared in the lyophilized urine dissolved in D_2O. The relaxation times (T_1 and T_2) of water protons were measured at the concentrations of 1 - 10 M for urea, 0.01 - 0.8 M for creatinine, 1 - 10 mM for uric acid, and 0.01 - 3 M for glycine solutions. With the increase of the concentration, T_1 decreased linearly to 2 - 3 sec, and T_2 decreased exponentially to 0.1 - 2 sec with all compounds examined. The hydration number (mol H_2O/mol) calculated was 40 for glycine, 20 for creatinine, 3 for urea and 0.1 for uric acid.

14

EFFECT OF LiCl ON THE HYDRATION OF FIBRINOGEN AND FIBRIN-GEL ESTIMATED BY H-NMR RELAXATION TIMES OF WATER PROTONS. TANAKA, Y., YOSHIOKA, Y. NAKAYA, S. & KUROSAWA, N. 2nd Dept. Physiol., Schl. Med., Iwate Med. Univ., Morioka, Iwate, 020

When the fibrinogen(Fbg) solutions(0.2 M borate buffer) were converted to the fibrin-gel(Gel) by addition of thrombin, the turbidity of resulting Gel decreased with the increase of concentration of salt in the buffer (0.02 - 0.50 M). It has been reported that the higher the concentration of salt such as NaCl and KCl, the more transparent the Gel and the smaller the hydration. In this report, the effect of LiCl was examined by the same manner. H-NMR relaxation times, T1 and T2, of water in Fbg and Gel were determined at various concentrations of LiCl (0.02 - 1.0). T1 of Fbg and Gel varied little from the buffer(3.367 sec) to 2.943 for Fbg and 2.665 for Gel(10 mg/ml) at 0.05 M LiCl. T2 of Fbg and Gel were 1.133 and 0.685 sec, respectively, while that of buffer was 2.026. The hydration values were caliculated from these T1 and T2 according to Kumosinski and Pessen(1984). They were 0.22 g of water/g of protein for Fbg and 0.49 for Gel. The contribution of L-ion to the protein hydration is larger than that of Na and K.

15

APPLICATION OF NMR SPECTROSCOPY TO THE DYNAMICS OF METABOLITES IN RAT LIVER TISSUE

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The dynamic behavior of metabolites in excised rat liver was studied by using 80 MHz H-NMR spectroscopy (Bruker WP80SY-WG). The NMR spectrum of 20 mg wet tissue was recorded in 3 mm NMR tube at 30 ^{o}C with presaturation of the water resonance. The peakes of the spectrum were so broad that the assignment and band width measurements were hardly done. This spectrum was reconstructed by using the spectra of the extracts obtained by Folch's method. The assignment and the band width measurement were easily made by chacking the chemical shift and the broadning parameter in reconstruction process. The resonances at 0.8 - 1.4 ppm were assigned to lipids and at 3 - 4 ppm to hydrophilic compounds, and their band widths were estimated to be 7 Hz and 4 Hz. This difference of widths indicates that hydrophilic compounds reorient 2 times faster than lipids. The main components of hydrophilic group were glucose, maltose, glycine, choline, phosphocholine and carnitine. Lactate and alanine were only observed in the extract.

16

CIRCULAR DICHROIC (CD) AND ^{1}H-NMR STUDIES ON THE N-B TRANSITION OF IODOACETAMIDE-BLOCKED BOVINE PLASMA ALBUMIN (IA-BPA) IN NEUTRAL pH REGION.

ERA, S., KUWATA, K., AMANO, H., FUJII, H., SOGAMI, M. and WATARI, H*. Dept. Physiol., Sch. Med., Gifu Univ., Gifu 500 and *Dept. Mol. Physiol., Natl. Inst. Physiol. Sci., Okazaki 444

IA-BPA and/or BPA show the N-B transition over the pH range from 7.0 to 9.0. Though pH-profiles of magnitudes of $[\theta]_{262}$ and $[\theta]_{268}$ showed significant decreases in the N-B transition in 0.10 M KCl, no significant changes in $f(\alpha)$, $f(\beta)$, normal ^{1}H-NMR spectra, spin-echo ^{1}H-NMR spectra and cross-relaxation times (T_{IS}) were observed on going from the N-(pH or pD 7.0) to B-forms(pH or pD 9.0). These results might suggest that the N-B transition in 0.10 M KCl or NaCl involves only changes in conformation of disulfide bonds and/or side chains, resulting in the increase in the mutual movement of subdomains, connected by flexible hinges. In the N-B transition with no added salt, the significant decreases in $f(\alpha)$(N→B, $f(\alpha)$, 0.70→0.62), approximately 1.5 times increases in T_{IS} values and spin-echo ^{1}H-NMR spectra of the B-form might indicate that the B-form with no added salt has mobile structure.

17

STRUCTURAL FLUCTUATION AND N-A ISOMERIZATION OF BOVINE MERCAPTALBUMIN (BMA).

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In alkaline pH region, BMA isomerizes to the A-form by the intramolecular SH, S-S exchange reaction. The rates or equilibria of the reaction were strongly affected by environmental factors. In salt-free solution, non-aged iodoacetamide-blocked BMA (IA-BMA) showed characteristic changes in the secondary structure in the N-B transition ((N, pH 6.8), $f(\alpha)$=0.70, $f(\beta)$=0.12 ; (B, pH 9.0), $f(\alpha)$=0.62, $f(\beta)$ =0.20). However, $f(\alpha)$ and $f(\beta)$ of the IA-A-form over the pH range from 6.5 to 9.1 in salt-free solution or 0.10 M KCl were 0.60 and 0.20, respectively and were similar to those of the non-aged IA-BMA at pH 9.0(B-form) in salt-free solution. Cross-relaxation times (T_{IS}) of the IA-A-form at pD 9.3 in salt-free solution were longer than those at pD 7.20. Spin-echo ^{1}H-NMR spectra of the IA-A-form at pD 7.20 and 9.3 in salt-free solution indicated that side chains of the IA-A-form, such as ε-CH_2 of Lys, -CH_3 are more mobile than those of the non-aged IA-BMA.

18

FURTHER STUDIES ON THE RESOLUTION OF HUMAN MERCAPT- AND NONMERCAPT-ALBUMIN BY HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC). SOGAMI, M., ERA, S., KUWATA, K. AND FUJII, H. Dept. Physiol., Sch. Med., Gifu Univ., Gifu 500

Human serum albumin (HSA) is the mixture of mercapt- (HMA) and nonmercaptalbumin (HNA). It was reported by several groups that HNA are composed of mixed disulfide compounds, that is, mixed disulfide compounds with cysteine(HNA(CYS)) or glutathione(HNA(GSH)) and oxidation products higher than mixed disulfide, such as sulfenic, sulfinic and sulfonic states(HNA(OXI)). Ion-exchange HPLC on an Asahipak ES-502N column(0.76 x 10 cm ; column temperaure, 35 $\pm$ 0.02°) was carried out by gradient elution with ethanol concentration from 0 to 10% in 0.05 M sodium acetate, 0.40 M Na_2SO_4, pH 4.80. HPLC profiles of commercial HSA showed the clear resolution of HSA into three components. From experimental evidences on HMA, synthesized HNA(CYS), HNA(GSH) and HNA(OXI), it was concluded that the primary, secondary and tertiary components correspond to HMA, (HNA(CYS), HNA(GSH)) and HNA(OXI), respectively. Fracitons of HMA in commercial HSA preparations, obtained by ES-502N HPLC were comparable to those by GS-520 HPLC(Sogami et al, 1984).

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INHIBITORY EFFECTS OF GYMNEMIC ACID ON PLAQUE FORMATION AND GLUCAN SYNTHESIS. Miyoshi,M., Watanabe,T.*+ and Imoto,T. Dept. Physol. and Dept. Oral and Maxillofacial Surgery+ Tottori Univ. Sch. Med., Yonago 683

The effects of gymnemic acid(GA), a triterpene glycoside extracted from the leaves of Gymnema sylvestre, on the plaque formation of Streptococcus mutans cells and the glucan synthesis by crude glucosyltransferase(GTase) of S.mutans were examined in vitro. The formation of plaque adherent to a glass surface was almost completely inhibited by GA at a final concentraion of 1mg/ml. The synthesis of water-insoluble glucan(WIG) from sucrose with cell-free GTase of S.mutans was significantly inhibited by GA at this concentration. Furthermore, the synthesis of WIG adherent to a glass surface was markedly inhibited by GA at 0.1mg/ml. Inhibitory effect of WIG synthesis among several components of homologues separated from GA by means of high perfomance liquid chromatography system was found to increase with increasing hydrophobic degree of each component.

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HIGH-PERFORMANCE LIQUID CHROMATOGRAPHIC (HPLC) STUDIES ON THE STRUCTURAL ALTERATION OF HUMAN SERUM ALBUMIN (HSA) IN THE ELDERLY. ERA, S., KUWATA, K., KAWAI, K.*, SOGAMI, M., FUJII, H., KITAZAWA, Y.*, OKABE, H.**, NOMA, A.*** AND UJI, Y.*** Dept. Physiol. and *Dept. Ophthalmol., Sch. Med., Gifu Univ., Gifu, **Dept Lab. Med., Sch. Med., Kumamoto Univ., Kumamoto and ***Tokyo Metropolit. Geriat. Hospit., Tokyo

HSA is the mixture of mercapt-(HMA, reduced form) and nonmercaptalbumin(HNA, oxidized form). While conducting HPLC studies on HSA, the present authors found the convenient HPLC system for the resolution of HSA into HMA and HNA. Mean value of fraction of HMA($\bar{f}$(HMA)) for healthy male adults, obtained by 8 columns of GS-520H(sulfate buffer), was 0.75 $\pm$ 0.03(n=28). $\bar{f}$(HMA) for healthy eldery subjects(range of ages from 60 to 90), obtained by 8 columns(sulfate buffer) and 2 columns(citrate buffer) of GS-520H were 0.48 $\pm$ 0.05 and 0.47 $\pm$ 0.06(n=114), respectively, indicating the significant difference between healthy eldery subjects and healthy male adults. It was reported by Kuck et al(1982) that the sulfhydryl content of human lenses falls with ages Low $\bar{f}$(HMA) of HSA in the elderly might be in agreement with findings by Kuck et al.

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HIGH-PERFORMANCE LIQUID CHROMATOGRAPHIC (HPLC) STUDIES ON MERCAPT-NONMERCAPT (HMA-HNA) CONVERSION OF HUMAN SERUM ALBUMIN (HSA) IN RENAL TRANSPLANTS.

ERA, S., KUWATA, K., KIDA, K., SUZUKI, E.*, FUJII, H., SOGAMI, M., KUMANO, K.**, SAKAI, T.** AND KOSHIBA, K.** Dept. Physiol., Sch. Med., Gifu Univ., Gifu 500, *Dept. Mol. Physiol., Natl. Inst. Physiol. Sci., Okazaki 444 and **Dept. Urol., Sch. Med., Kitazato Univ., Sagamihara 228

HSA is the mixture of HMA and HNA. Fractions of HMA (f(HMA)) were obtained using HPLC on Asahipak GS-520 columns at neutral pH. Mean value of f(HMA) ($\bar{f}$(HMA)) for patients with chronic renal failure (CRF) of 0.51 $\pm$ 0.096 (n=28) was significantly lower than that for healthy male adults of 0.75 $\pm$ 0.028 (n=28). $\bar{f}$(HMA) values of renal transplants of A-Hospital, with or without using cyclosporin A were 0.63 $\pm$ 0.064 (n=26) and 0.63 $\pm$ 0.083 (n=166), respectively, indicating the HNA→HMA conversion of HSA in patients with CRF by the renal transplantation. Corresponding values of B-Hospital were 0.49 $\pm$ 0.089 (n=33) and 0.55 $\pm$ 0.080 (n=68), respectively, indicating significant differences in $\bar{f}$(HMA) values between A- and B-Hospitals ($P<0.01$).

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STRUCTURAL ALTERATION OF HUMAN SERUM ALBUMIN (HSA) BY ANESTHESIA.

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HSA is the mixture of mercapt- and nonmercaptalbumin (HMA and HNA). Fractions of HMA (f(HMA)) in patients with normal liver function before and after elective surgery under anesthesia were studied using high-performance liquid chromatography(HPLC). f(HMA) values were obtained using HPLC on 8 columns (column temperature, 28 ℃) or 2 columns (32 ℃) of Asahipak GS-520H (0.75 x 25 cm) at neutral pH. Eluent buffer for 8 and 2 columns were 0.03 M soium phosphate buffer, 0.15 M Na_2SO_4, pH 6.87 (sulfate buffer) and 0.03 M sodium phosphate buffer, 0.03 M trisodium citrate, pH 6.86 (citrate buffer). f(HMA) values indicated that two HPLC methords are equivalent. Analytical time on 2 columns of GS-520H with citrate buffer was one third of that on 8 columns with sulfate buffer. f(HMA) increased at the end of anesthesia and on the 1st postoperative day and then decreased for 2 weeks.

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HIGH-PERFORMANCE LIQUID CHROMATOGRAPHIC (HPLC) STUDIES ON PARTIALLY HYDROLYZED BOVINE PLASMA ALBUMIN (BPA*) FORMATION IN ACIDIC REGION.

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Bovine plasma albumin (BPA) has known to contain small amount of proteolytic enzyme, which catalyzes a specific cleavage of BPA between Gln-392 and Cys-435 in one or two portions near pH 3.8. The proteolytic products, BPA* has a tendency to form transparent gel in D_2O around pD 4 above 7%. Using ion exchange HPLC on TSK SP-5PW at pH 5.0, kinetic studies on BPA* formation in 0.10 M NaCl at pH 3.8 at 35° were carried out on various BPA preparations. After 50 hrs incubation at 35° at pH 3.8, BPA* fractions were from 0.01 to 0.57, indicating significant difference in amount of proteolytic enzyme among BPA preparations. CD-resolved secondary structures ($f(\alpha)$ and $f(\beta)$) of BPA* and BPA at pH 5.5 in 0.10 M NaCl were (0.61, 0.19) and (0.70, 0.12), respectively. Spin-echo ^{1}H-NMR spectra of BPA*-gel in D_2O at pD 4.0 indicated that side chains of His and Lys involve in the gel-formation.

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^{1}H-NMR STUDIES ON THE WATER STRUCTURE OF NORMAL RAT LIVER AND HEPATOCELLULAR TUMOR.

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Water structure was studied by measuring spin-lattice relaxation times(T_1) and cross-relaxation times(T_{IS}) from irradiated protein protons to water protons. Plots of $1/T_1$ or $1/T_{IS}$ of normal rat liver (ACI/N rat) vs dry weight(W(%)) were steeper than those of hepatocellular tumor and regenerating rat liver, with significant difference in plot of $1/T_{IS}$ vs W(%). These results might indicate that the water structure of normal rat liver is gel-like state. All of these experiments were carried out before July 1985. In experiments after January 1986, plots of $1/T_1$ and $1/T_{IS}$ vs W(%) for normal rat liver and hepatocellular tumor were shifted to the right-hand side with similar gradients to those before July 1985 and the significant differences in plots of $1/T_1$ or $1/T_{IS}$ vs W(%) were retained. These parallel shifts in plots of $1/T_1$ or $1/T_{IS}$ vs W(%) might be affected by nutritional conditions.

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^{1}H-NMR STUDIES ON WATER STRUCTURE IN PERITUMORAL EDEMATOUS BRAIN TISSUE.

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Water structures of normal rat brain, peritumoral edematous brain and T9-glioma were studied by measuring ^{1}H-NMR spectra, spin-lattice relaxation time(T_1), cross-relaxation time(T_{IS}) from irradiated protein protons to water protons, tissue hydration and electrolyte concentrations. Tissue hydration, Na^+ content and T_1 of T9-glioma were significantly increased in comparison with normal brian tissues. T_{IS} values of peritumoral edematous brain tissues were significantly reduced, even though hydration, electrolyte content and T_1 did not differ significantly between peritumoral edematous brain and normal control brain tissues. These results might indicate that the water structure in brain tissues is changed at an early stage of edema formation, that is, an amount of bound water to macromolecules is increased in edematous brain tissues without increases in total hydration.

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SPECTRA CHANGE OF ^{1}H-NMR WITH A INTERACTION BETWEEN PHOSPHATIDYL CHOLINE AND MONO-L-ASPARTIL CHLORIN e_6.

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Mono-L-aspartyl chlorin e_6 (NPe_6) has been shown to have a higher affinity for sarcoma than for various normal internal organs. In the tumor, NPe_6 is more likely to be bound to membrane lipid than a protein component. A study of the binding of phosphatidyl choline dioleoyl(P.C.) to NPe_6 by ^{1}H-NMR was performed. The ^{1}H-NMR spectrum of each group of P.C.(2×10^{-2}mol/l) in $CDCl_3$ solution were detected as follows: in oleic acid, $C\underline{H}_3$ 0.88ppm,-$(C\underline{H}_2)_{18}$-1.28 ppm,-$C\underline{H}$=$C\underline{H}$-5.32ppm, in the hydrophilic region,-$N^+(C\underline{H}_3)_3$ 3.33ppm,-$C\underline{H}_2$-N^+ 3. 77,-P-O-$C\underline{H}_2$-CH_2-N^+3.99ppm. To a $CDCl_3$ solution of P.C.(2×10^{-2}mol/l),a water solution of NPe_6 was added to increase its concentration to observe the change in the ^{1}H-NMR spectrum. As NPe_6 concentration increased, the signal of the hydrophilic region shifted toward the higher magnetic field, and the signal in oleic acid did not shift. Therefore, it is likely that the interaction occurs between thehydrophilic region of phosphatidyl choline and NPe_6.

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THE EFFECT OF PHOTOSENSITIZER UPON NERVE FUNCTION

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The effect of white light upon nerves accumulated with HpD and PH-1008 especially has been investigated.

Sciatic nerves of Xenopus were incubated with HpD and PH-1008 liquids in different concentrations for an hour, and divided into two groups (control and test), after then their action potentials were measured in dark room and in light radiation especially.In dark room, no change could be seen in both groups. When test groups were radiated with white light (power 2.0mW), their potentials decreased gradually depending on the concentrations of HpD, and PH-1008 and radiation duration. Maybe it is becourse of that when nerves accumulated HpD and PH-1008 were irradiated with white light, singlet oxygen was activized, and the later broke action potentials of the nerves.

Besides the above, after being radiated for one hour with 2.0mW white light, the fact that action potentials of nerves incubated with 10^{-3} mol/l HpD were 47.5% and those incubated with 10^{-4} mol/l PH-1008 were 31.7% can be seen. It shows the effect of PH-1008 is greater than HpD.

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THE ACCUMULATION OF HpD AND PH-1008 IN ASCITES TUMORS

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Solid tumors accumulate lage amounts of hematoporphyrin derivative (HpD) and other photosensitizers. The effectiveness of photodynamic therapy (PDT) after administration of HpD has been demonstrated. On the other hand, almost nobody has investigated the acumulation of photosensitizers in non-solid tumors.

In this study, we measured fluorescence spectra of HpD and 13,17-di tetra ammonium protoporphyrin(PH-1008) in ascites tumors of mice by excimer dye laser.

Ascites Balb/c mice to which Meth-A fibrosarcoma was transplanted into the peritoneal cavity were chosen. The ascites-induced mice received injections of 20mg/kg HpD or PH-1008 into their tail veins, and detection procedures were started 30mins, 2, 6, 24 and 48hrs later.

The results show that the accumulation of PH-1008 in ascites tumors is about 31.4 times greater than that of HpD .

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AFFINITY OF HpD AND SERUM COMPONENTS (NO.2)

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There has been increasing interest in use of porphyrin for tumor localization and therapy. Hematoporphyrin derivative (HpD) is well-known tumor-specific photosensitizer. HpD has been used clinically as a photosensitizer in photodynamic therapy (PDT). PDT is performed after HpD i.v. injection. Therefor, HpD may interact with serum components. Last year, we should the binding affinity of HpD to albumin, one of the serum components. In this study, we investigated relation between tumor accumulation HpD and albumin binding HpD. HpD accumulation in tumor and albumin binding HpD were measured by HPLC. HPLC is able to select in several components of HpD. Retention time of these components has 5'55",8'56",22'23" and 25'23". Retention time of accumulated components in tumor has 4'12",6'00",8'40",21'46" and 24'43". Retention time of tumor-specific components is 8'40". It's HPLC pattern is similar to HpD components binded to mouse serum albumin. These results suggest that albumin may be tumor-specific carrier protein of HpD.

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APPLICATION OF THE ^{31}P-NMR DESPOT METHOD TO THE MEASUREMENT OF SPIN-LATTICE RELAXATION TIME IN BIOLOGICAL SYSTEMS. SUZUKI,E., MAEDA,M., SEO,Y., KUKI,S., NAKAYAMA,S., TSUKAMOTO,K., KAWAKAMI,T., MURAKAMI,M. and WATARI,H. Dept. of Mol. Physiol., Natl. Inst. for Physiol. Sci., Okazaki 444

It was reported by several groups(Homer(1985), Seo(1987)) that the DESPOT method(Driven-Equilibrium Single-Pulse Observation of T_1) is very convenient for the measurement of spin-lattice relaxation time (T_1). However, in order to measure the accurate T_1 of phosphorus-containing metabolites in biological systems, it is necessary to use its suitable pulse repetition time(t) of ^{31}P-NMR DESPOT method. The results indicated that the T_1 of multiple kinds of phosphorus-containing metabolites, including PME, 2,3-DPG, Pi, PDE, PCr and ATP were significantly different and those were between 0.15 ± 0.02 and 8.50 ± 1.57 sec, indicating that a suitable t for the biological systems was generally 0.6 sec. However, T_1 of phosphorus-containing metabolites of rat liver were between 0.15 ± 0.02 and 1.10 ± 0.07 sec and those of rat kidney were between 1.06 ± 0.12 and 8.50 ± 1.57 sec, indicating that suitable t were 0.3 and 1.0 sec, respectively.

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FACILITATED TRANSPORT OF OXYGEN THROUGH HEMOGLOBIN SOLUTIONS. HASHIMOTO, M, HATA, R., TYUMA, I., ISOMOTO, A.*, AND UOZUMI, M.** Dept. Physico-chemical Physiol., Osaka Univ. Med. Sch., 4-3-57, Nakanoshima, Kita-ku, Osaka 530, *Dept. Gen. Educ., Kinki Univ., Higashiosaka 577, and **Osaka Pref. Inst. Public Health, Higashinari-ku, Osaka 537.

A method for quantitative analysis of hemoglobin color to estimate the oxygen saturation was developed. The method uses an image-input and -processing system composed of a 3-tube video camera and a digital image analyzer. Using the system connected to a microscope, facilitated diffusion of oxygen in hemoglobin solutions was observed and analyzed in a position-sensitive way. So, an empirical formula $J = kCY$ was obtained, where J is the flux of oxygen, C is the concentration of hemoglobin, Y is the oxygen saturation of hemoglobin, and k is a constant.

We have now examined the effect of the oxygen affinity of hemoglobin and the effect of the viscosity of solution on the oxygen transport and have obtained the following results. (1) The empirical formula $J = kCY$ is valid as well as in our earlier experiments. (2) Both the oxygen affinity of hemoglobin and the viscosity of solution have no effect on the k value. (3) The oxygen affinity of hemoglobin affects the rate of transport through the change of Y value. These facts may suggest the molecular mechanism of the facilitated transport but cannot be explained by the Fick's diffusion law.

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OXYGEN BINDING PROPERTIES OF AMPHIBIAN HEMOGLOBINS: A COMPARISON WITH HUMAN HEMOGLOBIN. IMAI, K., TSUNESHIGE, A*, TYUMA, I., KIHARA, H*[1], SHINOZAKI, N*[2] Dept. Physicochem. Physiol., Osaka Univ. Med. Sch., Nakanoshima, Osaka 530; [1]Jichi Med. College, Minamikawachi, Tochigi 329-04; [2]Nippon Amphibian Lab., Nikko, Tochigi 321-16.

The amphibian hemoglobin (Hb) is interesting from a viewpoint of a wide variety of respiration which switches during metamorphosis. We investigated oxygen binding properties of four kinds of salamander Hbs and compared them with those of human adult Hb (Hb A). The sources of Hb samples were Onychodactylus japonicus, Megalobatrachus sligoi, Andrius japonicus, and Cryptobranchus alleganiensis. Both red cells and Hb solutions of these salamanders showed low oxygen affinities and almost diminished or very small Bohr effects. The oxygen equilibrium curve of the salamander Hbs was little shifted on the addition of Cl^-, CO_2, ATP, IHP (inositol hexaphosphate), and inorganic phosphate. Cooperativity of the salamander Hbs was somewhat smaller than that of Hb A. Thus, the salamander Hb seems to be a primitive Hb which lacks part of important allsteric effects. We thank Mr. Shogetsu at Nippon Salamander Center (Nabari, Mie) for blood samples of A. japonicus and C. alleganiensis.

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EFFECTS OF OSMOTIC PERTURBATION ON THE DIELECTRIC PROPERTIES OF CULTURED MURINE LYMPHOBLASTS (L5178Y).

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The dielectric constant and electrical conductivity of cultured cells (mouse lymphoma L5178Y) in suspension were measured over the frequency range from 0.01 to 500 MHz at various medium osmolalities (170-590 mosmolal). By combining the observed dispersion curves and morphological parameters obtained from light and electron microscopy, we examined the cell's dielectric behavior on the basis of a newly-introduced "composite-shell" model, which consists of three concentric shells (implying the cell membrane and the outer and inner membranes of the nucleus) and smaller shells (implying mitochondria). Analysis by a computerized curve-fitting procedure revealed that the specific electrical capacity of the plasma membrane (Cm) increased, as a function of external medium osmolality, from 0.8 $\mu F/cm^2$ (at 170 mosmolal) up to 1.5 $\mu F/cm^2$ (at 590 mosmolal).

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DIELECTRIC BEHAVIOR OF THE LENS AND ITS CHANGE DUE TO EXPERIMENTAL CATARACTS.

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In order to study the passive electrical properties of the lens and their changes with cataract formation, we have examined the dielectric behavior of the bullfrog lens over a wide frequency range of 100 Hz - 500 MHz. At least three dielectric dispersions were observed in this frequency range. An application of an ellipsoidal cell model based on the ultrastructural features of the lens gave a good fit between theory and experiment. The curve fitting analysis revealed that the first dispersion appearing around 2 kHz is assigned to fiber cells in the peripheral cortex, where the fibers run parallel to the applied electric field, and the second dispersion around 2 MHz to central cortical fibers and nucleus. The third dispersion around 50 MHz could not be fully explained by the model analysis alone; it might be due to protein-bound water. Cataractogenic treatment such as microwave irradiation resulted in the disappearance of the first dispersion, suggesting that the membranous structures of fiber cells in the cortex were affected by microwave irradiation. The dielectric dispersion method is useful for non-destructive detection of cataractous lenses.

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AGONIST-INDUCED CHANGES IN CELL MEMBRANE CAPACITANCE AND CONDUCTANCE IN SINGLE ACINAR CELLS OF RAT PANCREATIC GLAND.

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Single acinar cells of rat pancreas were studied by the whole-cell recording in a chemically defined cytosolic environment. Changes in membrane capacitance (C) and conductance (G) were monitored by a lock-in amplifier, where C and G were reflected by the process of exo/endocytosis and activity of ion channels. C and G increased in response to Ach (0.1 μM) when pipette [Ca] was weakly chelated by 70 μM-EGTA. The respose was pro-longed with cytosolic GTPγS (50-100 μM), while inhibited with GDPβS (200 μM). The peak size of C varied between 200 and 1000 fF, suggesting 20-100 zymogen granules can fuse with the cell membrane in response to Ca-mobilizing receptor stimulation.

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CHANGES IN THE ABILITY OF REGULATORY VOLUME DECREASE DURING CELL DIFFERENTIATION OF MOUSE B LYMPHOCYTES. HAZAMA, A. AND OKADA, Y. Dept. Physiol., Kyoto Univ. Sch. Med., Kyoto 606

A variety of cell species, including T lymphocytes, can readjust their volume in a hypotonic medium after the initial osmotic swelling due to KCl effluxes. However, no regulatory volume decrease (RVD) has been found in mature human B lymphocytes (Grinstein, 1983). Supporting this observation, we found that a mature murine B cell line (No. 101) had little ability of the volume regulation under hypotonic conditions. In addition, mouse pre-B cell lines (DW 34, DW 8 and an Abelson leukemia virus-transformed pre-B cell line) were also found to exhibit no RVD within several tens of minutes. In contrast, prepre-B cell lines (SCID 7, Abelson virus-transformed prepre-B) could show rapid volume regulation upon hypotonic stress. The RVD was suppressed by elevating the extracellular K^+ concentration and facilitated by reducing the extracellular Cl^- ions. A K^+ channel blocker (quinine) and a Cl^- channel blocker (SITS) inhibited the RVD of prepre-B cells. When a cationic ionophore (gramicidine) was added, the RVD was observed in hypotonically swollen pre-B cells was observed. It is concluded that the RVD mechanism (presumably K^+ transporters) become impaired during the mouse B-cell lineage differentiation at the pre-B stage. (The authors are indebted to Drs. Shin-Ichi Nishikawa (Kumamoto Univ.) and Haruo Sugiyama (Osaka univ.) for gifts of B-lineage cell lines.)

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STUDY ON PRECURSOR T CELL PROLIFERATION INDUCING FACTOR. TOYOKAWA, T., TOHJI, Y., OSHITANI, N., KIN, T., HATO, F., KIMURA, S., KINOSHITA, Y. Dept. Physiol., Osaka City Univ. Med. Sch., 1-4-54, Asahi-machi, Abeno-ku, Osaka 545

Although many investigators reported that thymus humoral factors secreted from thymus epithelial cells might play critical roles in T cell differentiation and maturation process, the pricise mechanisms of intrathymic thymocyte proliferation remains unclear. The authors separated precursor T cells by combining rosette-formation method with one-step density gradient centrifugation method and succeeded to isolate biologically active polypeptide fraction (M.W. about 10,000) which could specifically induce proliferation of precursor T cells from culture supernatant of a rat thymus epithelial cell line, TAD3, by high-performance liquid chromatography equipped with a gel-filtration column. In the polypeptide fraction, neither interleukin 1 activity nor interleukin 2 activity could be detected. Therefore, humoral factors which are secreted from thymus epithelial cells might have close relation to early events of thymocyte proliferation in thymic subcapsular region, as well as to thymocyte differentiation and maturation pathway.

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THE BIOLOGICAL ACTIVITIES OF POLYPEPTIDE FRACTIONS FROM CULTURE SUPERNATANT OF RAT THYMUS EPITHELIAL CELL LINE (IT-45R1). MORIOKA, K., TOMINAGA, K., TANIYAMA, T., HATO, F., TOYOKAWA, T., KIMURA, S. and KINOSHITA, Y. Dept. Physiol. Osaka City Univ. Med. Sch., 1-4-54, Asahi-machi, Abeno-ku, Osaka 545

To study the effects of the thymic hormonal factors secreted by thymus epithelial cells on thymocytes, we separated four polypeptide fractions (I, II, III, and IV) from culture supernatant of a rat thymus epithelial cell line, IT-45R1, and examined their biological activities to three small thymocyte subsets which were separated by density grdient centrifugation and adhesion method. Each of the fractions enhanced Con A responsiveness in the lighter subset consisting mainly of immature thymocytes, and II and IV increased PHA responsiveness of the heavier subset into which relatively mature thymocytes were separated. The results suggested that II and IV have biological activities, but not only one, to the subsets at different stage of maturation. It was, thus, presumed that several active factors, whose target cells are different, are isolated into the fractions.

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FLUOROALUMINATES STIMULATE HISTAMINE SECRETION IN THE DIGITONIN-PERMEABILIZED RAT MAST CELLS. SORIMACHI, M., YAMAGAMI, K., NISHIMURA, S. AND YADA, T. Dept. Physiol., Kagoshima Univ. Med. Sch., Kagoshima, Kagoshima 890

GTP or its stable analogues stimulate histamine secretion from digitonin-permeabilized mast cells, only when the micromolar concentration of free Ca is provided. To see further the role of GTP binding protein, we investigated the effects of fluoroaluminates on histamine secretion in the presence of contaminating free Ca (1-2 uM). Combination of NaF and AlCl , but not the individual agent, stimulated secretion in digitonin-permeabilized, but not in intact, cells. The addition of 1mM EGTA completely inhibited this secretion without altering the amount of each species of fluoroaluminates formed. This secretion was inhibited by simultaneous addition of neomycin or p-Bromophenacyl bromide. Pertussis toxin treatment little affected the response to fluoroaluminates, though the treatment inhibited markedly the response to compound 48/80. The response to the maximal dose of GTP S(0.2mM) was further increased by the simultaneous addition of fluoroaluminates, but its magnitude was smaller than that expected from an additive effect of the individual agents. These results suggest that fluoroaluminates stimulate secretion through GTP binding protein-dependent and -independent mechanisms.

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MEMBRANE CURRENTS ACTIVATED BY COMPOUND 48/80 IN RAT PERITONEAL MAST CELLS. KUNO, M. Dept. of Physiol., Osaka City Univ. Med. Sch., Abeno-ku, Osaka 545.

Membrane currents induced by stimulation with a secretagogue, compound 48/80, were recorded from rat peritoneal mast cells, using patch clamp technique. In whole cell recordings, the addition of compound 48/80 induced currents with an increase in input conductance. The currents appeared within 10-60 sec after stimulation and lasted for 2-10 min with a gradual decay, and were suppressed by cadmium or EGTA. The current-voltage relation was fairly linear over -100$\sim$+50mV and the reversal potential ranged from +10 to +30mV, with pipettes containing isotonic K-glutamate or CsCl solutions. Lowering the external Ca^{++} to luM for 1-2 min before stimulation greatly suppressed the secretagogue-induced currents. In the cell-attached patches, an addition of compound 48/80 induced or enhanced Ba^{++} currents at the resting potential. These results suggest that compound 48/80 activates Ca^{++}-permeable channel in mast cells and that the channel might be involved in the Ca^{++} entry during the stimulus-secretion coupling.

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STIMULATION OF MORPHOLOGICAL CHANGES AND GROWTH OF MOUSE MAMMARY TUMOR CELLS BY 12-O-TETRADECANOYL-13-ACETATE (TPA). KAWAMURA,K.[1], ENAMI,J.[2], KOGA,M.[2], [1]Biomaterials Reserch Institute Co.,Ltd., Yokohama, Kanagawa 244, [2]Dept. Physiol., Dokkyo Univ. Sch. Med., Mibu, Tochigi 321-02.

Mouse mammary tumor cells obtained from spontaneous mammary tumors of the SHN mice were cultured in monolayers and in collagen gels. In monolayer culture, the cells changed morphology from flattened to compact after addition of TPA, the most potent tumor promotor. These morphological changes were associated with the disappearance of actin filaments. Following the morphological changes, TPA stimulated the growth of the tumor cells. Growth stimulation was also seen with EGF. However, morphological changes were not observed. In collagen gel embedded culture, mammary tumor cells showed fibroblastic morphology after addition of TPA. In contrast to the observations in monolayer culture, both stimulation and inhibition of growth were seen in different tumors in collagen gel embedded culture.

From these observations, it is concluded that TPA induced different morphological changes and growth patterns depending on the nature of the substrata.

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FUNCTIONAL ROLES OF ASTROCYTES ON NEURONAL DEVELOPMENT.

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Our previous studies demonstrated that subcultured astrocytes enhanced the neurite outgrowth and the survival of the cultured neurons from embryonic rat cerebral hemisphere, but suppressed the proliferation of the neuroblasts. The mechanisms of the action of strocytes were further investigated. It was revealed that the enhanced survival and the anti-mitotic effects were regulated by soluble factors produced by astrocytes. It was also suggested that the neurite promoting effect was mediated by the cell-cell contact. The neurite promoting effect was found to be specific to astrocytes among various types of cells examined. Membrane surface molecules of astrocytes associated with the neurite promoting effect were currently investigated by using monoclonal antibodies.

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EFFECTS OF DISRUPTION OF CYTOSKELTAL FILAMENTS ON PLASTICITY OF NEURAL CELL MEMBRANES.

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Cell membrane elasticity has been measured in erythrocytes by the method of Elastic Area Compressibility Modulus(EACM). A dissociated neuron is aspirated by a negative pressure into a siliconized capillary, the diameter of which is about a half that of the neuron. Cell surface area can be calculated from pictures of the aspirated neuron on a TV monitor screen. Dorsal root ganglion neurons from fetal and 3-month-old mice were dissociated and their values of the area compressibility modulus (K) were measured. The K value of adult mouse neurons was 21.3±10.3 dyn/cm which is about 1/10 that of erythrocytes. The K value of fetal mouse DRG neurons was 2.8±0.5 dyn/cm. The cell membrane elasticity decreases with aging. Since neuronal cell membrane functions closely relate to intracellular cytockeltal filaments, elasticity of the membrane may be affected by disruption of the filaments. When 10uM cytochalasin D was treated to adult cultured neurons , the elasticity scarecely changed. However, when 10uM colchicine was applied to the neurons, the K value decreased to 7.80 dyn/cm. This result suggests that intracellular microtubules in a neuron may mechanically bind to the cell membrane.

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INTRODUCTION OF MACROMOLECULES INTO PRIMALY CULTURED NEURONAL CELLS BY ERYTHROCYTE GHOST FUSION INJECTION.

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In order to study of the macromolecular functions in the cells, erythrocyte ghost fusion injection method is the easiest technique for introducing biologicaly active macromolecules into cultured living cells. But, the recipient cells used in this method have been limited in the tumor cells. The purpose of the present study was to introduce macromolecules into primaly cultured neuronal cells by this injection method.

FITC-BSA or FITC-IgG was trapped in human erythrocyte ghosts, and the ghosts were fused with primaly cultured mouse dorsal root ganglion cells by 45% polyethylene glycol(PEG1000) for 2 min. This fusion resulted in introduction of these molecules into the cells. The injection efficiency was about 30%, and the recipient cells extended neurites.

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ROLE OF CELL INTERACTION IN EMBRYONIC DEVELOPMENT OF XENOPUS STUDIED IN A CELL CULTURE SYSTEM. OKAMOTO, H. AND MITANI, S. Dept. Neurobiol., Institute of Brain Research, Faculty of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113

The role of cell interaction in embryonic development of Xenopus laevis was studied in an in vitro micro-culture system of early gastrula cells. The desired number of dissociated cells were distributed into micro-culture wells and cultures were started with or without centrifugation which facilitated reaggregation of cells. The differentiated cells in culture wells were identified with monoclonal antibodies to muscle, epidermal or neural cells. It was found that reproducible cellular differentiation of muscle and epidermis was dependent on the intimate reaggregation of dissociated cells and on the size of resultant aggregate. A minimum of about 20 cells of the lateral marginal zone and 100 cells of the ventral ectoderm of early gastrula were required, when put into a culture well, for the successful muscle and epidermal differentiation, respectively. When 150 cells of the ventral ectoderm were co-cultured with dorsal marginal zone cells, about 20 of the latter were enough for supporting the reproducible neural differentiation, which was also dependent on the intimate reaggregation of both types of cells. Finally, a possible contribution of readily diffusible substance(s) was suggested for the muscle, but not for the epidermal or neural differentiation in experiments where the volume of culture medium in a well was varied.

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IONIC ENVIRONMENTS AFFECTING INTERCELLULAR COUPLING BETWEEN EPITHELIAL CELLS IN FROG SKIN. KATAKURA,T. Department of Physiology, Kitasato University School of Medicine, Sagamihara, Kanagawa, 228

We have previously shown that the epithelial cells of abdominal skin of the frog, Rana japonica, are highly coupled only under short-circuited condition (s.c.c.) by dye transfer method. The elevation of cytosolic free calcium level, achieved by 1×10^{-6} M calcium-ionophore A23187 plus 10 mM calcium chloride in bathing solution, altered the cell-to-cell coupling in s.c. skin. Namely, each epithelial cells were uncoupled in high $(Ca^{2+})_i$ level even in s.c.c., consistent with the results from other tissues by many investigators. On the other hand, the increase in pH of bathing solution from normal pH7.5 to 8.0 in s.c.c. or the decrease in pH from 7.5 to 6.5 in open-circuited (o.c.) skin both failed to alter the manner of intercellular coupling. In order to measure accurate intracellular proton activity (pH_i) during extracellular pH (pH_o) variation indicated above under both s.c.c. and o.c.c., proton-sensitive, liquid membrane type theta-microelectrodes were prepared according to Meyer and others(1985). The resistance of ion-sensitive barrel ranged $60\text{-}150\times10^9$ ohm and slope constant ranged 54-57 mV per 10 fold change in proton activity. Preliminary measurements revealed that intracellular pH (pH_i) is about 0.3 unit lower than pH_o at pH_o=7.5 in o.c. skin and that pH_i is lower than pH_o(=7.5) by about 0.5 unit in s.c. skin.

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SPREADING AND SURVIVAL OF BSC-1 CELLS INDUCED BY COLLAGEN AND CALF SERUM. SHIBA, Y., SASAKI, Y., HIRONO, C., AND KANNO, Y. Dept. of Physiol., Hiroshima Univ. Sch. of Dent., Hiroshima 734

Effects of collagen and serum on cell spreading and survival were investigated in cultured BSC-1 cells to clarify the possible involvement of cell spreading and of serum factors in the maintenance of cell viability. BSC-1 cells (kidney cell line derived from the african green monkey) were cultured in Dulbecco's modified Eagle's medium supplemented with 10% calf serum and were harvested with 0.02% EDTA solution. More than 70% of the cells on the normal culture dishes did not spread and did not survive in the absence of calf serum after 24 hr culture. Addition of calf serum induced spreading and survival of the cells on the normal dishes, but not on the bacteriological dishes. Addition of type IV collagen, but not type I collagen, induced spreading and survival in the absence of calf serum. Fibronectin and epidermal growth factor induced spreading and survival on the normal dishes in the absence of calf serum. These results suggest that cell spreading is indispensable for the maintenance of viability induced by type IV collagen, and by epidermal growth factor and fibronectin in calf serum.

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INHIBITION OF INTERCELLULAR COMMUNICATION OF ACINAR CELLS FROM RAT SUBMANDIBULAR GLAND BY CHOLINERGIC AND ADRENERGIC AGONISTS. SASAKI, Y., SHIBA, Y. AND KANNO, Y. Dept. of Physiol., Hiroshima Univ. Sch. of Dent., Hiroshima 734

The effects of cholinergic and adrenergic agonists on intercellular communication of acinar cells were investigated. When Lucifer Yellow CH was microinjected into one of the acinar cells in an isolated acinus, the fluorescent dye was transferred to neighbouring cells within 2 min. Addition of acetylcholine (ACh) and carbachol (CCh) at concentrations higher than 10^{-6} M rapidly suppressed the transfer of injected dye. The inhibition of transfer of dye by 10^{-4} M ACh or 10^{-4} M CCh was blocked by the addition of 10^{-6} M atropine. The inhibitory effects of 10^{-4} M adrenaline and 10^{-4} M noradrenaline were weaker than those of 10^{-4} M ACh. The transfer of dye was not inhibited by 10^{-4} M isoproterenol. The inhibition of transfer of dye by 10^{-4} M adrenaline was blocked by the addition of 10^{-5} M phenoxybenzamine. These results indicate that the muscarinic action of cholinergic agonists and the α-action of adrenergic agonists rapidly inhibit the intercellular communication of the acinar cells from rat submandibular gland.

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STRETCH AND HYPOSMOTIC SOLUTION ACTIVATE SINGLE K OUTWARD CURRENT ON XENOPUS KIDNEY PROXIMAL BASOLATERAL MEMBRANE. KAWAHARA, K. Dept. Physiol., Faculty of Med. Univ. Tokyo, Tokyo 113

Single K channel of basolateral membrane of the kidney proximal tubule was studied in isolated single cells using the patch-clamp technique. The kidney of Xenopus was perfused with Ca/Mg free solution and then dissected in 0.05 % collagenase containing Ringer solution. The single cell seems to keep a polarity under optical microscope (x 400). At the cell-attached patch configuration K channel current flows into the cell from the pipette (100 mM KCl). The channel activity is voltage sensitive (Open probability(Po) increases at hyperpolarization). Thus, K outward current through the channel was rarely seen at a control condition. However, a small negative hydrauric pressure in the pipette (-15 cm·H_2O) increases Po. When the pressure was returned to zero, Po decreased to control level. A hyposmotic solution also activates this channel. In conclusion, the basolateral K channel can be activated by a slight degree of cell swelling.

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SEROTONIN STIMULATES MITOGENESIS IN RAT RENAL MESANGIAL CELLS. TAKUWA,N., TAKUWA,Y.*, STERZEL,R.B.* & RASMUSSEN,H.* Dept. Physiol. Faculty of Medicine, Univ. of Tokyo, Tokyo 113 and Yale Univ. School of Medicine, CT, USA.

A vasoactive inflammatory amine, serotonin, stimulates DNA synthesis in cultured rat glomerular mesangial cells in a dose-dependent manner, and acts synergistically with insulin and epidermal growth factor (EGF). Serotonin stimulates phosphoinositide turnover , resulting in a transient rise in intracellular Ca^{2+} concentration as measured by the photoprotein aequorin, and a transient increase in ^{45}Ca efflux from prelabeled cells. It also induces a prompt and sustained 3-fold increase in Ca^{2+}influx rate across the plasma membrane. Serotonin induces a rapid and sustained 2-fold increase in cellular 1,2-diacylglycerol (1,2-DG) content, and the phosphorylation of an acidic 80k-Da protein, a specific substrate for protein kinase C. Activators of protein kinase C (TPA and dioctanoylglycerol) mimic the mitogenic effect of serotonin. Insulin and EGF do not potentiate serotonin-induced increase in 1,2-DG, but do potentiate serotonin-induced phosphorylation of the 80k-Da protein. These results indicate that activation of protein kinase C plays a role in serotonin-induced mitogenesis in mesangial cells and that one of the effects of insulin and EGF is to enhance this action of serotonin.

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EFFECTS OF EXTRACELLULAR pH (HCO_3^-) ON PERITUBULAR MEMBRANE POTENTIAL, INTRACELLULAR pH AND SODIUM ACTIVITY IN THE PROXIMAL TUBULE OF BULLFROG KIDNEY. KUBOTA,T., SHOSAKU,T., HAGIWARA,N., INOUE, A., and FUJIMOTO, M. 2nd Dept. of Physiol., Osaka Medical College, Takatsuki, Osaka 569

To study the effects of extracellular pH (HCO_3^-) on peritubular membrane potential (E_M), intracellular pH (pH_i) and sodium activity (aNa_i) in the proximal tubule of perfused bullfrog kidney, we used double-barreled ion-selective microelectrodes. The results show that 1) decreasing peritubular pH from 7.6 to 6.6 by lowering HCO_3^- at constant PCO_2 (1.5%) for 1 min produced a depolarization of E_M by 25 mV and a decrease of pH_i by 0.3 without significant change of aNa_i. 2) lowering peritubular HCO_3^- from 15 to nominally 0 mM by changing PCO_2 at constant pH (7.6) for 1 min also caused a depolarization of E_M by 20 mV and a decrese of pH_i by 0.2 without any significant change of aNa_i. 3) addition of 0.5 mM SITS (4-acetamido-4'-isothiocyanostilbene-2,2'-disulfonate) to the peritubular perfusate for 1 hour inhibited pH- or HCO_3^--induced depolarization of E_M by 60-80 %. 4) administration of 4 mM Ba^{2+} inhibited partially a depolarization or hyperpolarization of E_M produced by increased peritubular K^+ or HCO_3^- at constant pH. The conclusions were obtained as follows: 1) HCO_3^- exit across the peritubular membrane could be explained by a simple diffusion process. 2) K^+ permeability in the peritubular membrane would be decreased by intracellular acidification.

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MECHANISM OF BRADYKININ-EVOKED CATECHOLAMINE SECRETION FROM THE PERFUSED RAT ADRENAL MEDULLA. WARASHINA,A., FUJIWARA, N., HIRANO, T. & SHIMOJI, K. Dept. of Physiol. and Anesthesiol. Niigata Univ Sch. of Med., Niigata 951

Catecholamine (CA) secretion in perfused rat adrenal medulla stimulated by bradykinin(BK) was continuously monitored using an electrochemical detector and quantitatively measured after separation of adrenaline from noradrenaline by HPLC. The BK-evoked secretion consisted of two distinct phases, a brief transient release lasting for the initial few minutes followed by a maintained release during continuous stimulation. Since bradykinin was reported in the literature to stimulate phosphatidylinositol4,5-bisphosphate breakdown in the plasma membranes of neuroblastoma and chromaffin cells, inositol trisphosphate (IP_3) that mobilizes intracellular Ca^{2+} may be a putative second messenger on BK stimulation. However, Ca^{2+}-antagonists, TMB-8 (100 uM) and dantrolene-Na (25 uM) failed to suppress the BK-evoked CA secretion. As one possibility, BK-stimulated inositol metabolism causes the activation of some pathway which introduces extracellular Ca^{2+} to evoke CA secretion. Although this pathway is inhibited by inorganic Ca^{2+}- channel blockers, Co^{2+} and Cd^{2+}, voltage-dependent Ca^{2+}-channels are not involved in this pathway because of its low sensitivity to D600.

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URINARY UROKINASE RECEPTOR MIGHT INFLUENCE THE MIGRATION OF TUMOR CELL. Takahashi, K. and Masumura, S. Dept. Physiol., Shimane Medical University, Izumo 693

Highly purified human urokinase was labeled with either ^{125}I or with FITC and used as a probe for the binding to a human metastatic carcinomatous cells, Detroit 562, at cellular and membrane protein level. Two-color cytofluorometric determinations demonstrated that the binding of the probe was specifically receptor-mediated and that the cell population was heterogeneous in the composition of cells with different expressional level of the receptors. Those could be separated into homogeneous ones by cell coloning or by the use of cell sorter; higher receptor-producing cells had a characteristic moving-tracks on a surface coated with gold particles and collagen, which had fibrinolytic activities as well. Followed by radioreceptor assays, the receptors having two different affinity populations were characterized as a surface glycoprotein. Those results and the data obtained by the analyses of proteins separable on SDS-polyacrylamide gels led us to suggest that the receptor-captured membrane urokinase might stimulate local proteolysis, facilitating the migration of the tumor cell.

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RELATIONSHIP BETWEEN KALLIKREIN RELEASE AND RECEPTOR BINDING OF MUSCARINIC CHOLINERGIC RECEPTOR IN RAT SUBMANDIBULAR GLAND. HIRAMATSU, Y., YOSHIMURA, K., KAMEDA, K. AND FUKUDA, H.#* Dept. Oral Physiol. and Dept. Oral Surg.#, Hokkaido Univ. Sch. Dent. Sapporo 060

Muscarinic cholinergic agonists such as carbamylcholine(CCh), methacholine(MCh) and acetylcholine(ACh) stimulated kallikrein release(KR) and the maximum amount of KR by these agonists was almost comparable to that by α-adrenergic agonists. But oxotremorine(Oxo) and pilocarpine-(Pilo) did not stimulate KR. [^{3}H]QNB binding studies showed that the CCh inhibition curve was less steep (Hill coefficient(n_H)=0.65), suggesting the presence of heterogenous binding sites. Presence of Gpp(NH)p shifted the CCh inhibition curve to the right, and increased the "steepness" of the curve (n_H=0.82). Computer analysis of displacement of CCh indicated that the curves were best fitted to the model of two affinity states of the receptor in the absence, but not in the presence, of Gpp(NH)p. Similar results were obtained by ACh and MCh. In contrast, the inhibition curves of Oxo and Pilo were steep (n_H is about one) in the absence and presence of Gpp(NH)p. These results suggest that only the muscarinic agonists which induce a low affinity state can stimulate KR.

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ACTIVATION OF PROTEIN KINASE C STIMULATES INSULIN RELEASE FROM RINm5F CELLS VIA INCREASE IN CYTOSOLIC Ca2+. YADA, T. and SHARP, G.W.G., Dept. Physiol., Kagoshima University School of Medicine, Kagoshima 890, Cornell University, Ithaca, New York 14853, USA.

In studying the mechanism by which protein kinase C (PKC) regulates insulin scretion, we examined the effect of PKC on cytosolic Ca2+ concentration ([Ca2+]i). We used the Ca2+ indicator fura2 in the rat B-cell line RINm5F, and measured [Ca2+]i in parallel with the rate of insulin release. The phorbol ester TPA, an activator of PKC, stimulated insulin release under static incubation conditions and caused an increase in [Ca2+]i. Ca2+ free conditions eliminated the increase in [Ca2+]i and inhibited the stimulation of insulin release. The Ca2+ channel blocker nitrendipine also inhibited both. The action of TPA was compared with that of depolarizing concentration of KCl (25mM), which stimulates secretion solely by opening Ca2+ channels. Compared to KCl, TPA induced greater release of insulin with a smaller rise of [Ca2+]i. From these results, it is concluded that (1) the activation of PKC by TPA opens Ca2+ channels in the RINm5F cell membrane and brings about a rise in [Ca2+]i, (2) this rise in [Ca2+]i results in insulin secretion and (3) PKC potentiates the stimulatory action of the increased [Ca2+]i on insulin secretion.

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ANALYSIS OF THE OUTWARD CURRENT IN XENOPUS OOCYTE MEMBRANE. Kurata,Y.*, Ohtahara,A.* and Ichikawa,O. Dept. Physiol., Tottori Univ. Sch. Med., Yonago 683

Time and voltage dependent outward current was studied in Xenopus oocyte membrane using the voltage-clamp technique. It was activated during depolarization from the resting potential(-65mV) to voltages more positive than -10mV. Time course of activation was fitted by a single-exponential curve with the time constant longer than 10sec. The mechanism of this current could be explained, at least phenomenologically, by the existence of the channel of Hodgkin-Huxley type with a single activation gate in the membrane. The reversal potential(r.p.;-15mV) for this current was close to the equilibrium potential of Cl^-, however, substitution of external Cl^- with propionate had no effect on the r.p.. Replacement of Na^+ with choline or increment of K^+ in the external solution produced a small shift in the r.p.. The rate of activation was much dependent on the temperature, the current was activated above 10 °C and grew at the higher temperature. Those observations suggest that the current is due to the non-specific cation channel.

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HETEROGENEOUS DISTRIBUTION OF CYTOPLASMIC FREE CALCIUM CONCENTRATION $[Ca^{2+}]_i$ IN VARIOUS CELLS REVEALED BY DIGITAL IMAGING MICROSCOPE EQUIPPED WITH A MICROSPECTROFLUOROMETER. TASHIRO, Y., TSUNODA, Y. AND YODOSAWA, S. Dept. Physiol., Kansai Medical University, Moriguchi, Osaka 570

Cytoplasmic free calcium concentration, $[Ca^{2+}]_i$ was estimated by digital imaging microscope which is composed of Olympus epifluorescence inverted microscope (IMT-2-RFL), high sensitive SIT camera (Ikegami, CTC-9000) a color image analyser (Olympus CIA-102) and a host computer (Hewlett Packard HP-310). This system is also equipped with a microspectrofluorometer (Olympus OSP-II). Following cells were analysed: Gastric parietal and chief cells, hepatocytes, blood platelets, mast cells, vascular endothelial cells outer and inner hair cells. In general, there are two kinds of $[Ca^{2+}]_i$ gradients; one is contrinuous gradient in the peripheral cytoplasm increasing towards the plasma membrane and another is discintinuous gradients (Ca^{2+} plateaus) in some restricted regions of the endoplasm. When stimulated by various agonist, $[Ca^{2+}]_i$ increased markedly and the heterogeneous Ca^{2+} gradients disappeared.

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Ca^{2+} SIGNAL TRANSDUCTION IN THE GASTRIC PARIETAL CELL. TSUNODA, Y., YODOZAWA, S. AND TASHIRO, Y. Dept. Physiol. Kansai Medical University, Moriguchi, Osaka 570

Gastrin-induced Ca^{2+} mobilization comprises two components; a rapid Ca^{2+} mobilization from the intracellular store(s) and a more prolonged and localized Ca^{2+} entry from the extracellular space. Among others, first internal Ca^{2+} mobilization is mediated by myo-inositol 1,4,5-trisphosphate (IP_3). Our digital imaging microscope visualized the IP_3-mediated Ca^{2+} mobilization and ATP-promoted Ca^{2+} (re-)uptake in the store(s) of the sapon-permeabilized parietal cells. When treated with IP_3, the high plateaus enlarged to the entire cytoplasm and new higher plateaus appeared and enlarged again, in a transient manner.

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DISTRIBUTION AND TEMPORAL CHANGE OF INTRACELLULAR Ca^{2+} CONCENTRATION IN A CULTURED HEPATOMA CELL LINE H-35. YODOZAWA, S., YOSHIMORI, T., TSUNODA, Y., and TASHIRO, Y. Dept. Physiol., Kansai Medical University, Moriguchi, Osaka 570

Addition of norepinephrine, epinephrine and ionomycin to cultured H-35 hepatoma cell caused a rapid increase in intracellular Ca^{2+} concentration. By digital imaging microscope single H-35 hepatoma cell loaded with fura-2, we visualized distribution and temporal change of intracellular Ca^{2+} concentration before and after addition of norepinephrine or ionomycin. Ca^{2+} transient by norepinephrine was blocked by pretreatment with an α blocker phentolamine.

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Ca MOBILIZATION BY CYCLIC AMP IN CULTURED INTESTINAL EPITHELIAL CELLS. Okada, Y. and Hazama, A. Dept. Physiol., Kyoto Univ. Fac. Med., Kyoto 606

A human epithelial cell line derived from neonatal small intestine (Intestine 407) is known to respond with hyperpolarizations not only to Ca-mediated intestinal secretagogues such as acetylcholine but also to cyclic AMP-mediated secretagogues such as VIP (Yada & Okada, 1984, J. Membr. Biol. 77, 33). Since these electrical responses were inhibited by a blocker of epithelial Ca-activated K conductances (quinine), cyclic AMP-mediated secretagogues may somehow induce Ca mobilization within the cells. Thus, the cytosolic free Ca^{2+} concentration was measured by a fluorescence-microscopical ratio-image technique with fura-2. Transient Ca^{2+} increases were actually observed in fura2-loaded cells in response to CCh and VIP. Dibutyryl cyclic AMP (dcAMP) was also effective in inducing similar Ca^{2+} increases. The Ca response to CCh was inhibited by deprivation of extracellular Ca^{2+} or by applying a Ca-channel blocker (nifedipine). In contrast, VIP- and dcAMP-induced responses were not affected by these maneuvers. When the cells were prior treated with drugs such as caffeine, adenine and procaine, which are known to affect the Ca transport in ER, the Ca responses to VIP and dcAMP (but not CCh) were abolished. It is concluded that cyclic AMP accumulation induced by stimulation of VIP-receptors brings about Ca mobilization (presumably from the ER) in Intestine 407 cells.

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ETHANOL ON THE MUCOSAL SIDE OF GASTRIC MUCOSA AFFECTS MUCOSAL PHYSIOLOGICAL PARAMETERS OF BULLFROGS. YAMAGUCHI, M. AND TAKEGUCHI, N. Fac. Pharmaceu. Sci., Toyama Med. & Pharmaceu. Univ., Toyama 930-01

Ethanol (ETOH) on the mucosal side of Ussing chamber affected parameters of gastric mucosa of bullfrogs. Both mucosal and submucosal solutions were exchanged every 20 min. ETOH higher than 10 % decreased the acid secretory rate, PD and the resistance of the mucosa. PD seems to be a good index for the mucosal damage. One hour incubation with 15% ETOH induced partially-irreversible damage. 20% ETOH induced irreversible damage. However, the 1-h incubation without solution exchange induced partial damage, indicating that the mucosa secreted protecting material(s) into the mucosal solution. We also determined efflux rates of glutathione (GSH) and GSSG (or GSH and GSSG-like compounds) into the solution. The ratios were increased by ETOH. As a candidate for the protecting material, the roles of GSH and GSSG are discussed.

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INHIBITION OF NA^+,K^+-ATPase ACTIVITY AND ENDOGENOUS SUBSTRATE MOBILIZATION ABOLISHES CYTOCHROME REDUCTION AND OXYGEN CONSUMPTION INDUCED BY HIGH POTASSIUM. SAITO, T. AND KANNO, T.,Dept. Physiol., Fac.Vet.Med., Hokkaido Univ., Sapporo 060

Under ether anesthesia, rat brains were perfused with oxygenated HEPES-buffered Ringer solution containing 5% dextran 70 and heparin,decapitated and then removed. The pyriform cortex slices by horizontal cut (about 0.5 mm in thickness) were perifused with oxygenated HEPES-buffered Ringer solution at a constant flow rate of 3ml/min at about 20°C. Perfusion with high potassium (60mM K^+) solution caused reduction of cytochromes, a transient increase in ATP/ADP ratio, and an increase in oxygen consumption. These responses were abolished with ouabain(0.1mM)treatment.The reduction response was also inhibited by iodoacetate (3mM), a glycolytic inhibitor, aminooxyacetate(1mM),an inhibitor of amino transferase and bromooctanoate (3mM), an inhibitor of β-thiolase in β-oxidation of fatty acids, but remained in the presence of 2-deoxy-D-glucose (10mM). These results show that high potassium may cause the activation of active transport systems including Na^+, K^+-ATPase to consume oxygen and the mobilization of endogenous substrates, which induce reduction of cytochromes under the condition of the limited oxygen supply.

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METABOLIC SUBSTRATE REQUIRED FOR SECRETORY RESPONSES INDUCED BY CCK-8 IN THE RAT PANCREAS.
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Influences of glucose removal and/or various metabolic inhibitors on the CCK-8 induced secretory responses(pancreatic protein output and juice flow)were examined in the isolated perfused rat pancreas. The responses induced by continuous stimulation with 100pM CCK-8 were remained unchanged when glucose was removed from the perfusing solution. The responses were inhibited when 10μM rotenone, an inhibitor of the mitochondrial respiratory chain, was added to the perfusing solution but remained unchanged when 0.1mM iodoacetate, a glycolysis inhibitor, 5mM 2-deoxy-D-glucose, a hexokinase inhibitor or 1mM aminooxyacetate, an aminotransferase inhibitor was added to the perfusing solution. The secretory responses were dose-dependently inhibited by addition of bromooctanoate(0.12mM, 0.6mM and 3mM), an inhibitor of β-thiolase in β-oxydation. The inhibitory effect of bromooctanoate was not influenced by addition of 5 mM glucose or 1 mM aminooxyacetate. These results are compatible with the view that the substrate for energy metabolism maintaining CCK-8-induced secretory responses may be endogenous fatty acids.

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PURIFICATION OF PHYSIOLOGICAL ACTIVE B-CELLS FROM PANCREATIC ISLETS.
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It has been well established that the mammalian pancreatic islet is composed of heterogeneous cell populations. Within islet there are several regulatory factors for insulin secretion. These are hormone combinations and cell-cell communications. Thus, an attractive hypothesis has developed that the secretory function of insulin is modulated by the structure of the islet. To clarify this hypothesis, the isolation of B-cells from other cell populations is very relevant. We show the simple method to purify B-cells in this study.

Pancreas were aseptically removed from new-born rats, and islets were obtained by collagenase digestion. The dispersed tissue were then pelleted and cultured in a complete medium, containing RPMI 1640 supplemented with 10% fetal calf serum. After 48hr, the medium was collected and the cells were precipitated for 10min at 1000rpm. Each fractions were isolated by the Percoll discontinuous gradient centrifugation (20,25,30,35, and 40% of each 1ml) for 30min at 3000rpm. Purified B-cell was collected at Fr. 2 between 20% to 25%. The cells of Fr. 2 were responsible for the treatment of 25mM glucose, and insulin was secreted biphasically. Purification hold was more than thousand times, and purity was 80-85% according the data of immunohistochemical study.

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ANALYSIS OF PROTEIN PHOSPHORYLATION IN PURIFIED PANCREATIC B-CELLS ASSOCIATED WITH INSULIN SECRETION
TOKUDA, M., ITANO, T., MATSUI, H., YAMAMOTO, Y., ETOH, S., NAKAMURA, M., MINAMOTO, Y. & HATASE, O. Dept. of Physiol, Kagawa Med. Sch., Kagawa, 761-07

Three proteins phosphorylation was induced by glucose stimulation in B-cell fraction. Enhanced phosphorylation of the peptides (Mr. 10,000 - 20,000 dalton) was observed throughout the reaction time. The phosphorylation of a peptide (Mr. 26,000) coincided with the 2nd peak of insulin secretion in B-cells, and that of a peptide(Mr. 55,000) with both the 1st and the 2nd peak. However once B-cells were purified by the Percoll discontinuous gradient centrifugation, the total phosphorylation was remarkably diminished. The reconstitution experiments using each Percoll-separated fractions were performed to solve this problem. The addition of the 5th layer to B-cells(2nd layer) showed remarkable stimulation of phosphorylation, but the addition of 3rd and 4th layer to (2nd+5th) layer inhibited the phosphorylation. These data suggested the importance of the cell-cell interaction in B-cell response, especially with 5th layer cells.

K252b, a potent inhibitor of protein kinase C, inhibited the phosphorylation of a peptide(Mr. 35,000). W-7, a calmodulin inhibitor, as well as gliclazide, one of the sulfonylureas, diminished the phosphorylation of the high molecular weight peptides of the purified B-cells.

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EFFECT OF CHOLINERGIC STIMULATION ON CYTOSOLIC Ca^{2+} CONCENTRATION IN THE RAT LACRIMAL GLAND ACINI. TAKAHASHI, H., SAITO, Y., OZAWA, T., OKADA, M., NISHIYAMA, A., Dept. of Physiol., Tohoku Univ. Sch. of Med., Sendai 980.

The effects of carbamylcholine (CCh) on cytosolic Ca^{2+} concentration ($[Ca]_i$) in suspensions of quin2-loaded dispersed acini have been studied by means of fluorescence spectroscopy. Resting $[Ca]_i$ was 155±10nM. Addition of 0.1mM CCh caused an increase in $[Ca]_i$ which consisted of an early transient phase (1274±161nM) and a late steady phase (790±80nM). In a low Ca (0.3uM) solution, the sustained increase in $[Ca]_i$ disappeared. Subsequent admission of Ca increased $[Ca]_i$. Addition of TMB-8 (50uM) reduced markedly the early increase in $[Ca]_i$ in Ca-free suspensions, but did not affect the recovery of the late increase by admission of Ca. Nifedipine (10uM) had a similar action to that of TMB-8. La (1mM) reduced significantly the late increase in $[Ca]_i$ but did not affect the early one. In Na-free NMDG suspensions, the increase in $[Ca]_i$ induced by CCh stimulation was reduced, however recovered fully by subsequent addition of Na (100mM). The results indicate that CCh stimulation increases $[Ca]_i$ initially by releasing Ca from the intracellular Ca store and secondarily by increasing Ca influx from the ECF and that extracellular Na is required for activating the agonist-induced Ca influx.

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SINGLE CALCIUM-ACTIVATED POTASSIUM CHANNELS RECORDED FROM CULTURED MAMMARY GLAND CELLS. FURUYA, K., ENOMOTO, K.[1], YAMAGISHI, S., EDWARDS, C.,[*2] OKA, T.[*2] Nat. Inst. Physiol. Sci., Okazaki, 444, (1)Shimane Med. Univ., Izumo, 693, (2)NIH, Bethesda, MD20892, USA.

The properties of Ca-activated K^+ channels in mouse mammary epithelial cells in primary culture were studied by the patch-clamp technique. In cell-attached patches using a physiological solution in the pipette, spontaneous channel openings were sometimes observed and its slope conductance was about 12pS at the negative membrane potential. External application of A23187, a calcium ionophore, activated this channel. In excised inside-out patches, the channel was activated by increasing the internal Ca^{2+} concentration (10^{-7} to 10^{-6}M). No voltage dependence of the channel activity was observed. The channel was highly selective for K^+ and the internal Na^+ blocked the outward K^+ current by the voltage dependent manner. That caused the non-linear I-V relationship of this channel at the positive membrane potential. The channel was blocked by internal Ba^{2+} (0.1 mM) and TEA (20 - 50 mM). Ba^{2+} reduced the open provability but not the single channel conductance. In the case of TEA, that was reversed. The single channel conductance of this channel, measured as inward currents by using a high-K solution in the pipette, was large (40 - 80 pS), and showed an inward rectification. These results suggest that this channel is different type from usual small conductance Ca-activated K channels observed in other cells.

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Ca-ACTIVATED K CHANNEL IN RAT PAROTID GLAND. SHIGETOMI, T., TOKUNO, H. AND TOMITA, T. Dept. Oral Surg. and Dept. Physiol., Sch. Med., Nagoya Univ., Nagoya 466

In inside-out patches, the most commonly observed ionic channel in the rat parotid membrane was the K channel which was activated by Ca at a concentration of more than 0.4 μM. Full activation occurred at about 2.5 μM. In the presence of a Ca concentration, the channel was also activated by depolarization of the membrane. In the cell-attached patch-clamp, the open probability of this channel was very low, but it was greatly increased by carbachol or adrenaline, probably due to an increase in intracellular Ca concentrations, as previously reported for other glands. In the whole-cell clamp mode, clamped at -40 mV, both carbachol (10 μM) and adrenaline (10 μM) produced a transient outward current of about 10 pA, lasting for about 1 min, and markedly increased the membrane conductance. Since the conductance increase was not essentially modified by reducing the external concentration of either Na or Cl ions, it was concluded that carbachol and adrenaline open mainly Ca-activated K channels, probably due to an increase in intracellular Ca concentration by releasing Ca from the store.

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PATCH-CLAMP STUDIES OF K^+-CHANNELS IN GUINEA-PIG PANCREATIC ACINAR CELLS.

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K^+-channels in plasma membrane of isolated guinea-pig pancreatic acini were studied by patch-clamp techniques. Three types of K^+-permeable pores were found in excised patch experiments: Ca^{2+}-activated non-selective cation channel with a unit conductance of about 25 pS that could be inhibited by ATP (adenosine 5'-triphosphate) acting on the membrane inside and two kinds of Ca^{2+}-and voltage-activated K^+-selective channels with unit conductances of about 200 pS and 30 pS, respectively. The small conductance K^+-channel was inhibited by 10 mM TEA (tetraethylammonium) acting on membrane outside. In intact cells pentagastrin activated a current through the 30 pS K^+-selective channel. In these experiments pentagastrin was added to the bath solution and had no contact with the electrical isolated membrane patch from which the current were recorded, suggesting that the activation is mediated via an intracellular messenger. Pentagastrin-stimulation of the K^+-current was also observed in whole-cell recording. Present results suggested that in the stimulated condition the membrane of guinea-pig pancreatic acinar cell were dominated by the 30 pS K^+-channel.

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IMMUNOCHEMICAL STUDY AND ANALYSIS OF mRNAs OF Na^+,K^+-ATPase ISOZYME

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Previously, we have reported the presence of a new immunoreactive Na^+,K^+-ATPase α subunit isoform (tentatively designated S90) in rat submandibular gland (SMG); it is not a protein artificially formed from α present in SMG microsomes. When microsomes from the kidney, brain and SMG were incubated with [γ-^{32}P]ATP and subjected to electrophoresis, S90 as well as α and α(+) was radio-labelled, suggesting that S90 is one of catalytic subunits of Na^+,K^+-ATPase.

Using the specific probe (TACTTCCCGCGGGGACTT), and northern hybridization technique, the mRNAs of α subunit of Na^+,K^+-ATPase was examined. The mRNA bands from SMG and kidney had a same electrophoretic mobility with a molecular weight of 5,600 kilobase, whereas the band from brain had a slightly larger molecular weight, 6,000 kilobase. Since SMG apparently gave only a single band, it is still unclear whether the SMG indeed contains two different mRNAs corresponding to two α subunits or the gland only contains a single species of mRNA. If the latter is the case, α subunit synthesized in the SMG might be processed to yield S90.

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CALCIUM UPTAKE AND ECTO-ADENOSINE TRIPHOSPHATASE ACTIVITY OF A431 CELLS

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When cells of A431 (human epidermoidal carcinoma) were incubated with ATP, the radioactive calcium was incorporated into the cell. These cells also had stong activity to hydrolyze extracellular ATP (ecto-ATPase activity). When ecto-ATPase activity on these cells was inhibited by adenosine diphosphate, adenylylimidodiphosphate or sodium pyrophosphate, the ATP-dependent calcium uptake was decreased.

ATP-dependent calcium uptake was also decreased when the cells were preincubated in medium which does not contain magnesium ion (ecto-ATPase activity was not inhibited under such a preincubating condition). The decreased ATP-dependent calcium incorporation recovered its activity when the cells were further preincubated with the medium containing magnesium, calcium, cobalt or cupric ions. It is suggested therefore that ecto-ATPase activity and magnesium ion associated with the cell membrane are essential for ATP-dependent calcium uptake by A431 cells.

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THE DIFFERENCE OF THE PROPERTIES OF PHOSPHOFRUCTOKINASE BETWEEN ADULT AND IMMATURE RAT SUBMANDIBULAR GLANDS. HAMANO, E., YAMAZAKI, T. and FURUYAMA, S. Dept. Physiol., Nihon Univ. Sch. Dent. at Matsudo, 2-870-1, Sakaecho-nishi, Matsudo, Chiba 271

Phosphofructokinase (PFK) was purified from adult and immature (2 weeks old age) rat submandibular glands, and the enzymological properties and the subunits composition were studied. Although ATP played a dual role as a substrate and an inhibitor on adult PFK, immature PFK was less sensitive to ATP inhibition. Saturation curve for fructose 6-phosphate (F-6-P) was sigmoidal on adult PFK. In immature, however, PFK was less sigmoidal. Fructose 2,6-bisphosphate ($F\text{-}2,6\text{-}P_2$) relieved ATP inhibition on PFK in adult, but this effect of $F\text{-}2,6\text{-}P_2$ did not observe clearly in immature. On SDS-PAGE, the purified PFKs were composed of three different subunits, which corresponded to M-, L- and C-type subunits. The difference of subunits composition on SDS-PAGE was shown in adult and immature PFKs. These results implied that the difference of regulatory properties between adult and immature PFKs might be caused by the difference of the subunits composition.

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SUBSTANTIATION OF THE CONCEPT OF HOMEOSTASIS BY CARNOSINE. NAGAI, K., SUDA, T., KAWASAKI, K.*, YAMGUCHI, Y. Department of Pathophysiology, Dental Research Center, School of Dentistry, Nihon University

Homeostasis introduced by Cannon has been studied with regard to equilibration of terminal physiologic parameters such as respiration and blood pressure, but not as a barrier achieved by immune and reparative functions of the body to maintain the internal environment of the essential physiological functions of life, particularly concerning its control output. We examined the modulatory effects of carnosine (CAR) and β-alanine (ALA) on antibody production in the DDY-SRBC-PFC system. CAR and ALA reduced elevated immune responses in immature mice but increased physiologically weakened immune responses in aged mice (30-week-old or above). They also non-specifically enhanced immune responses suppressed by the administration of anti-cancer agents such as MMC, 5FU, and CPD, transplantation of sarcoma-180, and γ-irradiation. These findings suggest that CAR and ALA are physiologically active agents that act on homeostasis and stimulate spontaneous healing ability by promoting reparative activities, modulating immune functions, and enhancing non-specific immune responses.

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ELECTROMAGNETIC INTERACTIONS WITH HEPATIC TRANSMEMBRANE ION TRANSPORT. KOBAYASHI,S.,OMOTE,Y.,AND NAKAJIMA,S. Tateisi Inst. Life Sci.,Kyoto 616 & Dept.Surg.,Asahikawa Med.Col.,Asahikawa 078-11

Electromagnetic interactions with transmembrane ion transport were studied using perfused, ethanol-added rat livers exposed to low-frequency, pulsed magnetic field (PMF). Livers from male Wistar fed rats were perfused via portal vein with $95\%O_2\text{-}5\%CO_2$ saturated with KHBB ($2.5mMCa^{2+}$ or $0.025mMCa^{2+}$) maintained at 37°C. PMF(N) generated from a solenoid (165φ,100T) was applied. The frequency was 200Hz and the intensity was 0.0055T. The effluent was analyzed for Ca^{2+},Mg^{2+},K^+, and Cl^-.

[RESULTS] (1) Effects of EtOH addition : with $2.5mMCa^{2+}$-perfusate, Ca^{2+} influx increased and effluxes of other ions decreased, and with $0.025mMCa^{2+}$-perfusate, Ca^{2+} efflux and Mg^{2+} influx decreased.
(2) PMF showed reversed effects upon EtOH-added livers in relation to transmembrane ion fluxes.

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EFFECTS OF POLYETHYLENE GLYCOL (PEG) ON THE REVERSIBLE AGGREGATION-DISAGGREGATION PHENOMENON OF LECITHIN LIPOSOMES

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Multilamellar liposomes of lecithin aggregate below the pretransition temperature (Tp) and make a lot of colonies. Increasing temperature of liposomes from below Tp at a lecithin concentration of 5㎎/㎖, the colonies suddenly disaggregate at Tp. Decreasing temperature, the liposomes begin to aggregate at Tp.

We observed the reversible aggregation-disaggregation phenomenon on the lecithin liposomes-PEG-water system by a light microscope. Results are following;

1. The phenomenon were observed at Tp in low concentration of PEG.
2. Increasing PEG concentration, the phenomenon were observed at the main transition temperature (Tc).
3. Still more PEG concentration, the phenomenon were not observed at even above Tc.

We also investigated a relationship PEG concentration and molecular weight of PEG on the phenomenon.

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URSODEOXYCHOLATE (UDC) PREVENTS HEPATOCELLULAR DAMAGE CAUSED BY OTHER BILE SALTS.

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Previous studies in our laboratory have shown that taurine- or glycine-conjugate of UDC, when administered simultaneously, prevents the cholestasis induced by infusion of more toxic bile salts such as taurocholate (TC) and taurochenodeoxycholate (TCDC). In order to examine whether UDC in an unconjugated form also posesses this cytoprotective effect on bile salt induced liver damage, TC (1.2 μmol/min/100 g) or TCDC (0.4 μmol/min per 100 g) was continuously infused for 2 hr with and without a simultaneous UDC infusion (0.6 μmol/min/100 g). TC or TCDC, when administered alone, caused a decrease in bile flow accompanied by drastic increase in biliary leakage of various proteins (lactate dehydrogenase, alkaline phosphatase, 5'-nucleotidase and albumin) which was dramatically prevented by the simultaneous infusion of UDC. It was concluded that UDC is as effective as its conjugates in preventing bile salt induced liver damages.

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DIELECTRIC PROPERTIES OF RAT RED BLOOD CELLS OXIDIZED WITH OXIDANTS

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Vitamin E prevents the cell membrane from oxidation and maintains the membrane stability. To examine the mechanism of oxidation and the membrane damage induced oxidant, frequency dependence (5 -- 110 MHz) of relative permittivity (dielectric const.) and conductivity of vitamin E sufficient and deficient red cell suspension were measured .As oxidant of red cells, the hypoxantine-xantine oxidase reaction (HX-XOD) and 2,2'-azobis (2-aminopropane)hydrochrolide (AAPH) were used. When red cells were oxidized with the HX-XOD complex plane plots of experimental data were circular arcs of Cole-Cole type in both suspensions of vitamin E sufficient and deficient red cells. On the other hand,Cole-Cole plots of red cells oxidized with AAPH were different with arcs. In the case of HX-XOD, by the impedance analysis using Pauly-Schwan theory the time course of product of size parameter of a red cell and membrane capacitance was the same process as that of $\Delta\varepsilon$.

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EFFECTS OF INTRACELLULAR MONOVALENT IONS ON Na^+, K^+, Cl^- COTRANSPORT OF HeLa CELLS. IKEHARA, T., YAMAGUCHI, H., HOSOKAWA, K., MIYAMOTO, H., Dept. Physiol., Sch. Med., Univ. Tokushima, Kuramoto-cho, Tokushima 770

Effects of the contents of Na^+ and K^+ ($[Na^+]c$, $[K^+]c$) on the affinities of the cations for the diuretic-sensitive cotransport pathway were studied, using Rb^+ as an analog for K^+. The cells were preincubated for various periods in media containing 10 μM ouabain to change the Na^+ and K^+ contents, keeping the sums of the two cation contents constant. Ouabain-insensitive, furosemide-sensitive Rb^+ influx (J_{Rb}) was increased on increase in $[K^+]c$ and decrease in $[Na^+]c$. J_{Rb} was examined as functions of the extracellular Rb^+ concentration ($[Rb^+]e$) for three groups of the cells with higher $[Na^+]c$ and lower $[K^+]c$ than control. Double-reciprocal plots of the data showed three straight regression lines, which converged at around a point situated closely above the abscissa. Similar plots were again made including the normal cells, indicating that the normal cells have lower value of the apparent Km for Rb^+ (K_{Rb}) than those for the high-Na^+, low-K^+ cells. Relation between J_{Rb} and $[Na^+]e$ were observed. Double-reciprocal plot showed similar aspect but the normal cells showed higher value for K_{Na}.

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INVOLVEMENT OF CYTOSKELETONS IN PROLIFERATION OF ADULT RAT HEPATOCYTES IN PRIMARY CULTURE. II. HASEGAWA, K., WATANABE, K. AND KOGA, M., Dept. Physiol., Dokkyo Univ. Sch. Med., Mibu, Tochigi 321-02

Colchicine (an inhibitor of microtubule polymerization) inhibited DNA synthesis in adult rat hepatocytes in primary culture. Since lumicolchicine did not affect DNA synthesis, inhibition of DNA synthesis by colchicine is thought to be caused by depolymerization of microtubules. To confirm these results, microscopical observation of microtubules were done by using FITC-labeled anti-tubulin. Polymerized microtubules were observed at cell periphery as soon as 1 or 2 h after plating. Thereafter, elongated microtubules were seen all over the cells. When colchicine was added to the medium, concentration-dependent depolymerization of microtubules was observed. Colchicine at 10^{-7} M inhibited DNA synthesis by 50% and it depolymerized microtubules in about 50% of hepatocytes. At 10^{-6} M, DNA synthesis was inhibited by over 90% and almost all hepatocytes showed depolymerized microtubule figures. Taxol (a stabilizer of microtubules, 10^{-6} M) also inhibited DNA synthesis by 83%. At this concentration of Taxol, thick microtubules were observed. These results confirmed the previous suggestion that polymerization , but not stabilization, of microtubules is necessary for the induction of DNA synthesis in primary cultures of adult rat hepatocytes.

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PURIFICATION OF ACTIN FROM MITOCHONDRIA AND ITS IMMUNOCYTOCHEMICAL LOCALIZATION BY ELECTRONE MICROSCOPY. ETOH, S., MATSUI, H., ITANO, T., TOKUDA, M., NAKAMURA, M., HOSOKAWA, J. & HATASE, O. Dept. of Physiology, Kagawa Med. Sch., Kagawa, 761-07

Mitochondria (Mt) contain Mt-genes and own protein synthesis system and can divide. They drastically change their configuration depending on their energy and respiratory state. Although the molecular mechanism of mitochondrial division and configrational change have not been well clarified, the presence of cytoskeletal system in MT is suggested. In this report, we prepared highly purified mitochondria by differential percoll gradient method. (Hatase et al., Biochem. Biophys. Res. Commun., 132, 63-66)

We purified actin-like protein(s) from the matrix fraction of percoll purified mitochondria by DNase I affinity column. The apparent molecular weight of this protein was 42K dalton and it was recognized by antiserum immunized against rabbit skeletal actin. Since the affinity purified fraction contained other proteins than actin, it was suggested that mitochondria matrix contained not only actin but also actin binding proteins. The immunohistochemical study by an electrone microscope confirmed that actin was actually present in mitochondrial matrix, and that was not the contamination from the outside of mitochondria.

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JUNCTIONAL PERMEABILITY IN MATURE AND IMMATURE RAT SALIVARY GLANDS.
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Tight junctions in salivary glands maintain the separation between luminal spaces and intercellular and interstitial spaces and thus have a barrier function. The aim of this study was to examine the permeability of the tight junctions to moderate- or large-sized tracers from blood to saliva in the three major salivary glands of mature and immature rats. Male Wistar rats (mature, 8 weeks old; immature, 2-5 days old) were used. Moderate-sized (horseradish peroxidase or HRP, MW=40,000) and large-sized (lactoperoxidase or LP, MW=93,000) were injected separately and intravenously under pentobarbital anesthesia. The glands were dissected out 5 minutes later and processed for TEM; and the tracers were detected cytochemically by the DAB method. In the immature rat, the tight junctions of sublingual and submandibular glands were permeable to HRP, but impermeable to LP; whereas those in parotid glands were permeable to both tracers. In contrast, in the mature rat the tight junctions of all 3 glands were impermeable to both molecules. These results suggest that the tight junctions in the 3 major salivary glands of mature rats serve as a barrier to both moderate- and large-sized proteins, whereas the junctions of sublingual and submandibular glands of immature rats have no barrier function with respect to moderate-sized molecules.

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Calmodulin-binding proteins in rat salivary glands. YOKOYAMA, N. AND FURUYAMA, S., Dept. Physiol., Nihon Univ. Sch. Dent. at Matsudo, Matsudo, Chiba 271.

Calmodulin(CaM) is an ubiqitous protein in various tissues and is an intracellular Ca^{2+} receptor which mediate various Ca^{2+}-dependent cellular processes. The diversity of physiological function of CaM depends on the properties of CaM-binding proteins. Calcineurin(CaN), CaM-dependent phosphatase, is the major CaM-binding protein in brain. Recently we purified CaM-dependent phosphatase from bovine parotid gland.

In rat, CaM-binding proteins were found in the cytosol fractions of both submandibular and parotid glands utilizing a gel overlay procedure of CaM. To identify the nature of CaM-binding proteins in salivary glands, immunobloting analysis was done with antibody against bovine brain CaN. Immunobloting data showed one of CaM-binding proteins in rat submandibular and parotid glands was CaM-dependent phosphatase. Immunohistochemical studies using antibodies against bovine brain CaN revealed that CaM-dependent phosphatase was localized in both acinar and duct cells in rat salivary glands.

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INVOLVEMENT OF GTP-BINDING PROTEIN IN SIGNAL TRANSDUCTION OF SPERM-EGG INTERACTION AT FERTILIZATION OF HAMSTER EGGS. MIYAZAKI, S., IGUSA, Y., AND SWANN, K*. Dept. Physiol. Jichi Med. Sch., Tochigi-ken, 329-04.

The mechanism involved in the signal transduction of sperm-egg interaction causing periodic increase of intracellular Ca ions in golden hamster eggs was examined by microinjection methods. Ca transients were monitored by the hyperpolarizing response and/or aequorin luminescence. Injection of GTPγS into unfertilized eggs produced periodic Ca rises similar to those seen in fertilized eggs. The occurrence of both GTPγS- and sperm-induced Ca rises was blocked by injection of GDPβS, suggesting the invelvement of GTP-binding protein in the signal transduction. The supposed G-protein was insensitive to pertussis toxin and cholera toxin. Iontophoretic injection of F^- ions causes 2-3 Ca transients. In Ca-free external medium, injection of GTPγS or F^- produced only one response, and the sperm-induced Ca rises disappeared. Iontophoretic injection of inositol 1,4,5trisphosphate (IP_3) induced a Ca release in an all-or-none manner, followed by the refractory period lasting for 90-120 sec. When IP_3 was continuously injected possibly by leakage from the pipette, it produced periodic Ca rises. It is proposed that the periodic Ca rises occur when intracellular Ca stores are reloaded by Ca influx due to increased Ca permeability and the stores are stimulated by the continuous existence of IP_3 causing Ca release.

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INVESTIGATION OF G-PROTEIN THAT IS NOT SENSITIVE TO BACTERIAL TOXIN

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The identification of the G-protein as coupled to phospholipase C (PLase C) is one of the important problems to elucidate signal transduction processes as mediated by the calcium mobilizing receptors. It has been reported that the relevant G-protein in the different cell types can be classified into two groups: one is pertussis toxin sensitive and the other is insensitive. For identifying the G-protein as involved in the latter case, our first strategy was to purify G-protein that was not sensitive to bacterial toxin. We obtained the fraction of GTPγS binding activity from rat liver membrane extract that was free of both pertussis and cholera toxin substrate. However in the course of this investigation, we found the endogenous inhibitor activity of the ADP-ribosylation of G-protein as catalyzed by pertussis toxin. In the presence of such endogenous inhibitor it is concieved that some toxin-sensitive G-proteins might be coupled to PLase C without being modified by pertussis toxin treatment. To examine this possibility, the purification and characterization of the inhibitor is now in progress.

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HISTOLOGICAL ANALYSIS OF SPLEEN IN EXPERIMENTAL HEMOLYTIC ANEMIA (2).

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It is known that phenylhydrazine hydrochloride produces serious hemolytic anemia (J.Clin,. Invest.,43,1329.1964). At the same time leukocytosis occurs, but its pathological significance is unknown yet. Serum free Fe combines with transferrin, and in macrophages and leukocytes of spleen ionic states of Fe consists of Fe^{2+} and Fe^{3+}. The concentrations of Fe in serum and in granulocytes are measured by the bathophenanthroline direct modified method. The concentration of Fe^{2+}, Fe^{3+} and total Fe in serum were as follows: Fe^{2+} 45 (control 23), Fe^{3+} 306 (control 73), total Fe 351 μg/dl (control 97 μg/dl) respectively. Fe^{3+} was 87% of total Fe. On the other hand, the concentrations of Fe in granulocytes were as follows: Fe^{2+} 0.4 (control 0.2), Fe^{3+} 6.0 (control 5.0), total Fe 6.4 $\mu g/10^{11}$Cells (control 5.4 $\mu g/10^{11}$ Cells). The Fe^{3+} was 96% of total Fe. These results indicate that in granulocytes, Fe^{2+} is oxidated Fe^{3+} by ferroxidase rapidly.

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The protective effect of coenzyme Q_{10} on generation of field potentials from the guinea pig cortical slice incubated under a cycle of normoxia-hypoxia.

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Ubiquinone (Coenzyme Q_{10}, Co Q_{10}) is one of coenzymes of respiratory chain in mitochondria of mammalian cells. It functions to produce ATP in oxidative phosphorylation system. When exogenous Co Q_{10} is added in incubation medium of nervous tissues, it is not clarified whether or not Co Q_{10} is absorbed into the cells and then utilized in their mitochondria. The present experiment was conducted in order to ascertain whether exogenous Co Q_{10} is effective or not for the levels of tissue ATP and for the amplitudes of field potentials evoked by electrical stimulation of lateral olfacory tract in guinea pig olfactory cortical slice. The results were as follows. 1) Exogenous Co Q_{10} was effective for the recovery of field potentials in amplitude when the brain slices were incubated with oxygen gas after the replacement of nitrogen gas. 2) The recovery level of tissue ATP was significantly high when the slices were again incubated with oxygen gas after nitrogen gas flow under the condition of the solution containing Co Q_{10}. 3) Post-tetanic potentiation after tetanic stimulation (100Hz, 20sec) was prominent in amplitude when the slices were incubated with the solution containing Co Q_{10}.

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ELECTROGENIC SODIUM PUMP ACTIVITY EVOKED BY SUSTAINED STIMULATION WITH ACETYLCHOLINE IN MOUSE PAROTID ACINAR CELLS. *HAYASHI, H., NISHIYAMA, A. AND TAKAHASHI, H., *Coll. of Med. Sci., Tohoku Univ., Dept. of Physiol., Tohoku Univ. Sch.of Med., Sendai 980.

With a microelectrode technique, mechanism of ACh-induced electrogenic Na pump activation was investigated in the cells of the superfused segment. In control or Cl-free Br solutions resting potentials were about -60mV and ACh (5×10^{-8}M) stimulation for 2-5 min evoked sustained hyperpolarizations of about 20mV. In conditions inhibiting Na-K ATPase by addition of ouabain or by removal of external K, ACh evoked only transient hyperpolarizations. In conditions inhibiting Na-K-Cl cotransport such as in Na-free NMDG, Cl-free NO_3 or gluconate solutions or in the presence of furosemide (1.2×10^{-3}M) in normal or Cl-free Br solutions, ACh evoked sustained hyperpolarizations which were little affected by addition of ouabain or by removal of K. Followings were suggested. (1) The ACh-evoked potential change consists of hyperpolarizations caused by activations of a K-conductive pathway and an electrogenic Na-K pump in the basolateral membrane and a depolarization by an activation of a Cl-conductive pathway in the luminal membrane. (2) ACh causes an increase in both Na and Cl influxes mainly via an activation of the Na-K-Cl cotransport, and the increased cellular Na activates the electrogenic Na Pump and the Cl elevates a driving force for the Cl exit across the luminal membrane.

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Na^+-H^+ AND Cl^--HCO_3^- ANTIPORTERS IN THE MOUSE PANCREATIC ACINAR CELLS. OZAWA, T., SAITO, Y., OKADA, M. AND NISHIYAMA, A. Dept. of Physiol. Tohoku Univ. Sch. of Med., Sendai 980.

Using double-barreled Na^+ and H^+ selective microelectrodes, intracellular Na^+ (aNa_i) and H^+ (pH_i) activities of the mouse pancreatic acinar cells have been measured. In HCO_3^--free solution the membrane potential (V_m) and aNa_i in the resting state was -36 ± 2mV and 9 ± 1mM, respectively. Cholecystokinin (CCK-8 0.1nM) depolarized V_m by about 10mV. While aNa_i was increased only slightly by CCK-8, simultaneous presence of ouabain (1mM) enhanced CCK-8-induced increase in aNa_i (+6mM) and this increase was markedly inhibited by amiloride (0.3mM). Acid loading with NH_4^+ (10mM) prepulse method increased aNa_i by a few mM and the presence of amiloride significantly inhibited the increase. pH_i in the resting state was 6.9-7.0 and addition of CCK-8 increased pH_i by about 0.2 unit. CCK-8-induced increase in pH_i was abolished by amiloride. In HCO_3^-/CO_2 buffered solution, replacement of all Cl^- in the superfusate with gluconate$^-$ increased pH_i by about 0.2 unit. The presence of DIDS (0.2mM) inhibited the pH_i increase. These results suggest that Na^+-H^+ and Cl^--HCO_3^- antiporters exist in the basolateral membrane and the Na^+-H^+ antiport is activated in the stimulated conditions.

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HCO_3^- SECRETION BY GUINEA PIG ANTRAL MUCOSA IN VITRO. SUZUKI, A. AND SUZUKI, Y. Dept. Physiol. and Surg., Yamagata Univ. Sch. Med., Yamagata 990-23

HCO_3^- secretion and bidirectional fluxes of $^{36}Cl^-$ and $^{22}Na^+$ by guinea pig antral mucosa was studied by Ussing chambar. HCO_3^- secretion was measured by a pH stat method. Basal HCO_3^- secretion was about $0.5\,\mu$Eq/h・cm and was inhibited by anoxia. Bethanechol significantly increased HCO_3^- secretion. Removal of serosal HCO_3^- markedly reduced the basal and the bethanechol-induced HCO_3^- secretion. Methazolamide significantly reduced the bethanechol-induced HCO_3^- secretion. Removal of Cl^- from the bathing solution did not affect the basal and the bethanechol-induced HCO_3^- secretion. On the other hand, both the removal of Na^+ from the bathing solution and the application of ouabain to the serosal side abolished the bethanechol-induced increase in HCO_3^- secretion. The antral mucosa secreted Cl^- while net flux of Na^+ was almost zero at the basal state. Bethanechol increased both short-circuit current and the secretory fluxes of Na^+ and Cl^-. These finding indicated that 1) guinea pig antral mucosa secretes HCO_3^- by active transport, 2) most of HCO_3^- secretion at the basal condition as well as stimulated state may originate in serosal HCO_3^- and also be partly dependent on carbonic anhydrase, 3) Cl^- is secreted spontaneously, 4) muscarnic receptors may be involved in the regulation of HCO_3^-, Cl^- and Na^+ secretion.

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BICARBONATE SECRETION IN GUINEA PIG CECUM.
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Bicarbonate secretion in the guinea cecum was studied in vitro in Ussing chamber under short-circuit conditions. The serosal side was bathed with bicarbonate-CO_2-containing solution and the alkalinization rate of the mucosal unbuffered solution (J(OH)) was measured by a pH-stat method. J(OH) under the control condition was 2-2.5 and the addition of ouabain to the serosal side reduced the rate to 1-1.5 (in $\mu mol/cm^2 \cdot h$). The ouabain-sensitive component of J(OH) was dependent on mucosal Na and Cl while it was independent on serosal Na and Cl. The mucosal addition of Cl channel blocker, diphenylamine-2-carboxylic acid (10^{-3} M), reduced the ouabain-sensitive J(OH), and decreased the short-circuit current and the transepithelial conductance. The serosal addition of 4-acetamido-4'-isothiocyanostilbene-2,2'-disulfonic acid ($5x10^{-4}$ M) decreased the ouabain-sensitive J(OH). These results suggest that bicarbonate is taken up across the basolateral membrane through the Cl/HCO_3 exchange and exits across the mucosal membrane through the anion channel. The mucosal Na and Cl are essential for the bicarbonate secretion but the mechanisms of their actions remain to be explored.

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MECHANISM OF ELECTROGENIC TRANSPORT OF BASIC AMINO ACID (L-LYSINE) ACROSS RENAL PROXIMAL TUBULE.
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The effect of Na^+ and pH in the perfusion fluids on the lysine-induced membrane deporarization were studied in Triturus proximal tubule. The depolarization induced by introduction of L-lysine into the lumen was independent of both Na^+ concentration and pH of the luminal solution, excluding the possibilities of coupling with Na^+ or H^+. In the absence of Na^+, coexistence of 20mM L-alanine completely suppressed generation of the lysine-depolarization, indicating the importance of ε-NH_3^+ in electrogenic transport. Membrane potential-dependence of the depolarization did not differ in feature in the presence and absence of Na^+. These findings suggest that lysine entry across the luminal membrane is carrier mediated electro-diffusion. In the absence of Na^+, repeated introduction of lysine caused gradual decrease of amplitude of depolarization with growing rebound hyperpolarization. Addition of Na^+ to the peritubular fluid caused restoration of the depolarizing response and disappearance of the hyperpolarization. These findings suggest that the exit of lysine across the basolateral membrane is Na^+-dependent and its mechanism is non-electrogenic.

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ACTION OF SUBSTANCE P ON ION TRANSPORT OF GUINEA PIG DISTAL COLON.
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Substance P-like immunoreactivity is found in enteric neurons in guinea pig colon; however, the role of substance P in the regulation of colonic ion transport is unknoun. The present study examined the mechanisms of action of substance P on the ion transport of guinea pig colonic mucosa. Segments of muscle-stripped distal colon that contained submucosal ganglia were set up in Ussing flux chambers. Short-circuit current, a measure of net ion transport, was recorded continously. Serosal addition of substance P increased in short-circuit current in a dose-depedent manner over the concentration range of 5 nM to 10 uM. The action of substance P was transient and returned to baseline levels within 20 minutes. At 10 uM doses of substance P, the increase in short-circuit current averaged 337.2±28 uA/cm from a baseline of -38±7 uA/cm. Neural blockade with 0.1 uM tetrodotoxin or antagonism of muscarinic receptors with 10 uM atropine siginficantly decreased the substance P-evoked increase in short-circuit current in 8 tissues to 6.6 ± 1.5 % and 67.7±9.1% of control values, respectively. Pyrilamine also decreased the maximum response to 51.1± 16.3% of control value. The results suggest that substance P mediates changes in colonic ion transport by acting cholinergic and non-cholinergic neurons, as well as releasing histamine from intestinal mast cells.

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ISOLATION OF ACTIVE TRANSPORT PROCESS AT ORGAN LEVEL IN THE PERFUSED SALIVARY GLAND. Murakami,M., Suzuki,E., Watari,H., *Miyamoto,S. and *Imai,Y., Natl. Inst. Physiol. Sci., Okazaki 444. and *Osaka Medical College, Takatsuki 569.

The intracellular K (K_{in}) of the isolated perfused mandibular gland was measured with NMR spectroscopy during activation with acetylcholine and inactivation of Na^+/K^+ ATPase by ouabain. K_{in} decreased by 30 % of the resting value during secretion with 1 uM ACh. By overloading of 1 mM ouabain, the intracellular K decreased by additional 40 % of the resting level (30% of the resting level). Removal of both drugs restored the intracellular K level within 20 min. Applying 135 mmol/l ICF as the resting K_{in}, K_{in} was calculated as 95 mmol/l ICF during secretion and 40 mmol/l ICF during inactivation of Na^+/K^+ ATPase, which balanced with K loss to the effluent and saliva. K uptake during withrawal of ouabain and ACh was compared with the time course of oxygen consumption; ca.70 umol/g of K uptake required ca.80 umol/g of ATP during redistribution of intracellular electrolytes.

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DISSOCIATION BETWEEN EXOCRINE SECRETION AND ENERGY SUPPLY IN RAT PANCREAS DURING STIMULATION WITH HIGH DOSES OF SECRETAGOGUES. MATSUMOTO, T.[1], KANNO, T.[1], SEO, Y.[2], MURAKAMI, M.[2] & WATARI, H.[2] 1:Dept. Physiol., Fac. Vet. Med., Hokkaido Univ., Sapporo 060. 2:Dept. Molecular Physiol., Natl. Inst. Physiol. Sci.(Seiriken), Okazaki 444.

Effects of high doses of secretagogues (CCK-8 and ACh) on kinetics of phosphorus energy metabolites during exocrine secretion were studied in isolated perfused rat pancreas by ^{31}P-NMR method at 25°C. Although continuous stimulation with low doses of secretagogues (10 and 100 pM CCK-8, 0.1 μM ACh) caused a sustained increase in pancreatic exocrine secretion, it did not induce any change in the tissue level of ATP. Continuous stimulation with high doses of secretagogues (1 nM CCK-8, 0.3 and 3.0 μM ACh) caused tachyphylactic secretory responses and decreased the tissue level of ATP, whereas it kept the tissue level of creatine phosphate (PCr) almost unchanged or inceased. These findings suggest that stimulation with high doses of secretagogues inhibits creatine phosphokinase (CPK) system near ATP-consuming sites or disturbs PCr transport between a CPK system near ATP-consuming sites and another CPK system near mitochondria in pancreatic acinar cells.

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INSULIN INCREASES [^{3}H]-OUABAIN-BINDING IN FROG SKELETAL MUSCLE.
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To elucidate the mechanism of stimulation of Na/K transport by insulin, the density of [^{3}H]-ouabain-binding sites was examined. Satorius muscles of bull frog (Rana catesbeiana) were used for these experiments throughout. Muslces were loaded with [^{3}H]-ouabain by incubating in a variety of test solutions containing [^{3}H]-ouabain for one hour at room temperature. From competition experiment with cold ouabain, the amount of [^{3}H]-ouabain specifically bound to the binding sites on plasma membrane was estimated to be 80 - 90% of the total [^{3}H]-ouabain in muscle. The concentration of cold ouabain required to suppress the specific [^{3}H]-ouabain-binding to one half was 1.2×10^{-6}M. The [^{3}H]-ouabain in muscle increased 1.7 times when the muscle was incubate with insulin for one hour. Monensin (10^{-5}M) completely blocked the stimulating effect of insulin on [^{3}H]-ouabain-binding. The rate of dissociation of specifically bound [^{3}H]-ouabain was 0.54±0.006/h in control intact muscle and was 0.033±0.003/h in insulin-exposed muscle.

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REGULATION OF Na,K-ATPase IN FROG SKELETAL MUSCLE BY INSULIN.
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Insulin is known to stimulate Na/K-transport activity in muscle cells. Na,K-ATPase activity of plasma membrane fractions was increased by exposing muscles to insulin before preparing membrane fractions: the activity of control was 9.1 ± 0.5 and that of insulin-treated muscles was 16.5 ± 0.4 μmol Pi/hr/mg protein. However, an addition of insulin to plasma membrane fractions was uneffectable. Cytosols were prepared from muscles treated with or without insulin and fractionated by ion-exchange chromatography. In the case of control muscles, a fraction not bound to S-Sepharose Fast Flow, a strong cationic exchanger, had Na,K-dependent ATPase activity of 2.4 ± 0.7, but in the case of insulin-treated muscles, the fraction not bound to S-Sepharose Fast Flow showed only 0.82 ± 0.2 μmol Pi/hr/mg protein. The activities of 5'-nucleotidase and UDP-galactosyltransferase, a marker enzyme of plasma membrane and Golgi membrane,respectively, were not detected in all fractions of cytosols prepared from control and insulin-treated muscles. These results suggest that units or subunits of Na,K-ATPase were stored in cytosols and insulin enhances the translocation of those proteins from cytosols to the plasma membrane.

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Ca MOBILIZATION BY CYCLIC AMP WITHIN RAT PARIETAL CELLS IN PRIMARY CULTURE.
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Intracellular recordings in cultured rat parietal cells showed that the cells respond with quinine- and TEA-sensitive hyperpolarizations to Ca-mediated acid secretagogues (CCh and gastrin) and to cyclic AMP-mediated secretagogues (histamine plus IMX). Since histamine-induced hyperpolarizing responses were inhibited by deprivation of extracellular Ca^{2+} ions, there is a possibility that increases in the cytosolic Ca^{2+} concentration are involved in the K^+ conductance activation upon stimulation with not only Ca-mediated but also cyclic AMP-mediated secretagogues. Thus, the cytosolic free Ca^{2+} concentration was measured by a fluorescence-microscopical ratio-image technique with fura-2 under the stimulation with these secretagogues. Increases in the cytosolic Ca^{2+} level were actually detected in fura-2-loaded parietal cells in response to CCh or gastrin, but not histamine. When the cells were prior treated with IMX, however, histamine was found to increase the free Ca^{2+} ions within the cells. Stimulation with dibutyryl cyclic AMP was also effective in increasing cytosolic Ca^{2+} ions. It is concluded that intracellular cyclic AMP accumulation induced by histamine receptor stimulation does somehow induce Ca mobilization into the cytosol in the cultured rat parietal cells.

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WHOLE-CELL POTASSIUM CURRENTS AND HISTAMINE-INDUCED RESPONSES IN CULTURED INTESTINAL EPITHELIAL CELLS.
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Cultured human epithelial cells derived from the neonatal small intestine (Intestine 407) are known to exhibit hyperpolarizing responses to a vareity of intestinal secretagogues including histamine (Yada & Okada, 1984, J. Membra. Biol. 77, 33). To identify responsible ionic currents, whole-cell recordings were carried out with patch electrodes. The resting cells have outward-rectifying currents (activated over +20 mV under control electrolyte conditions) and inward-rectifying currents (activated below -80 mV). Both currents were inhibited by extracellular Cs^+ and Ba^{2+}. The slope conductance of inward-rectifying currents was dependent on the 0.5 power of the extracellular K^+ concentration. Both types of currents were not affected by stimulation of the cells with histamine. Upon the stimulation with histamine, however, another type of voltage-dependent currents was activated. The I-V curve was bell-shaped and had a peak value at about +40 mV. When the extracellular K^+ concentration was altered, the reversal potential became shifted according to changes in the E_K values. When cytosolic Ca^{2+} ions were chelated with 10 mM EGTA, the histamine-induced current activation was abolished. It is concluded that the cultured intestinal epithelial cells have three types of K^+ channels; 1) outward-rectifying K^+ channels, 2) inward-rectifying K^+ channels, and 3) Ca^{2+}-activated K^+ channels.

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POTASSIUM CHANNEL CURRENTS IN PARIETAL CELLS ISOLATED FROM THE GUINEA PIG GASTRIC FUNDUS. Kotera, T., Hashimoto, A., Ueda, S. and Okada, Y.* *Dept. Physiol. and Dept. Intern. Med., Kyoto Univ. Fac. Med., Kyoto 606

Whole-cell recordings were performed in parietal cells isolated from guinea pig gastric fundus by proteolytic digestion. In addition to so-called leakage currents, the cells exhibited activation of two types of voltage-gated currents upon applying command pulses. Outward-rectifying currents were activated at positive potentials, while inward-rectifying currents were below -90 mV under control ionic conditions. Both currents were not affected by extracellular Na^+ and Cl^- concentrations. When the extracellular K^+ concentration was changed, the I-V curves of both currents became shifted according to changes in the equilibrium potential to K^+. The slope conductance of inward-rectifying currents were dependent on the 0.5 power of the extracellular K^+ concentration. The outwardly rectifying currents were suppressed by extracellular Cs^+, Ba^{2+} and TEA^+, whereas inwardly rectifying currents were by Cs^+ and Ba^{2+} but not TEA^+. Ca^{2+}-activated K^+ currents were not observed even during exposure to ionomycin. Ionomycin increased voltage-independent leak currents but rather suppressed inward- and outward-rectifying currents. By single-channel recordings in excised patch membranes, cation channels (the conductance of about 25 pS) permeable to both K^+ and Na^+ were frequently observed. It is concluded that guinea pig parietal cells have both outward- and inward-rectifying K^+ channels as well as non-selective cation channels.

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APPLICATION OF THE VOLUME FLOW EQUATION TO SALIVARY SECRETION OF A PERFUSED RAT MANDIBULAR GLAND

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In this report we have tried to expand the volume transport equation of Kedem & Katchalsky and to use it to analyze driving forces of water transport. The experiments were carried out on rat mandibular glands perfused with HEPES-Ringer solution. A main duct was intubated and a vertical tube of 60 cm length was connected to one end and a pressure transducer was connected to another end. During acetylcholine stimulation, secreted saliva climbed up in the vertical tube and the level of it could be monitored by pressure. At resting condition, the pre-filled fluid in the vertical tube was gradually absorbed into a gland, so the decay of pressure could be observed. The results about the relation between volume flow and pressure revealed that our equation was very useful in analyzing the water transport mechanism of a salivary gland.

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SHORT CIRCUIT CURRENT OF FROG SKIN IN THE NON-STEADY STATE

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Short circuit currents (SCC) in the non-steady conditions were studied in ouabain treated frog skins by changing the ionic contents of bathing solutions. Ussing's chambers were used to measure SCC and transepithelial conductance. The whole skin pre-incubated with 10^{-3}M ouabain (60 minutes), showed an outward transient SCC when the normal Ringer solutions in both chambers were replaced with high K Ringer solutions containing ouabain. An inward transient SCC reappeared when K Ringer solutions were replaced with normal Ringer solutions. In a split skin, transient SCC changed more rapidly than those of a whole skin. The rate constants of the inward currents, and the integration of the inward currents were larger than those of outward currents. Ionic composition study of a split skin showed that passive movement of Na and K owing to asymmetrical permeability of composed membrane caused the transient SCC without active Na transport.

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IMPEDANCE MEASUREMENT IN PERFUSED SUBMANDIBULAR GLAND OF RABBITS

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Impedances of perfused submandibular gland were measured by YHP 4192a Impedance analyzer and 4193a Vector Impedance meter. Measured frequency was ranged from 10 Hz to 110 MHz. The measured impedances were corrected the residual inductance and expressed as conductivity and relative permittivity. The rabbit submandibular gland was perfused by Krebs-Henseleit solution and acetylcholine (10^{-6}M) was used for stimulation. The conductivities of low frequencies incresed during stimulation, and the dispersion of relative permittivity shifted to low frequencies. The conductivity increase suggests the decrease in cellular volume because the coductivity of the cell membrane was negligible. For continuous measurement of the changes of conductivity at low frequencies and relative permittivity, the impedances at 10 KHz and 200 KHz were measured at intervals of 10 sec. The conductivity at 10 KHz increased rapidly with the start of stimulation and recovered slowly after the stop of stimulation. The relative permittivity at 200 KHz decreased during stimulation and recovered rapidly after the stop of stimulation.

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SODIUM-INDEPENDENT SECRETION OF H ION IN THE PROXIMAL TUBULE OF BULLFROG KIDNEY.

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In secretion of H^+ in the proximal tubule, both Na^+-dependent and Na^+-independent processes have been postulated to occur via some antiport of H^+/Na^+ or H^+/K^+ across the luminal membrane. To investigate actual behavior of H^+ and Na^+, we used H^+ or Na^+ selective double-barrelled microelectrodes in combination with in vitro acridine orange fluorescence microscopic technique, and demonstrated that H^+ distribution and Na+ activity within the cell were dissociated. These were affected more or less by endogenous humoral agents, such as cyclic AMP and insulin, and exogenous transport inhibitors, such as ouabain. Luminal perfusion of amiloride (10^{-3}M) or lowered Na+ (0.5 mM) blocked the luminal acidification. In the absence of Na^+, the H^+-blocking effect of amiloride was lowered, supporting the concept of Na^+/H^+ exchange. Dibutyryl-cyclic AMP (10^{-4}M) induced a remarkable accumulation of H^+ in the vesicle with cytosol alkalosis and a blockade of H^+ secretion into the lumen. Peritubular insulin (200 mIU/L) or ouabain (10^{-5}M) caused a transient acidification of luminal fluid and sustained fall of pH in cytosol with a dissipation of vesicle H^+ accumulation. These transient changes in luminal pH would be mediated by exocytosis or some intracellular metabolic changes in primarily Na^+-independent mechanism.

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THE ELECTROPHYSIOLOGICAL STUDY ON THE EFFECT OF INSULIN IN THE PROXIMAL TUBULE CELL.

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Since our immunological binding assay detected insulin receptors in the bullfrog kidney, we started the present study to examine the effect of this hormone on the ion transport in the proximal tubule. Double-barrelled H^+ or Na^+ selective microelectrodes were employed for direct cellular impalements in doubly perfused proximal tubule. We also measured subcellular H^+ distribution with a fluorescence microscopic method using the in vitro acridine orange technique. Peritubular application of insulin (200mIU) or ouabain (10^{-4}M) caused a transient luminal acidification. This effect was not blocked by luminal application of low Na^+ (0.5 mM) perfusate or that containing amiloride (10^{-3}M). Ouabain in 10^{-5} M caused a cytosol acidification and the cell Na^+ was increased, and after ouabain administration insulin caused a transient fall of cell pH but increased Na^+ continuously. Insulin dissipated vesicle H^+ accumulation. After ouabain application insulin dissipated it diffusely toward cytosol. Thus, insulin stimulate H^+ transport from the vesicle to cytosol. The luminal acidification induced by insulin would be mediated by some Na^+-independent mechanism and it could be secondary phenomenon of a stimulation of Na^+/H^+ exchange or Na^+-K^+ pump in the cell membrane.

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IMMUNOELECTRON MICROSCOPIC LOCALIZATION OF (Na^+, K^+)ATPase α-SUBUNIT IN THE TYMPANIC WALL OF THE RAT COCHLEAR DUCT. IWANO, T., YAMAMOTO, A., OMORI, K., KUMAZAWA, T. AND TASHIRO, Y. Dept. Physiol. and Otolaryngology, Kansai Medical University, Moriguchi, Osaka 570

Tympanic wall of rat cochlear duct was fixed by perfusion with 4% paraformaldehyde and embedded in LR-gold. The ultrathin sections were incubated with affinity purified antibody against α-subunit of rat kidney (Na^+, K^+)ATPase, subsequently with protein A gold complex. In the organ of Corti, the plasma membranes of inner and outer hair cell were hardly labeled with gold particles, whereas many gold particles were found on the basolateral plasma membranes of the border cell and inner phalangeal cell which surround the inner hair cells. In the spiral limbus, numerous gold particles were found on the basolateral membrane of the interdental cells.

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EFFECTS OF HCO_3^-/CO_2 BUFFER ON WATER ABSORPTION ACROSS THE SEAWATER EEL INTESTINE. ANDO, M. Lab. of Physiol., Fac. of Integrated Arts & Sci., Hiroshima Univ., Hiroshima 730

Although Na^+-K^+-Cl^- transport system has been reported in various cells and tissues, effects of HCO_3^- on such cotransport system is not well studied. To elucidate a role of HCO_3^- in the Na^+-K^+-Cl^- and water transport, effects of HCO_3^- on the transepithelial potential difference (PD) and the net water flux were examined in the seawater eel intestine. When HCO_3^-/CO_2 buffer was replaced with other buffer system such as phosphate, Tris, HEPES or TES, both the PD and the net water flux decreased gradually, as well as a reduction in NaCl absorption, indicating that Na^+-K^+-Cl^- transport depends on HCO_3^-/CO_2 buffer system. However, when only HCO_3^- was removed from the bathing media while 5% CO_2 continued to be bubbled, the serosa-negative PD increased, whereas the net water flux decreased. In contrast, removal of CO_2 alone diminished the PD without remarakable influence on the net water flux. These results indicate that HCO_3^- contributes to the water absorption and CO_2 to the serosa-negative PD.

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ANION EXCHANGE MECHANISMS AND INTRACELLULAR pH IN ISOLATED CHICK ENTEROCYTES. KINOSHITA, Y. and IRIMAJIRI, A.
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By monitoring pHi changes with the acridine orange dye, we examined anion exchange mechanisms mediating anion substitution-induced changes in intracellular pH (pHi) of isolated, metabolically-intact chick enterocytes in nominally HCO_3-free media. DIDS-inhibitable pHi increases caused by replacement of medium Cl with SO_4 were also observed with replacement by SCN or NO_3, an anion more permeant than Cl. Methazolamide treatment of cells to minimize HCO_3 ions available did not suppress the pHi increase. The pHi increase was independent of medium Na. Thus, the anion substitution-associated pHi shift is likely to be mediated by electroneutral Cl/OH exchange, although the possible exchange mode of Cl/HCO_3 cannot be excluded. The contribution of electrical coupling through conductive pathways should be minimum. When the Na concentration was reduced in Cl-medium, a pHi decrease was observed which could not totally be attributed to the Na/H antiport activity detected as an amiloride-sensitive component. This suggests the possible occurrence of a Na-dependent anion exchange activity, which may underlie a DIDS-induced pHi decrease in Cl-medium, a pHi change unexplainable by the Cl/OH exchanger's function of extruding base (OH) in exchange for Cl.

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Cl SECRETION AND METABOLIC STUDIES IN THE COLONIC MUCOSA. SUZUKI, Y., *MURAKAMI, Y., *SEO, Y. AND *WATARI, H. Dept. Physiol. Yamagata Univ. Sch. Med., Yamagata 990-23 and *Dept. of Molecular. Physiol., Natl. Inst. Physiol. Sci., Okazaki 444.

Phosphorus nuclear magnetic resonance (^{31}P NMR) was used to study energy metabolism in the isolated and muscle-stripped colonic mucosa from guinea pig. The tissue was superfused with phosphate free buffered solution and set in the NMR tube. Six peaks were identified from low field as: sugar phosphate and nucleotide monophosphate; inorganic phosphate; creatine phosphate; γ peak of nucleotide triphosphate and β peak of nucleotide diphosphate; α peak of nucleotide di- and triphosphate; NAD and NADH; β peak of nucleotide triphosphate. When the Cl secretory activity by the mucosa was stimulated by simultaneous addition of bethanechol and prostaglandin E_1, the oxygen consumption rate determined polarograhically was found to increase by 30%. On the other hand, the similar stimulation failed to alter the ^{31}P NMR spectra noticeably. The results suggest that the tissue content of phosphorus compounds remains essentially unchanged when the tissue metabolic rate is enhanced during stimulation of Cl secretion in the colonic mucosa.

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ION CHANNELS IN THE PLASMA MEMBRANE OF SUBMANDIBULAR GLAND EPITHELIAL CELLS IN CULTURE. Y. SAITO, A. NISHIYAMA, *M. KAN, *M. OBINATA, Departments of Physiology, Sch. of Med., and *Cell Physiology, Res. Institute for Tuberculosis and Cancer, Tohoku University, Sendai 980, Japan.

In order to elucidate the ion transport mechanisms across the plasma membranes of submandibular gland epithelial cells, patch clamp experiments have been made on cells in culture. Submandibular glands from mice were excised and digested by collagenase treatment. The isolated cells were incubated in dishes under serum-free, low-Ca^{2+} culture medium (WAJ 404 with supplements). Epithelial-like cells grew as a colony over many weeks. Some cells contained numerous vacuoles. The apical membranes of cultured cells were excised as inside/out patches and analyzed for the ion channels. The frequency distribution of single channel conductance suggested that at lease several different kinds of channels existed in the patches. Among these channels, characterized by the ion-selectivity were (i) Ca^{2+}- dependent Na^+/K^+ channel of the conductance of 20-30pS, (ii) Ca^{2+}- dependent Cl^- channel, 20-30pS and (iii) Cl^- channel, $>$ 200pS, which was activated mostly when pipette potential was $< \pm$40mV. However, maxi-K^+ channel, though, whose presence in the cells isolated from this tissue has been reported, has not been found among 100 patches studied.

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RELATIONSHIP OF SECRETION AND ECF VOLUME IN DOG SUBMANDIBULAR GLAND
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Salivary secretion consists of two phases, the initial phase which has a rapid secretory rate , and the steady phase which has a lower secretory rate. In the present study, we show that two phases of secretion can be separated by stimulation during circulatory arrest and by stimulation after arterial reopening. The salivary secretion rate decreased with decrease in extracelluler fluid volume. We have also measured the decreasing hydrostatic pressure and the increasing Cl concentration in the interstitium during secretion. It is suggested that the change of osmolality and hydrostatic pressure in ECF affects the rate of salivary secretion.

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THE MECHANISM OF CCK-8 EVOKED FLUID SECRETION IN THE ISOLATED PERFUSED HYPERTROPHIED RAT PANCREAS. ISHIKAWA, T. and KANNO, T., Dept. Physiol. Fac. Vet. Med., Hokkaido Univ., kita-ku Sapporo 060

Possible contribution of various ion transport systems in CCK-8 evoked fluid secretion was studied in the perfused rat pancreas isolated from rat after inducing hypertrophy of the pancreas. Hypertrophy of rat pancreas was produced by oral administration of a synthetic protease inhibitor (FOY-305) once a day for 3 weeks. Perfusion with CCK-8 evoked a maximum level of fluid secretion at concentration of 100 pM in the hypertrophied pancreas. Lowering extracellular Na^+ or Cl^- caused diminution of the CCK-8 evoked fluid secretion in the hypertrophied pancreas. Ouabain (0.1 and 1 mM) or furosemide (1 mM) abolished the CCK-8 evoked fluid secretion in the hypertrophied pancreas. These results led us to conclude that ouabain sensitive Na-K pump activity and furosemide sensitive Na-K-2Cl contransport system contribute to the CCK-8 evoked fluid secretion in the hypertrophied pancreas.

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DETERMINATION OF INTRACELLULAR SODIUM LEVEL BY SODIUM-NMR SPECTROSCOPY IN THE PERFUSED RAT LIVER. TSUKAMOTO, K., MURAKAMI, M., SEO, Y., WATARI, H., NONAKA, M., OKA, T. Dept. Molecular Physiol., Natl. Inst. Physiol. Sci. Okazaki 444. and Dept Surg., Kyoto Prefectural Univ. Med. Kyoto 602.

The intracellular Na content was measured in the perfused rat liver by sodium nuclear magnetic resonance (NMR) spectroscopy. Dysprosium triethylenetetramine hexaacetic acid (Dy(TTHA)) was used as a shift reagent to discriminate the intra- from extracellular Na signal. A right lobe of a rat liver was isolated and perfused with a modified Krebs-Henseleit solution containing 10 mM Dy(TTHA) at 37°C. The resonance peak of the intracellular Na was observed at 0.5 ppm, and those of the extracellular Na were observed at 2.7 and 4.5 ppm. In the basal condition, intracellular Na concentration was calculated as 9.0 $\pm$ 0.6 (mean $\pm$ SEM, n=7) mmol/ l. By the administration of ouabain (1 mM), intracellular Na level reversibly increased 28 mmol/l for 60 min. Thus sodium NMR spectroscopy permits us to observe continuous changes of the intacellular Na level in the perfused rat liver.

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INTRACELLULAR TRANSPORT OF IONS AND PROTEINS INTO THE LUMEN IN PIG PANCREATIC ACINAR CELLS. Sadao Sasaki, Ken-ichi Kamiya* and Ikuko Nakagaki. Department of Physiology, Osaka Medical College, Osaka 569 and *Department of Internal Medicine, Fukui Medical College, Fukui 910-11.

The effects of furosemide, oubain, omeprazole and monensin on the ion and protein transports in pig pancreatic acinar cells were studied using electron probe X-ray microanalysis and ^3H-leucine electron microscopic autoradiography. Previous X-ray microanalysis of freshly frozen thin sections of the acinar cells showed that the Na, Cl and Ca concentrations increased and K decreased in the cytoplasm, while the Na, Cl and K increased in both the secretory granules and the lumen, with CCK-8 stimulation. Addition of furosemide (10 μM) to the bath solution produced significant changes. There was an increase in K concentration and a decrease in Na and Cl in the cytoplasm, and the Cl decrease in luminal space. After oubain (100 μM) exposure, the Na and Cl increased, but K decreased in the cytoplasm, and there was a slight increase in Na and Cl in the luminal space. By the treatment of omeprazole (10 μM) , the K concentration in the lumen decreased, while the Na and Cl increased. In monensin (10 μM) treated acinar cells, K concentration decreased, and Ca, Na and Cl increased in the cytoplasm and intracellular recording of basal membrane potential of monensin treated cells showed deporalization and radioautographs showed enhanced exocytosis and inhibited transport of granules.

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ION AND PROTEIN SECRETION AND CYTOSKELETAL SYSTEMS OF THE POSTERIOR SILK GLAND CELLS.

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Intracellular ion and secretory protein transport and secretion in the posterior silk gland cells of the silkworm, Bombyx mori were investigated in relation to the cytoskeletal systems of the cells using the techniques of electron probe X-ray microanalysis and radioautography. The silk glands were pulse-labelled for 3 min with ^{3}H-glycine in vitro and then chased in media containing excess cold glycine and monensin, and the flow of the label was observed. By the treatment with monensin for 40 min and 120 min, the label still located in the basal cytoplasm, though in the control glands the grains were distributed in the apical cytoplasm. The spectra of X-ray microanalysis from the cytoplasm of the cells treated with monensin showed the higher Na, Cl and Ca peaks than those from the cytoplasm of normal cells. It may be suggested that the intracellular transport of secretory globule from basal cytoplasm to apical cytoplasm and lumen was inhibited with monensin, and the H gradient is responsible for intracellular transport which is regulated by the microtubule system in the posterior silk gland cells.

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EFFECTS OF CYCLIC NUCLEOTIDE ON THE MECHANISM OF PROXIMAL URINARY ACIDIFICATION OF BULLFROG KIDNEY.

HAGIWARA,N., KUBOTA,T., INOUE,A., YAMAGUCHI,J., and FUJIMOTO,M. 2nd Dept. of Physiol., Osaka Med. College, Takatsuki, Osaka 569.

To study the effect of dibutyryl-cyclic AMP (db-cAMP,10^{-4}M) on the mechanism of proximal urinary acidification, we used double-barrelled Na^{+} or H^{+} selective microelectrodes in doubly-perfused bullfrog proximal tubules. The peritubular membrane potential difference (E_M) and intracellular Na^{+} activities ($(Na)_i$) and intracellular and luminal pH were monitored continuously after peritubular application of db-cAMP. We also observed the change of intracellular distribution of H^{+} with db-cAMP by means of acridine orange fluorescence microscopic technique. Results: 1) 10^{-3}M amiloride, a blocker of Na^{+}/H^{+} antiport, suppressed proximal urinary acidification by 65%; 2) peritubular application of db-cAMP produced a transient increase of tubular fluid pH; 3) db-cAMP administration caused a decrease of $(Na)_i$ by 5-10 mEq/L and cytosol pH by about 0.1; 4) db-cAMP administration stimulated the intravesicular accumulation of H^{+}. Conclusions: 1) cAMP induced cytosol alkalinization by enhancing incorporation of H^{+} into subcellular vesicles; 2) cAMP suppressed the Na^{+}/H^{+} exchange mechanism in the luminal border and transiently inhibited the proximal urinary acidification.

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THE ELECTRIC CAPACITANCE AND SERIES AND PARALLEL RESISTANCES OF THE SQUID GIANT AXON AT REST AND EXCITATION. SAITO, T., Dept. Physiol., The Nippon Dent. Univ., Tokyo, Tokyo 102

By appling the direct or alternating potentials to the living bodys, it was clear that they had the resistances and capacitances. Formerly the equivalent circuit was the capacitance with series and parallel resistances by the direct potential. But it was the capacitance with series resistance or with parallel resistance by the alternating potential and it have not managed the circuit was the capacitance with both resistances. The auther measured the polarization by using the finite alternating potential. The capacitances, series resistances and parallel resistances were determind at six kinds of frequences and five kinds of amplitudes. The rest conditions were three cases and excition were two.

By these experiments the change of the series resistance was little and the parallel resistance became one tenth and the capacitance five times.

The sepiotheudes lessoniana was used for this research.

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INWARD RECTIFIER PRODUCED BY *XENOPUS* OOCYTES INJECTED WITH CARP OLFACTORY EPITHELIUM mRNA. YOSHII, K., KURIHARA, K., Faculty of Pharmaceutical Sci., Hokkaido University, Sapporo 060

mRNA was extracted from carp olfactory epithelium by guanidinium-CsCl method and injected into *Xeopus* oocytes. The oocytes produced inward rectifier and TTX-sensitive Na channel, which were not observed in uninjected oocytes. The inward rectifier was investigated under two electrode voltage-clamp conditions. The inward rectifier opened on hyperpolarization and the current decreased to a steady state. The magnitude of the current increased with increasing $[K^+]_{out}$. The relationship between 0 current potentials and $[K^+]_{out}$ was fitted by a straight line with a slope of 58 mV/decade when the $[K^+]_{out}$ was higher than 5 mM. The chord conductances of instantaneous current simply depended on voltage rather than $[K^+]_{out}$. The inactivation process in the current developed on hyperpolarization and with increasing $[Na^+]_{out}$ The time constant of decay in the current was shorter in depolarized potentials and high $[Na^+]_{out}$.

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THE EFFECT OF DIVALENT CATIONS ON THE SINGLE CHANNEL CONDUCTANCE OF K-CHANNEL FROM SARCOPLASMIC RETICULUM IN PLANAR BILAYER MEMBRANES. NOMURA,K.,NARUSE,K.,KATO,T.,SOKABE,M.,ITO,F., Dept. Physiol.,Nagoya Univ. Sch. Med. Nagoya 466

The effects of calcium(Ca) and other divalent alkaline earth metal cations on the single channel conductance of sarcoplasmic reticulum (SR) K-channel were investigated in artificial planar bilayer membrane. SR vesicles were prepared from rabbit back and leg muscles. The single channel conductance was reduced nearly equally from both sides of membrane in a dose dependent manner. The dose inhibition curve fitted a single site titration curve. The Ca blockade of the channel was also voltage dependent. Interpretation of the voltage dependent blockade by Woodhull's ionic blockade theory gave us the values of δ (fraction of the total electrical potential drop across the membrane) : δ =0.16 for cis block and δ =0.23 for trans block. (trans : side opposite to where SR vesicles were added) From these values it was indicated that the blocking sites were not the filter of the channel. Other divalent cations (Sr, Mg, Ba) blocked the channel with almost the same values of δ .

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Ca-SENSITIVE POTASSIUM CHANNEL IN *DROSOPHILA* LARVAL MUSCLE.

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Single Ca-sensitive K currents were recorded from vesicles derived from *Drosophila* larval muscles in a high K (130 mM) bath solution. This channel had a unit conductance of 50 pS at 0 mV and a reversal potential lower than -60 mV when the pipette contained a 2.5 mM K solution. The corresponding values were 70 pS and -20 mV with a 65 mM K solution, and 90 pS and 0 mV with a 130 mM K solution. The I-V relations of the channel can be described by the Goldman-Hodgkin-Katz constant field equation. Ca-dependence was determined by perfusion experiments using an inside-out configuration. In a bath solution containing 10^{-7} M Ca, the probability of being open (Po) at 40 mV was 0.82. In 10^{-8} M Ca, it was near zero. This channel also appeared voltage-dependent in that the Po increased as the membrane was depolarized. In 10^{-7} M Ca solution, the Po increased from 0.35 at -60 mV to 0.82 at 40 mV.

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STRUCTURE-ACTIVITY RELATIONSHIP IN THE MODIFICATION OF D-RING OF GRAYANOTOXIN (GTX).

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An attempt was made to develop a pharmacological tool from GTX for elucidating the functional structure of Na channel. Because of technical as well as chemical reasons, a systematic modification was conducted on the D-ring of GTX. Dose-response curve was made by using depolarization on squid axon with internal application of GTX. Comparison of the biological activity of GTX analogues in terms of ED_{50} and the maximum depolarization was made, referring to those of α-dihydro-GTX II. Since introduction of epoxy ring between 10 and 14 constrains C-D ring and eliminates depolarizing action, it appears that the biological action of GTX requires restriction of the movement of B-ring by preserving the spatial position of C-D ring. Introduction of alkyl group, primary and secondary amine and amido including TEMPO in D-ring decreases biological activity at various extent but does not totally deprive of the activity. Although modification of D-ring may exert a subtle effect on the activity, D-ring is the most promising position in introducing chemical groups which can function as pharmacological probe.

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GUANIDYL-SIDE ARMED CYCLAM BLOCKS SODIUM CHANNELS OF FROG VENTRICULAR CELLS IN AN UNUSUAL MODE.

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It has been shown that in pronase-treated squid axons internally applied guanidyl-side armed cyclam (G-cyclam) suppresses the Na current in a time course similar to that of Na inactivation process.

The mechanism of G-cyclam block of Na channel in frog ventricular cells was studied with the single channel recording technique. G-cyclam applied to the cytoplasmic face suppressed the single Na channel current in membrane potential and concentration dependent manners and an obvious burst caused by blocking events could not be observed. Irrespective of the presence of G-cyclam, mean open times obtained from open time histograms did not change and the values of the variance of the current records in open states at -3 °C remained unchanged.

These findings indicate that G-cyclam blocks the single Na channel in frog ventricular cells incompletely, that is, the flow of current through a single channel is reduced but not abolished. This incomplete block could hardly explain the fact that the block is potential and concentration dependent on both squid axons and frog ventricular cells.

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DIFFERENTIAL ACTIONS OF CHARGED AND UNCHARGED LOCAL ANESTHETICS ON THE SODIUM CURRENT OF ISOLATED MAMMALIAN CENTRAL NEURONS. IKEMOTO, Y., KANEDA, M., YOSHIDA, A. and AKAIKE, N. Department of Physiology, Faculty of Medicine, Kyushu University, Fukuoka 812,. Japan.

Single neurons were isolated enzymatically from hippocampus and hypothalamus of new born rats. Effects of extracellularly-applied QX-314 and benzocaine on the I_{Na} of the neurons were examined using the 'concentration clamp' technique. QX-314 did not affect the I_{Na} when the neurons were left silent. With stimulation of 1 Hz the I_{Na} was suppressed slowly to about a half in the presence of 1 mM QX-314, reaching a steady value in about 15 min. This finding may suggest that QX-314 reaches the binding site through the open channels. The steady state inactivation curve was shifted slightly to the left. Brief pre-applications of 1 mM benzocaine showed that the access time constant of the drug to the resting state of the Na channel was about 16 msec. While the access time constant to the open state, which was maintained by scorpion toxin, was about 8 msec. The dose-inhibition curve by benzocaine in the presence and absence of QX-314 showed that the two local anesthetics act at separate sites on the Na channel protein.

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INONIC CHANNELS IN PRIMARY CULTURED NEURONS OF THE CEREBRAL CORTEX OF MICE. TAKAGI,T., KAJIWARA,K., KOMATSUBARA,J., YUYAMA,T., SUGAYA,E., *SUGAYA,A., *TSUDA,T. AND *YASUDA,K. Dept. of Physiol. Kanagawa Dental College, Yokosuka and *Fac. Pharmaceut. Sci., Josai Univ., Sakado, Saitama

Characteristics of the calcium current of the primary cultured cerebral cortical neurons of mice were investigated. To clarify the role of the single calcium ion channel in the provocation of seizure discharges, effects of pentylenetetrazol (PTZ) were also examined.

Dissected cortical area cells were prepared from 17-day-old embryonic mice. Ionic currents were recorded using the whole-cell clamp method and cell-attached clamp method. A single calcium channel recording was performed with a pipette containing $BaCl_2$.

By application of PTZ in the cultured medium, about half of the examined primary culuted cerebral cortical neurons showed bursting-type inward current on examination by the whole-cell clamp method. By the cell-attached clamp method, open time and open frequency of the single calcium ions channel increased and sometimes showed bursting-type open and closed state after application of PTZ.

These findings suggest that PTZ induces bursting-type open and closed state of a single calcium ion channel of primary cultured cerebral cortical neurons.

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GANGLIOSIDES AND NEURITE EXTENSION OF THE PRIMARY CULTURED NEURONS OF THE CEREBRAL CORTEX OF MICE. KAJIWARA,K., TAKAGI,T., KOMATSUBARA,J. YUYAMA,T. AND SUGAYA,E. Dept. of Physiol., Kanagawa Dental College, Yokosuka

To clarify the ralationship between neurite extension and gangliosides, ganglioside compositions of primary cultured neurons of the cerebral cortex of mice in the various culture condition were examined.

Dissociated cortical area cells were prepared from 17-day-old embryonic mice. Isolation and identification of gangliosides were carried out by the modified method of Ledeen. Total gangliosides were designated according to the nomenclature used by Svennenholm.

The neurite extension was inhibited in the culture with serum-free culture medium. The serum-free culture medium inhibited the proliferation of astrocytes. Addition of astrocytes in the serum-free medium showed neurite extension. In these conditions, the content of the GD3 ganglioside was reduced; but GD3 ganglioside was hardly detected in the culture of pure astrocytes. Addition of the GD3 gangliodes promoted the neurite extension in the serum-free culture medium.

These findings suggest that contact with astrocyte is essential and the GD3 ganglioside is important for the normal extension of neurites.

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DIRECTION OF THE OPTICAL ACTIVITY SIGNAL OF LOBSTER NERVE. WATANABE, A., National Institute of Physiological Sciences, Myodaiji-cho, Okazaki 444.

The optical activity of the nerve changes transiently when the nerve is excited by electrical stimulation. The direction of the change is however not constant but varies according to the preparation. The purpose of the experiment was to find out conditions which determine the direction of the optical activity response. The direction did not change by changing the wavelength of the incident light between 450 and 575 nm. The direction was not correlated with the side of the walking legs of the lobster from which the nerve was dissected. Two conditions were found important in determining the direction of the optical response. One was the tension applied to the nerve. When the nerve was stretched by 5 - 20% of its resting length, the response changed its time course. Usually the increase in tension increased the rate of the change. The latency was shortened. Sometimes a new phase appeared which had the opposite sign to that of the relaxed nerve. Sometimes a complete reversal of the sign of the response was elicited. The second was the site of the stimulation. The direction of the response was reversed when the direction of the impulse propagation was reversed. It is likely that the spatial gradient of the membrane potential of nerve fibers is an important factor to determine the sign of the optical activity response.

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REAL-TIME IMAGING OF EVOKED ELECTRICAL ACTIVITY IN EMBRYONIC CHICK CERVICAL VAGUS NERVE FIBERS USING A VOLTAGE-SENSITIVE DYE. KOMURO, H., SAKAI, T., KATOH, Y. and KAMINO, K. Dept. of Physiol., Tokyo Ika-Shika Dai., Sch. Med. Tokyo 113.

Using a voltage-sensitive merocyanine-rhodanine dye (NK2761) and a high S/N vidicon camera, we have tried to image electrical activity in the embryonic chick cervical vagus nerve. The vagus nerve was stained with the dye and absorption change evoked by depolarizing pulse stimulation in the end of the nerve fibers with a suction electrode was monitored. The video output of the camera was fed into the digitizing input of a image processor which was under the interactive control of a computer. Digitized video images are stored in real time in the 512x485x16 bit volatile memory planes of the image processing system and data are transfered onto a hard disk by a computer. Finally, subtracting the control image, we have obtained the image of the action potential-related absorption change with a spatial resolution of 2.2 μm. In the present experiments, it is concluded that our good results were obtained because the fractional absorption changes ($\Delta A/A$) in cervical vagus nerve fibers stained with NK2761 are larger than 1 per cent.

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SPATIAL AND TEMPORAL VARIATIONS OF FREE CALCIUM IN NG108-15. OZAKI, K.* and MIYAKAWA, A. Biotechnology Group, Research Department, Olympus Optical Co., Ltd. 2951 Ishikawa-cho, Hachioji, Tokyo 192.

We have developed the digital imaging microscope consisted of an inverted microscope, a sillicon intensified target camera, an image processor, and a 16 bit personal computer. We examined the variations of free calcium in fura-2 loaded NG108-15 cells (cultured in 1 mM dibutyryl cAMP). When the cells were stimulated by 0.1 mM carbachol, the concentrations of intracellular free calcium increased in 3 cells but unchanged in most cells (30 cells) at least in 1 min. The finding suggests the cells have the individuality in response to the stimulations. We also examined spatial and temporal variations in cytoplasmic free calcium level of NG108-15 on exposure to 50 mM KCl and 5 μM bradykinin. On an exposure to high concentraions of KCl, cytoplasmic calcium level rose in peripheral earlier than in central of the soma, whereas on an exposure to bradykinin, that rose in central. These findings are explained by the calcium mobilization from the different sources: from the medium through voltage dependent calcium channels in the former and from intracellular pools in the latter.

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MODULATION OF ION CHANNEL ACTIVITIES BY INTRACELLULARLY APPLIED Ca AND Mg IONS IN SQUID GIANT AXONS. YAMAGISHI, S., FURUYA, K. and KUKITA, F., Dept. of Cell Physiology, National Inst. for Physiol. Sci., Myodaiji, Okazaki 444.

Effects of intracellularly applied Ca and Mg ions on ion channel activities were compared precisely using squid giant axons. The axons immersed in artificial sea water (ASW) were internally perfused with a KCl or K-glutamate solution as a control. By addition of 0.3 - 30 mM Ca or Mg ions to 25 - 100 mM K-salt solutions, action potentials were gradually suppressed with little change in resting potentials. Effect of Mg ion was less suppressive than that of Ca ion. Under voltage clamp experiments, a Na channel current (I_{Na}) and a K channel current (I_K) were measured before and after the addition of Ca or Mg ions to a 100 mM K-glutamate solution. Both of Ca and Mg ions commonly suppressed the I_{Na} and I_K. The apparent K_D's of I_{Na} suppression by Ca and Mg ions were 2.8 and 9.0 mM, and of I_K suppression were 5.8 and 10.2 mM respectively. Another common effects were shifts of I-V relations to a low voltage direction by Ca or Mg addition. The values of the shift were 7 and 11 mV respectively. In conclusion, the mode of modulation by Ca and Mg ions to the Na and K channel activities were essentially the same, but the effects of Ca ion were 2-3 times stronger than that of Mg ion.

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VOLTAGE-DEPENDENT CYTOSOLIC CALCIUM TRANSIENTS IN THE GUINEA-PIG SUBMUCOUS NEURONS. HIRAI, K., KATAYAMA, Y. AND TATSUMI, H. Dept. Autonom. Physiol., Med. Res. Inst., Tokyo Med. and Dent. Univ., Tokyo, 101

Submucous plexus preparations were made from the guinea-pig caecum. Intracellular calcium concentration ($[Ca^{++}]i$) of single cells was measured by using fura-2 intracellularly injected from the recording electrode. The $[Ca^{++}]i$ was transiently increased by an action potential elicited by a direct stimulation. The recovery time course of both the $[Ca^{++}]i$ and afterhyperpolarization (AHP) was single-exponential, but the time constant of $[Ca^{++}]i$ recovery was almost two times smaller than that of AHP. In a voltage-clamped neuron (Vhold = -70 mV), the $[Ca^{++}]i$ was increased by depolarizing command pulse (duration: 2 sec). The time course of rising and falling phase of $[Ca^{++}]i$ was almost single-exponential and almost linearly related to the amplitude of the depolarization. The $[Ca^{++}]i$ was decreased by a hyperpolarizing command. This decrease was dependent on the amplitude of the command, but an inverse relationship appeared when the command exceeded -120 mV. ω-conotoxin (0.5 μM) inhibited the $[Ca^{++}]i$ increase evoked by an action potential while the toxin enhanced the $[Ca^{++}]i$ increase induced by depolarizing pulse.

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EFFECTS OF HYPOXIA ON THE CYTOSOLIC Ca^{2+} CONCENTRATION IN HIPPOCAMPAL CA1 NEURONS. KUDO, Y.[1], OGURA, A.[1], SUGITA, S[2] and HIGASHI, H[2] . [1]Dept. of Neurosci. Mitsubishi-Kasei Inst. of Life Sci., Machida, Tokyo 194 and [2] Dept. of Physiol., Kurume Univ. School of Med., Kurume 830, JAPAN.

Effects of high K^+ or hypoxic medium on the cytosolic Ca^{2+} concentration in the guinea pig hippocampal CA1 neurons in tissue slice and the cultured rat hippocampal neurons were studied by fura-2 fluorometry. The depolarization induced by high K^+medium (15 - 75 mM) was accompanied by an increase in cytosolic Ca^{2+} concentration. The increase at st.radiatum was the most obvious and long lasting, while the changes in st. oriens and st.pyramidale were highly reversible. Flunarizine (5 uM) depressed the increase slightly but significantly. When the preparation was perfused with glucose-free hypoxic medium (N_2 95%, CO_2 5%), cytosolic Ca^{2+} concentration increased gradually. The change was the most obvious at the st.radiatum region. St.oriens and st.pyramidale region were resistant to such hypoxic condition. In the cultured rat hippocampal neuron the hypoxic medium-induced changes in cytosolic Ca^{2+} concentration were the most obvious at the dendrite. These results suggest that the neuronal death to hypoxia will be caused by massive invasion of Ca^{2+} into the cell from the dendritic region.

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TOPOGRAPHYCAL ANALYSIS OF SEROTONIN-EVOKED INTRACELLULAR Ca^{2+} ELEVATION IN C6Bu1 CLONAL GLIAL CELL. OGURA, A., AKITA, K.* and KUDO, Y. Department of Neuroscience, Mitsubishi-Kasei Institute of Life Sciences, Machida-shi, Tokyo 194

Intracellular Ca^{2+} concentration ($[Ca^{2+}]_i$) plays key roles in regulating various cellular functions. In astroglial cells, potassium transport, glycogenolysis, or cell division (gliosis) is postulated to be triggered by $[Ca^{2+}]_i$-rise due to activated neurotransmitter receptors. We have previously proposed that $[Ca^{2+}]_i$-elevatory response evoked by serotonin (5HT) in astroglioma C6Bu1 cells may serve as a good model system for analysis. Here we applied a microscopic Ca^{2+} fluorometrical technique recently established by us to single C6Bu1 cells to determine a source of Ca^{2+} in the 5HT-evoked response. When whole surface of a cell is exposed to 5HT (1-3uM, 1-10s), the earliest $[Ca^{2+}]_i$-rise occurred from some spots of irregular distribution at the periphery of the cell. The 5HT-evoked $[Ca^{2+}]_i$-rise was abolished by removal of Ca^{2+} from extracellular milieu. Caffeine (3-10mM, 30-60s), known to mobilize Ca^{2+} from intracellular storage organelles in muscle cells, induced a small, slow but recognizable $[Ca^{2+}]_i$-rise in C6Bu1 cells. However, the sites of preferred $[Ca^{2+}]_i$-rise by caffeine and 5HT applied successively to a single cell were unidentical. Trimethoxybenzoic acid 8-diethylaminooctyl ester (TMB8; 100uM) blocked the caffeine-induced slow $[Ca^{2+}]_i$-rise but not the 5HT-evoked fast $[Ca^{2+}]_i$-elevation. These results suggest that the source of Ca^{2+} in the 5HT-evoked response in C6Bu1 cell is predominantly extracellular. This conclusion was in line with the results of quantification of ^{45}Ca uptake carried out under conditions equivalent to the fluorometry.

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SPATIAL AND TEMPORAL DYNAMICS OF INTRACELLULAR Ca^{2+} FOLLOWING ACTION POTENTIALS IN THE BULLFROG SYMPATHETIC GANGLION CELL. NOHMI, M., KUBA, K. AND MINOTA, S. Dept. Physiol., Saga Med. Sch., Saga 840-01.

A change (Ca^{2+}-transient) in the intracellular free Ca^{2+} ($[Ca^{2+}]_i$) and a hyperpolarization or the underlying membrane current induced by a single or repetitive action potentials were measured using a fura-2 fluorescence and an intracellular electrode. The rising and falling phases of a Ca^{2+}-transient after a single spike paralled the decay phases of major and late components, respectively, of the afterhyperpolarization. The increase in the amplitude of Ca^{2+}-transients caused by an increment in the number of stimuli was smaller than that expected from simple summation in series of Ca^{2+}-transients induced by a single spike, while the prolongation was much greater than expected. A Ca^{2+}-transient after a tetanus was not simulated by assuming a constant Ca^{2+}-buffering activity, but by assuming that $[Ca^{2+}]_i$ alters both spatially and temporally due to the Ca^{2+}-dependent uptake and release at Ca^{2+} reservoirs, binding to proteins and Ca^{2+}-dependent transports at the cell membrane. Thus, a change in the $[Ca^{2+}]_i$ beneath the cell membrane (represented by membrane responses) following a spike(s) differs from a change in the $[Ca^{2+}]_i$ in the deeper cytoplasm (reflected by a Ca^{2+}-transient). Furthermore, these Ca^{2+} buffering systems appear not only to reduce an increased $[Ca^{2+}]_i$ but to maintain a high level of $[Ca^{2+}]_i$.

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PROPERTIES OF CARDIAC L-TYPE CALCIUM CHANNELS RECOVERED BY THE TISSUE EXTRACT FROM RUN-DOWN IN CELL-FREE PATCHES.
KAMEYAMA, M., KAMEYAMA, A., KAIBARA, M. AND NAKAYAMA, T. National Institute for Physiological Sciences, Myodaiji, Okazaki 444, Japan.

We have reported that the run-down of cardiac L-type Ca channel is prevented and the channel activity is recovered by a supernatant of cardiac tissue homogenate in inside-out patches (Kameyama et al. J Physiol Soc Jpn, 49, 501, 1987). We investigated electrophysiological properties of the channels activated by the tissue extract in guinea-pig ventricular cells by the inside-out patch-clamp method with 50 mM Ba ions and 3 μM Bay K 8644 in the pipette. The extract-induced channels had an unitary current of 1-1.5 pA at 0 mV, and a slope conductance of 20-25 pS. The open time had two components with time constants of ∿1 and ∿10 ms, and the closed time had ∿2 and 20-30 ms components at 0 mV. In an example of consecutive sweeps of the single-channel current, the blank sweeps was 68 %, and the mean life times of blank and non-blank sweeps were 7.80 and 3.64 ms, respectively. These results suggest that properties of the channel activity induced by the extract in the inside-out patch are quite similar to those of the Ca channel in the cell-attached patch mode.

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AUTONOMIC NERVE TRANSMITTERS MODULATE ACTIVITY OF IONIC CHANNELS IN THE MOUSE PANCREATIC B-CELLS. MURAYAMA, K. AND OHARA, A.† Dept. Physiol. and †Dept. Biol., Shiga Univ. Med. Sci., Ohtsu 520-21

It has been reported that activity of the autonomic nervous system and also direct application of autonomic transmitters modulate the insulin release from the pancreas induced by glucose. To elucidate the membrane mechanism of action of those, we studied the direct effects of autonomic transmitters (5 μM ACh, 2 mM Carbachol and 1×10^{-6} g/ml adrenaline) on the ionic permeability of the mouse pancreatic B-cell (cultured 12-37 days) membrane using the patch-clamp technique. In the whole-cell voltage-clamp mode, ACh and Carbachol caused a transient inward current lasting 1-2 min in the cells held at their resting membrane potentials (-63 to -73 mV), which depolarized the membrane under current-clamp. Adrenaline reduced the depolarization induced by 11.2 mM glucose. Single-channel recordings in the cell-attached mode showed that 1) ACh inhibited opening of a 118-pS K^+-channel for a long period of time (6-27 s) followed by normal bursts of opening, 2) ACh induced opening of a 169-pS K^+-channel, and 3) adrenaline after its transient increase slightly reduced the opening rate of a 68-pS K^+-channel. Although there is a divergence of their effects, the present results clearly suggest that the autonomic transmitters exert direct effects on the B-cell membrane to modify its ionic permeability.

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TWO TYPES OF CALCIUM CURRENTS IN RAT ANTERIOR PITUITARY CELLS IN SOMATOTROPH-ENRICHED PRIMARY CULTURES. IINO, M., TSUZUKI, K., *KATO, M., *SUZUKI, M. AND OZAWA, S. Dept. Physiol., Sch. Med., *Dept. Physiol., Inst. Endocrinol., Gunma Univ., Maebashi 371

The properties of Ca^{2+} channels were studied in rat anterior pituitary cells in dissociated cultures. Anterior pituitary cells from male rat were dissociated by an enzymatic treatment (0.5% trypsin), and the somatotroph-enriched fraction was obtained by centrifugal elutriation. Immunohistochemical staining showed that somatotrophs constituted about 80% of the total cell count in this fraction. Two types of Ca^{2+} currents were recorded with the whole-cell voltage-clamp technique. A transient inward Ca^{2+} current (T-type current) was evoked by a step depolarization from a holding potential of -95 mV to potentials more positive than -45 mV. A depolarization to potentials more positive than -20 mV caused a long-lasting inward Ca^{2+} currrent (L-type current). When preceded by a conditioning pulse to -40 mV, the step depolarization failed to induce the T-type current due to inactivation. The T-type current was sensitive to Ni^{2+}; 100 μM-Ni^{2+} markedly suppressed the T-type current without affecting much of the L-type current. On the other hand the T-type current was less sensitive to Cd^{2+} than the L-type current.

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INHIBITORY EFFECT OF Ni IONS ON HUMAN GROWTH HORMONE RELEASING FACTOR-INDUCED GROWTH HORMONE SECRETION IN PERIFUSED RAT PITUITARY CELLS. KATO, M., *OZAWA, S., *IINO, M., *TSUZUKI, M., and SUZUKI, M. Dept. Physiol., Inst. Endocrinol., *Dept. Physiol., Sch Med., Gunma Univ., Maebashi 371

It is widely accepted that human growth hormone (GH) releasing factor (hGRF) stimulates GH secretion via cAMP and that Ca^{2+} is indispensable for exocytotic release of GH. In hGRF-induced GH secretion, influx of Ca^{2+} is essential. Ca^{2+} enters the cells probably through Ca^{2+} channels. There have been identified two types of Ca^{2+} channels in somatotrophs, namely T- and L-type Ca^{2+} channels. Since Ni^{2+} selectively blocked T-type channels, we investigated the effect of Ni^{2+} on hGRF-induced GH secretion to determine whether T-type channels play any role in the secretory process stimulated by hGRF.

Acutely dispersed male rat pituitary cells were used. Ni^{2+} showed the inhibitory effect on 1 nM hGRF-induced GH secretion with a concentration of 30 μM or more. Ni^{2+} also suppressed 1 mM DBcAMP-induced GH secretion but the effective dose was more than 50 μM. cAMP production stimulated by hGRF was also inhibited by 20 μM-Ni^{2+}. However, 30 mM K^+-induced GH secretion was not affected by even 200 μM-Ni^{2+}. In conclusion, Ni^{2+} suppressed hGRF-induced GH secretion both by blocking T-type Ca^{2+} channels and by inhibiting cAMP production. Exocytotic process itself was not affected by Ni^{2+}.

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Patch-clamp study of neutrophils in the circulating blood of the newt. Kawa, K. Dept. Pharmacol., Sch. Med., Gunma Univ., Maebashi 371.

The blood obtained from the atria of the newts (Triturus pyrrhogaster) contains several types of leukocytes. Under a phase contrast microscope, three types of granulocytes could be identified. Using patch-electrodes, it was possible to investigate the whole-cell membrane currents in these cells. In the neutrophils (diameter, 19~23 μm), identified by characteristic features of lobulated nucleus, inward rectifying K^+ currents were evoked with hyperpolarization from the holding potential of -83 mV. In the presence of Cs^+ (1mM) or Ba^{2+} (1mM) in the external saline, the amplitudes of inward currents were reduced with time- and voltage-dependent manner. When the external concentration of K^+ was increased from 4 mM through 20 mM to 100 mM replacing isomolar choline in the perfusing salines, the threshold of the K^+ currents shifted from -83 mV through -43 mV to -3 mV.
The amplitude of the evoked K^+ currents also increased as that the chord conductance in each of these salines was nearly proportional to the square root of the external K^+ concentration.

In basophils and eosinophils, there evoked no major membrane currents under voltage-clamp conditions. Their I-V relations were almost linear, which suggested almost electrically non-excitable properties in these cells.

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SCHWANN CELL LAYERS REGULATE ACTIVITIES IN NERVE FIBERS.
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Physiological roles of Schwann cell layers in nerve activity were examined in squid giant axons. The structure of Schwann cell layers was changed by applying the osmotic water flow to the intracellularly perfused giant axon. A bundle of fine nerve fibers around the giant axon was an additional diffusion barrier to cause an error in this experiment, especially when the inward water flow was applied, so it was necessary to remove completely fine nerves. Comparing with non-cleaned axons, this preparation was much more sensitive to the osmotic gradient. With the outward water flow, periaxonal K^+ accumulation was removed and the resistances due to Schwann cell layer and periaxonal space (F-H space) decreased. On the other hand, with the inward water flow, K^+ accumulation and the resistance due to Schwann cells increased, as if the F-H space thickness and the permeability of Schwann cell layer decreased. These changes were accompanied with a change in Na and K currents: these currents increased under the outward water flow and decreased under the inward water flow. Anyhow, Schwann cell layers could regulate ionic currents in peripheral nerve fiber.

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CHARACTERIZATION OF MEMBRANE ELECTRICAL PROPERTIES OF CELLS OF A MOUSE CLONAL OSTEOGENIC CELL LINE. AMAGAI, Y. AND KASAI, S., Department of Physiology, Tohoku Dental University, Koriyama, Fukushima 963

Cells of MC3T3-E1 osteogenic cell line have the capacity to differentiate into osteoblasts and to form bone tissue *in vitro*. We studied membrane ionic currents of these cells on their growing or actively mineralizing stage by whole-cell variant of the patch-clamp technique. Cells in log-phase had resting membrane potential (Em) of -22.9± 1.2 mV and generated depolarization-dependent, fast-inactivating Ca inward current which was blocked by phenytoin. Threshold of the current was about -50 mV. After 21 days in culture, spherical cells appeared in group and they increased in number to form calcifying nodules. The Em of these cells was -64.8 ± 1.4 mV. In addition to the fast-inactivating channel, they also had long-lasting, slow-inactivating Ca current system which was activated by depolarizing pulse above -20 mV. This current was inhibited by cadmium and verapamil. These results demonstrate that the MC3T3-E1 osteogenic cells express two kinds of voltage-dependent Ca channel which correspond to T-, and L-type ones of excitable membranes. Of these, the L-type Ca channel may be developed as the cells acquire the osteoblastic function.

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THE CHANNEL CURRENTS IN THE PATCH MEMBRANES OF CRAYFISH NEURON SOMA.
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The currents through ionic channels in the crayfish neuron soma membrane were recorded by using the patch clamp technique. The neuron soma was isolated by treating with 0.1% collagenase. The unitary currents flowing through a single channel of the membrane were detected as current fluctuations due to the blocking and unblocking of the channel. The peaks in the ionic current fluctuations at three different levels of regular intervals were observed in some preparations. The relationship between unitary current and the holding potential was linear in the range between +30 and -70 mV in mechanically isolated membrane patch was linear and the single channel conductance was 180pS. The reversal potential was -30mV which was the same order of value obtained with intracellular micro electrodes. The channel current was blocked by application of 13mM TEA in the outside-out patch. Therefore, we concluded that the channel currents recorded were K current.

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CHLORIDE CHANNELS IN XENOPUS OOCYTES COUPLED BY INOSITOL TRISPHOSPHATE AND Ca^{2+}.
OOSAWA, Y., FURUYA, K., SUGIYAMA, H. AND YAMAGISHI, S. Dept. Cell Physiol., National Institute for Physiological Sciences, Myodaiji, Okazaki 444.

Ionic currents were studied in Xenopus laevis oocyte using the patch-clamp technique. Single-channel currents were recorded from the cell-attached patches in oocytes injected with rat brain mRNA when glutamate was applied locally outside the patch. Single-channel conductance was 3.66 pS, and the extrapolated equilibrium potential was -23.0 mV which indicated that the channels were chloride-selective. Single-channel currents with similar characteristics were observed in cell-attached patches in native oocytes in response to injection of inositol trisphosphate (IP_3) or calcium. The results indicate that: (1) glutamate receptors induced by rat brain mRNA are activated by glutamate, which lead to the formation of IP_3; (2) IP_3 induced calcium release from intracellular stores; (3) the increase of intracellular calcium concentration activated endogenous calcium-dependent chloride channels.

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MODIFICATION OF Ca-ACTIVATED K CHANNELS BY INTERNAL CATIONS.
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Single channel currents through Ca-activated K channels of guinea pig vas deferens were measured by using inside-out patch to determine the effects of internal cations on permeation through the single channel. Among cations Li, Tris and Na scarcely pass the channel from inside, while Rb and NH_4 passed the channel some extent. The permeable order among the cations from inside to outside are $K > NH_4 > Rb \gg Na, Li, Tris$. Although Na ion exist inside the membrane could not pass the channel, it shifted the voltage threshold of the channel opening towered hyperpolarizing direction. NH_4 ion exist inside the membrane changed the reversal potential of the single channel current towered depolarizing direction, while the other ions shifted the reversal potential opposite way. The order of the effect is $Tris > Li > Rb > Na$.

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INHIBITION OF K CURRENT BY NIK-247 IN THE CRAYFISH AXON.

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NIK-247, 9-amino-2,3,5,6,7,8-hexahydro-1H-cyclopenta[b]-quinoline hydrochloride hydrate, is an aminopyridine derivative, and has been suggested to block K current. The inhibition of K current by NIK-247 was examined in the artificial node of the crayfish giant axon under voltage-clamp, in the presence of TTX. NIK-247 in the bath reversibly depressed the K current in 10 min. The inhibition was voltage-dependent, and occurred in dose-dependent manner in a range of 0.01 - 5 mM, with IC_{50} at 10^{-3} M. Such effect of NIK-247 resembled that of 3-AP, with IC_{50} of the latter at 3×10^{-5} M. NIK-247, however, differed in certain respects from 3-AP. On repetitive stimulation, no frequency-dependent recovery was observed with NIK-247, while inhibition to 75 % with 3-AP was removed to 25 % at 1 Hz. In the presence of both NIK-247 and 3-AP, the K current was further depressed, and showed less frequency-dependent recovery, which seemed to suggest presence of different binding sites, or in addition, of different dissociation kinetics. In the absence of TTX, NIK-247 also reduced the amplitude and the rate of rise of the action potential, which further suggests additional effects on activation process of the Na current.

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CALCIUM ANTAGONISTIC EFFECTS OF EPERISONE AND ITS DERIVATIVES.

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The effects of eperisone hydrochloride as a Ca^{2+}-antagonist were examined vis-à-vis tolperisone and its isopropyl derivative under voltage clamp in a snail neurone, PON (periodically oscillating neurone). The possible mode of eperisone action was also evaluated. Dose-dependent inhibition of the calcium current (I_{Ca}) at holding voltage (V_h) of -50 mV was induced by eperisone. At the command voltage (V_c) of +20 mV, I_{Ca} was maximum both in the presence and absence of the drug. We compared the dose-response relationship for the inhibitory effects of eperisone (IC_{50} = 0.353 mM), tolperisone (1.170 mM) and its isopropyl derivative (0.351 mM). Lineweaver-Burk plot analysis of eperisone effects measured under various extracellular Ca^{2+} concentrations indicated a competitive type inhibition of the drug. The influences of different frequency stimulations were observed under eperisone, indicating that the drug effects were not use-dependent. The results are taken to suggest that the drug does not prefer to bind with the Ca^{2+} channel in the open state.

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CALCIUM-ANTAGONISTIC EFFECTS OF BROVINCAMINE.

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The effects of brovincamine on the calcium current (I_{Ca}) and their possible mechanisms were studied under voltage clamp in a snail neurone. At holding voltage (V_h) of -50 mV, brovincamine inhibited Ica dose-dependently (IC_{50} = 0.135 mM) without altering the activation time. These effects were much stronger than vincamine (0.705 mM), and almost comparable to verapamil (0.153 mM). Measured in varied $[Ca]_o$, brovincamine was proven to block the channel competitively with Ca^{2+} by Lineweaver-Burk plot analysis. The effects of brovincamine was use-dependent, which may reflect its binding with the channel in open state. Brovincamine shifted the steady state inactivation curve to the hyperpolarizing direction. The dissociation constant for binding with inactivated Ca^{2+} channel was 22.6 μM which was 6.0 times lower than its IC_{50}, indicating that it preferentially binds to the inactivated channels. At hyperpolarized V_h, -80 mV, brovincamine could hardly inhibit I_{Ca}, in which IC_{50} was estimated as 1.25 mM. It is concluded that brovincamine binds competitively to the Ca^{2+} channels with the different affinities which may be in the order of inactivated > opened > resting channels.

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SLOW GATING OF THE CARDIAC L-TYPE CALCIUM CHANNELS AFFECTED BY INTRACELLULAR PROTON.

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We previously reported that intracellular proton (H^+_i) little reduces the unit amplitude of Ba^{2+} current through the Ca^{2+} channel, does not alter the number of channels in patches, but markedly reduces the open-state probability in the guinea pig ventricular cells using open cell-attached patch clamp technique (Kaibara et al., J. Physiol. Soc. Jpn., 49, 507, 1987). We investigated the effects of H^+_i on the fast gating represented by C-C-O scheme and the slow gating related to the availability of the channel. In the fast open-close kinetics, H^+_i increased the slow time constant of the closed time, but little affected the open-probability within the kinetics. Lowering pH_i from 8.2 to 6.2 enhanced the percentage of blank sweeps from 27% to 60%, increased the duration of clusters of blank sweeps increased by 51%, and decreased the duration of non-blank sweeps by 64%. The above results indicate that H^+_i mainly affects the slow gating of the channel.

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ELECTRON MICROSCOPIC DISCRIMINATION OF SYNAPTIC VESICLES BY USING MONOCLONAL ANTIBODY.
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We tried to immunologically discriminate types of isolated synaptic vesicles (SVs) by using Mab 171B5 against SVP-38. The SVs were isolated from whole cerebral cortices of guinea pigs. Immunoreaction procedures were performed on the SVs which were first dispersed on a grid mesh covered with a Formvar membrane. The SV specimen was observed under electron microscopy after faint negative staining. The positive immunoreaction could be distinguished by halo formation of ferritin particles in periphery of the SV. The percentages of positive immunoreactions varied depending on SV sizes and SV types of spheroid (S-type) and flattened (F-type) SVs. For the SV classes of which diameters were 400 to 420 A, 500 to 520 A and 620 to 640 A, the positive percentages were much larger in the S-type than in the F-type. Whereas, the positive percentages in the SV classes of 440 to 460 A, 480 to 500 A, 520 to 540 A and 760 to 780 A were larger in the F-type than in the S-type. For both of the S-type and the F-type, the positive percentages were similarly less than 50% in the SV classes of 420 to 440 A, 460 to 480 A and 540 to 560 A. For other SV classes, the positive reactions were more than 50% for both of the S-type and the F-type. These results show that several types of the SVs are differentiated respectively in the S-type and the F-type.

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HOMOLOGY OF A MAJOR GLYCOPROTEIN IN PERIPHERAL MYELIN TO IMMUNOGLOBULIN-CELL ADHESION MOLECULE SUPERFAMILY.
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We determined the complete amino acid sequence of a major glycoprotein, P0 protein, in bovine peripheral myelin and examined its homology to immunoglobulin-cell adhesion molecule superfamily. A predicted secondary structure of the amino-terminal domain of the P0 revealed some similarities to all immunoglobulin domains consisting of two β-sheets with antiparallel β-strands. The amino-terminal domain including two cysteines showed a significant sequence homology with the variable domains of immunoglobulins and cell adhesion molecules by a computor homology search program. We concluded that the P0 protein is a member of the immunoglobulin-cell adhesion molecule superfamily and may be involved in primordial immunoglobulin domain. The amino-terminal domain of the P0 protein is located on the extracellular side and probably functions as an adhesion molecule to form the myelin intraperiod line.

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CHANGES OF BRAIN GANGLIOSIDE IN MATERNAL HYPERPHENYLALANINEMIC RATS.
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Maternal hyperphenylalaninemic (HyPhe) rats whose dams had received 2000 mg/kg of L-phenylalanine, t.i.d., from days 10 to 14 of pregnancy showed a considerable decrease in brain ganglioside contents. This phenomenon was examined further to determine what species of ganglioside are involved in the retardation of myelination and/or synaptogenesis that characterize HyPhe rats. The brain cortices were removed and the total lipid fraction was extracted with a chloroform-methanol mixture. The acidic glycolipid fraction separated by ion-exchange chromatography was subfractioned to mono-, di-, tri- and tetra-sialogangliosides by ganglioside mapping using a column of DEAE-Sephadex A25. Each subfraction was subjected to Iatrobeads column chromatography. An aliquot of each fraction was analyzed by HPTLC. The fraction that migrated more slowly than GM1 and GD1b were decreased while the fraction that migrated more slowly than GD1a was increased in the HyPhe rats. These ganglioside species may play an important role in myelination and/or synaptogenesis.

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DIFFERENCES IN ME-LI AND VIP-LI IN DISCRETE BRAIN REGIONS OF SEIZURE-NAIVE AND SEIZURE-EXPERIENCED EL MICE. KANAMATSU, T. AND HIRANO, S., Dept. 2nd Physiology, Toho Univ. School of Med., 5-21-16, Ohmori-nishi, Ohta-ku, Tokyo, 143.

In an attempt to elucidate the relationship between endogenous metionine-enkephalin(ME) and vasoactive intestinal polypeptide(VIP) with generalized seizures, we determined regional brain levels of ME-like and VIP-like immunoreactivity(ME-LI and VIP-LI) in El mice during and after seizures induced by repeated tossing stimulation. We also compared these changes to that in regional brain of control ddY mice after electroconvulsive shock(ECS) treatment. The level of ME-LI in the striatum of seizure experienced El mice(El+), sacrificed at 96 hours after three cosecutive seizures, was high, while levels of VIP-LI in the stratum and hypothalamus were low in comparison to that of seizure-naive El mice. In contrast, ECS treatment on ddY mice showed different results relative to those of El mouse seizures. These observations suggest that ME and VIP may play some role in El mouse seizures and that roles of these peptides in El mouse seizures may not be the same as in ddY mouse seizures induced by ECS.

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ROLE OF PROTEIN KINASE C IN THE RELEASE OF NEUROTRANSMITTERS. TANIYAMA, K. Dept Pharmacol., Kobe University School of Medicine, Kobe 650

The involvement of protein kinase C in the release of ^{3}H-acetylcholine (ACh), ^{3}H-norepinephrine (NE) and endogenous γ-aminobutyric acid (GABA) was studied in the strips of guinea pig small intestine. 12-*O*-tetradecanoyl phorbol 13-acetate (TPA), but not 4α-phorbol-12,13-didecanoate potentiated the A23187-evoked release of ACh and NE, and the potentiating effect of TPA was inhibited by polymyxin B. High K^{+}-evoked releases of ACh, NE and GABA in the presence of tetrodotoxin were also potentiated by TPA. These TPA-induced potentiation of the evoked release was greater at the low concentration of external Ca^{2+} (0.5 mM) than at the high concentration (2 mM), thereby indicating that the activation of protein kinase C potentiates the evoked release of neurotransmitters as the result in increasing apparent affinities for Ca^{2+}. The ouabain-evoked release of neurotransmitters was not altered by TPA. Since ouabain is considered to induce the non-vesicular release of neurotransmitter, the activation of protein kinase C by TPA may be involved in the vesicular release, but not the non-vesicular release of neurotransmitter.

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THE MECHANISM BY WHICH METHAMHETAMINE MODULATES STRIATAL DOPAMINE RELEASE:A BRAIN DIALYSIS STUDY. NAKAMURA,M.[1], ITANO,T., TOKUDA,M., MATSUI,H., HOSOKAWA,K.[1], & HATASE,O., Dept. of Physiol., & Neuropsych.[1], Kagawa Med. Sch., Kagawa, 761-07

An intracerebral dialysis method was used in the anaesthetized rat to further clarify the effect of methamphetamine(M-AMPH) to the striatal dopaminergic terminals. Cannula type dialysis probe was positioned in right striatum in vivo, and perfused with Ringer's solution(2μl/min). The dialysates collected for 10 min were analyzed for dopamine(DA) and related metabolites, DOPAC and HVA by HPLC-ECD.

Low dose of M-AMPH($2X10^{-10}$moles/min) induced gradual increase in DOPAC(+50.0%) and HVA(+61.5%), and their concentrations were kept higher than basal levels. DA showed the transit increase up to 20 min after DOPAC and HVA increase. High dose M-AMPH($1x10^{-8}$mole/min) induced drastic increase of the DA, DOPAC(+50.0%) and HVA(+68.0%) concentration. But after 60 min, both DOPAC and HVA were decreased suddenly below the basal levels.These findings suggest M-AMPH differently acts the striatal dopaminergic terminals depending on its concentration. At low dose M-AMPH, it only acts as a DA releaser from the vesicles. At higher concentration of M-AMPH, it acts not only a DA releaser but also a DA re-uptake inhibitor and monoamine oxidase inhibitor. This hypothesis must be further examined by the several drugs relating the DA metabolism such as apomorphine, pergiline and reserpine.

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NEUROTRANSMITTER RELEASE IN THE RAT STRIATUM AND HIPPOCAMPUS DURING CONVULSIONS INDUCED BY 2-GUANIDINOETHANOL (GEt). TODA, H.*, AKIYAMA, K.*, KABUTO, H.*, YOKOI, I., Department of Neurochemistry, Institute for Neurobiology, Okayama University Medical School, Okayama 700.

Differential pulse voltammetry was used together with treated carbon fiber electrodes to study the in vivo dopamine and 5-HT release in the rat striatum and hippocampus during convulsions induced by GEt (6 μmol, intraventricularly). The working electrode was implanted into the striatum (A;7.8, L;3, V;2.5mm) or hippocampus (A;3.2, L;2.5, V;2mm). Measurements were made under EEG recordings from epidural electrodes. In the striatum, the DOPAC peak increased to 150%, and in the hippocampus, the DOPAC peak increased extremely 3 hours after GEt administration. The hight of the 5-HIAA peak were not affected in both nuclei by GEt.

Contents of dopamine, DOPAC, 5-HT and 5-HIAA in the rat striatum and hippocampus 3 hours after GEt administration were measured by HPLC. Though contents of dopamine, 5-HT and 5-HIAA were not changed in both nuclei, contents of DOPAC increased to 170% in the striatum and to 3300% in the hippocampus. These data suggest that dopamine metabolism and release might increase during convulsions induced by GEt.

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PURIFICATION OF JELLYFISH VENOM AND ITS DEPOLARIZING ACTION. [1]ANRAKU, M., [2]KIHARA, H., [3]OHNO, M. AND [2]HASHIMURA, S. [1]Lab. of Physiol., Sch. of Allied Med. Sci. and [2]Dept. of Physiol., Fac. of Med., Kagoshima Univ., Kagoshima 890 and [3]Fac. of Sci., Kyushu Univ., Fukuoka 812.

The venom from jellyfish collected around the Truk Islands was purified by the combined use of CM-, DEAE-cellulose, Butyl Toyopearl, Hydroxylapatite and Sephadex G-200. The venom irreversibly depolarised frog skeletal and ventricle fibers, and rat diaphragm muscle depending on its concentration. Frog skeletal muscle was the most sensitive to the venom (0.006mg/ml~). The depolarization was a function of the external Na concentration and was reveresed only when Na ions were replaced by sucrose or choline. The addition of TTX(10^{-6}g/ml), 4-aminopyridine(1mM), Cd (5mM), La(0.5mM), nicardipine(2×10^{-5}M) or ouabain(0.5mM) showed no effect on this depolarization. These results suggest that the venom-induced depolarization does not use the channel for Na, K, and Ca, and also the venom does not interfere with the (Na,K) pump. On the other hand, the venom did not depolarized the membrane potential of the node of Ranvier and Onchidium neuron.

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EFFECT OF TENOTOMY, DENERVATION OR THEIR COMBINATION ON VARIOUS MUSCLE-RELATED PROTEINS IN RAT FAST AND SLOW MUSCLES. MATSUSHITA, H., YAMADA, S., SATOH, T. and #KATO, K., Dept. Physiol., Sch. Dent., Aichigakuin Univ., Kusumoto, Nagoya 464 and #Dept. Biochem., Inst. Develop. Res., Aichi Prefect. Colony kasugai 48003

We have measured the changes in concentration of four kinds of muscle-related proteins (β-type enolase, creatine kinase M, creatine kinase B and S-100ao) in the fast (extensor digitorum longus) and slow (soleus) muscles of the rat subjected to denervation, tenotomy or their combination. Denervation brought about a marked change in the concentration of β-enolase and CKB in the fast muscle, while tenotomy strongly affected CKM and S-100ao in the slow muscle. When denervation and tenotomy were performed in combination, the amount of change was usually not a simple sum of the results after denervation or tenotomy; in the slow muscle the concentrations of CKM and S-100ao were at the level of simple denervation, while the change in CKB was unexpectedly large. Furthermore, after combined denervation and tenotomy the relative amount of change in each marker protein became quite similar in the two kinds of muscle; the order of effectiveness being CKB > β-enolase > S-100ao > CKM. This might suggest that the innervating nerve and the tendon are regulating in a differential manner the concentration of various muscle-related proteins in the fast and slow muscles, but the total effect of nerve plus tendon on each marker protein is equipotent in the fast and slow muscles.

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MONOCLONAL ANTIBODY IMMUNOHISTOCHEMISTRY OF DEGENERATIVE AND RENEWAL PATTERN IN RABBIT OLFACTORY RECEPTOR NEURONS FOLLOWING UNILATERAL OLFACTORY BULBECTOMY.

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Staining pattern of the olfactory receptors of the lesioned side was compared with that of the intact side in the nasal septum at various postoperative periods (12 hours - 6 months) following lesion. Monoclonal antibodies, 112D5 and 114G12 (MAbs 2D5 and 4G12), produced against the rabbit olfactory bulb were used as histochemical markers. MAb 2D5 stained all receptor neurons including degenerating neurons, whereas MAb 4G12 showed a rapid decrease in immunostaining so that 4G12-positive cells disappeared within 7 days after lesion. 4G12-positive cells reappeared at 4 weeks following lesion. By three months, 4G12-positive cells were arranged in a line at the apical region of the superficial compartment of the receptor cell layer, suggesting a recapitulation of developmental pattern of the receptor neurons. Thereafter, the 4G12-positive cells increased progressively and staining pattern of the olfactory epithelium recovered by 6 months. MAb 4G12 is thus the first marker that is not specific to the olfactory neurons and that can be used to characterize certain embryonic traits during the degeneration and regeneration of the olfactory epithelium in the adult mammal.

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MONOCLONAL ANTIBODIES THAT RECOGNIZE THE CELL NUCLEI IN THE CENTRAL NERVOUS SYSTEM OF GUINEA PIG

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We produced monoclonal antibodies against the protein fraction extracted from the cell nuclei of guinea pig brains. The antibody 5E5 specifically recognized the cell nuclei of a subpopulation of neurons, but not those of other tissues such as heart, liver, intestine, kidney, muscle, and ovary. The antibody 2F7 selectively reacted the nuclear membranes of neurons and glia in the central nervous system. However the antibody 7F10 labeled the cell nuclei of all the tissues. With immunoblot analysis, it was revealed that 2F7 recognized a protein of M.W. 68K, whereas 7F10 recognized proteins of M.W. 18K and 36K. Although the antigen of 5E5 was unknown, the DNase treatment on the tissues sections markedly diminished the antigenecity of 5E5. These antibodies also crossreacted the rat tissues in a similar manner.

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MOLECULAR HETEROGENEITY OF MYELIN SPECIFIC ENZYME, 2',3'-CYCLIC NUCLEOTIDE 3'-PHOSPHODIESTERASE.

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2',3'-Cyclic nucleotide 3'-phosphodiesterase (CNPase) is a biochemical marker enzyme of myelin sheath in the nervous system. By the analyses using polyclonal and monoclonal antibodies to CNPase and limitting digestion with V8-Protease and Lysyl Endopeptidase, we have demonstrated a molecular heterogeneity of CNPase from the CNS and the PNS. Summarise are as follows; 1) CNPase of the CNS are consist of two molecules of different molecular weight. 2) The PNS CNPase is different from the CNS CNPase in terms of immunological antigeneicity. 3) CNPase in the retina has low molecular weight than that the CNS CNPase.

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FACILITATORY AND INHIBITORY EFFECTS OF cAMP ON THREE TYPES OF DOPAMINE RECEPTORS. TAKAHASHI, J., SASAKI, K., HAKOZAKI, S., MATSUMOTO, M., TAKASHIMA, K., & SATO, M. Dept. Physiol., Sch. Med., Iwate Medical University, 19-1 Uchimaru, Morioka, Iwate 020.

Application of dopamine (DA) on certain ganglion cells of Aplysia elicits three types of responses. One is slow hyperpolarization due to the increase in K^+-conductance (H_K-type), another is fast depolarization mainly due to the increase in Na^+-conductance (D_{Na}-type), and the other is slow depolarizing response due to the voltage-dependent increase in both Na^+ and Ca^{2+} conductances ($_VD_{Na,Ca}$-type).

During the intracellular application of cyclic AMP, the H_K-type of response was markedly depressed in a dose dependent manner, while $_VD_{Na,Ca}$-type of response was augmented significantly. However, cAMP did not affect the D_{Na}-type of response. Similar depressing effect of cAMP was observed on other K^+-dependent responses of ACh-, HA-, and FMRFamide-receptors. It was suggested that the increase in intracellular cAMP would inhibit the opening of K^+ channels while facilitate the opening of the voltage-dependent Na^+, Ca^{2+}-channels. Supported by the Ichirou Kanehara Fund and the Narishige Neuroscience Fund.

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CYCLIC GMP INDUCES INWARD CURRENT IN NEURON R14 OF APLYSIA. ICHINOSE, M., SAWADA, M. AND MAENO, T. Dept. Physiol., Shimane Med. Univ., Izumo, 693

The effects of cyclic GMP (cGMP) on the soma of neuron R14 in the abdominal ganglion of Aplysia were characterized. Cells were impaled with two glass microelectrodes filled with 3 M KCl for voltage- and current-clamping. Pressure ejected L-phenylalanyl-L-methionyl-L-arginyl-L-phenylalanineamide (FMRFamide) caused a slow inward current (peak at 0.5-1 min; duration, 2-3 min). The phosphodiesterase inhibitors IBMX (1 mM) and theophylline (1 mM) increased the FMRFamide-induced inward current, suggesting involvement of a cyclic nucleotide in this response. Injection of cGMP and cAMP into R14 induced an inward current and a conductance increase outward current, respectively. cGMP-induced inward current increased as the membrane holding potential was raised from -70 to -10 mV. The response decreased in Na^+-deficient seawater and disappeared in Na^+-free seawater. Changing $[K^+]_o$ (from 5 to 50 mM) had no effect. By reducing $[Ca^{++}]_o$ or $[Cl^-]_o$, amplitude of the response markedly enhanced, e.g., 271% of control in 2 mM $[Ca^{++}]_o$ and 430% of control in 109 mM $[Cl^-]_o$. These voltage- and ion-dependency of cGMP response are similar to those of FMRFamide-induced response. Present results show a possibility that cGMP mediates the FMRFamide-indued slow inward current in neuron R14 of Aplysia.

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PARTICIPATION OF CYCLIC AMP IN THE MODULATORY EFFECT OF NORADRENALINE ON THE DEPOLARIZING ACTIONS OF EXCITATORY AMINO ACIDS. MORI-OKAMOTO, J. AND TATSUNO, J., Dept. of Physiology, National Defense Medical College, Tokorozawa, Saitama 359

We have reported in intracellularly recorded cultured chick cerebellar neurons that noradrenaline(NA) iontophoresed or bath-applied slightly decreased spontaneous spike firings with a small hyperpolarization and a slight increase in input resistance, and in addition to these direct actions, NA enhanced the depolarizations induced by iontophoretically applied glutamate(Gl) or aspartate. For the purpose of examining a possible involvement of cyclic nucleotides in this modulatory NA effect, the effects of cyclic AMP(cAMP), dibutyryl cAMP(DBcAMP) and some compounds related to the cAMP system were intracellularly investigated in the cultured cerebellar neurons. NA-induced hyperpolarization and increase in input resistance, and the facilitatory effect of NA on the Gl response were all mimicked by cAMP applied intra- or extracellularly, and by extracellularly applied DBcAMP. The facilitatory effect of DBcAMP on Gl was further enhanced by iontophoretically applied theophylline and papaverine, phosphodiesterase inhitors. The effect of DBcAMP was also enhanced by bath applied forskolin, an adenylate cyclase activator, while it was inhibited by lanthanum, a potent inhibitor of brain adenylate cyclase. These results suggest that the modulatory effect of NA on the actions of excitatory amino acids in the cerebellum are mediated by the cAMP system.

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RE-EVALUATION OF THE EXCITATORY ACTION OF NMDA ON CEREBELLAR PURKINJE CELLS. SEKIGUCHI, M., OKAMOTO, K. AND SAKAI, Y. Dept. Pharmacology, National Defense Medical College, 3-2 Namiki, Tokorozawa, Saitama 359

Whether NMDA receptors are present and functioning in the cerebellum of mature animals has not yet directly investigated. For the purpose of examining the presence and absence of NMDA receptors in the cerebellum of mature animals, mRNA extracted from the cerebella of mature guinea pigs was injected into Xenopus laevis oocytes, and the properties of expressed "glutamate" receptors were investigated by intracellular recordings. mRNA-injected oocytes were dose-dependently depolarized by NMDA applied by superfusion at micromolar concentrations, and this response to NMDA was selectively blocked by APV, phencyclidine and ketamine. Voltage-clamp studies showed that NMDA-induced currents in mRNA-injected oocytes were suppressed by Mg^{2+} in a voltage dependent manner. The plateau potential component of climbing fiber responses induced in cerebellar slices and recorded from Purkinje cell dendrites was completely blocked by phencyclidine. These results clearly indicate that NMDA receptors are present in the cerebellum of mature guinea pig.

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EXCITATORY AND INHIBITORY DUAL ACTION OF GABA ON THE NEUROTRANSMISSION IN THE GUINEA PIG SUPERIOR COLLICULUS SLICES. ARAKAWA,T., OKADA,Y. Dept. Physiol., Kobe Univ. Sch. Med., Kobe 650

Laminar distribution of GABA in the superior colliculus(SC) of the guinea pig was determined. It was found that the highest amount of GABA was contained in the upper half of the superficial gray layer(SGL) of SC (37.4+ 1.1mmol/kg dry). To investigate the function of GABA in SGL,the effect of GABA on neurotransmission(postsynaptic potential -PSP) in SGL was studied using SC slices. Muscimol($GABA_A$ agonist), and baclofen($GABA_B$ agonist) were also tested. Bath-applied GABA at 100uM-1mM enhanced the amplitude of PSP in SGL in a dose dependent manner, and at over 1mM it depressed the PSP dose-dependently. A similer pattern of response was observed with muscimol (0.1-1uM, enhancement; 10uM, depression). However baclofen only inhibited the PSP(0.1-1uM). At 0.5mM of nipecotic acid, the excitatory effect of GABA was enhanced. With 1uM bicuculline the dose-response curve of GABA was shifted to tht right and the excitatory effect was also enhanced. These results indicate that GABA has a dual action on neurotransmission in SGL, excitatory effect, possibly mediated by $GABA_A$ receptors, and an inhibitory effect mediated by both $GABA_A$ and $GABA_B$ receptors.

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EFFECTS OF DEPRIVATION OF OXYGEN AND GLUCOSE ON THE NEURAL ACTIVITY AND THE LEVEL OF HIGH-ENERGY PHOSPHATES IN THE HIPPOCAMPAL SLICES OF IMMATURE AND ADULT RAT. OKADA,Y., KAWAI,S., YONETANI,M, and YONEDA,K., Dep. Physiol., Kobe Univ. Sch. Med., Chuo-ku, Kobe 650

Hippocampal slices(300-400μm thick) were prepared from 4,7,10 day old and adult rat. Postsynaptic potential(PSP) was elicited in the pyramidal cell layer of CA_1 area by stimulating the Schaffer's collateral. ATP, creatine-Phosphate(CrP) and lactate in the slices were determined during deprivation of oxygen and glucose. After the onset of deprivation PSP of the slices of 4,7,10 day old and adult rat was completely abolished in 22, 9, 5.6, and 4.6 min, respectively. From the change of the level of ATP, CrP and lactate during deprivation, the energy use rate were calculated. The rate(~Pmmol/g DNA/min) in 4,7,10 day old and adult slices was 1.09, 2.93, 3.42 and 4.75, respectively. Thus the differences in the energy use rate in immatue and mature brain corresponded well with those of the decay time of PSP during deprivation. The level of ATP at the time of abolishement of PSP of 4,7,10 day old and adult sample was 23, 39, 51 and 61% of the initial value. This indicates that the functional pool of ATP in the immature brain may be larger than that in the adult.

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EFFECT OF APV(2-AMINO-5-PHOSPHONOVALERATE) ON LONG-TERM POTENTIATION IN THE SUPERIOR COLLICULUS SLICES FROM THE GUINEA PIG MIYAMOTO,T., OKADA,Y. Dep. Physiol., Kobe Univ. Sch. Med., Kobe 650

Slices (400-600um thick) of superior colliculus (SC) from guinea pig were prepared by cutting sagittally and incubated in the standard medium. Postsynaptic potential(PSP) was recorded in the superficial grey layer(SGL) of SC by stimulating optic layer(OL). Tetanic stimutation increased the amplitude of PSP in SGL to 150-170% of control value and evoked long-term potentiation(LTP). Tetanic stimulations were applied to the OL at frequency of 50Hz and 100Hz, for 1,10, 20, and 30 sec. Tetanus of 50Hz and 20sec was the most suitable for LTP formation. Application of 500uM of APV with 50Hz and 20sec tetanic stimultaiton did not show the LTP formation. However, when APV was removed from the medium, the amplitude of PSP was increased to 150% of the control value in 15min. Thus APV, a specific NMDA receptor antagonist masked the appearance but did not prevent the formation of LTP itself. These results indicate that LTP formation in SC can be reliably recorded in in vitro preparation and suggest that presynaptic plasticity as well as postsynaptic NMDA receptor is involved in the formation of LTP in SC.

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HIPPOCAMPAL LONG-TERM POTENTIATION INDUCED BY LOW-FREQUENCY STIMULI IN MAGNESIUM-FREE CONDITION AND ITS BLOCKAGE BY GABA. Yoshioka, N. and Sakuari, M. Dept. of Physiol., Fac. of Med. Univ. of Tokyo, Hongo 7-3-1, Bunkyo-ku, Tokyo.

An attractive model has been proposed to explain the mechanism of LTP: opening of NMDA-receptor channels (NMDA-RCs) is of a primary importance, through which Ca^{2+} enters postsynaptic cells, leading to LTP; the role of postsynaptic depolarization is only to eliminate the voltage-dependent blockage of NMDA-RCs by Mg^{2+}. Accordingly, two predictions can be made from this model in Mg^{2+}-free condition: (1) high-frequency stimulation is not necessary, (2) depolarization is not required, either. To test these predictions, experiments were performed on CA1 area of hippocampal slices (CA3 was cut apart) prepared from guinea pigs. Both stimulation and recordings ("population EPSPs") were made in the stratum radiatum. Low-frequency stimuli (1 Hz, 150 times), which caused depression in normal Ringer solution, induced LTP in Mg^{2+}-free medium. This is consistent with the prediction (1). This potentiation was completely blocked by specific NMDA-R antagonist, APV. However, when GABA was iontophoretically applied during conditioning stimulation, this potentiation was prevented. This is contradictory to the prediction (2). Thus, the role of postsynaptic depolarization in induction of LTP may not be only to eliminate voltage-dependent blockage of NMDA-RCs by Mg^{2+}

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QUISQUALATE AND NMDA RECEPTORS ARE ESSENTIAL FOR INDUCTION OF HIPPOCAMPAL LONG-TERM FACILITATION. KATO, H., KATO, K., URUNO, K., IZUMI, Y. AND ITO, K. Dept. Physiol., Yamagata Univ. Sch. Med., Yamagata 990-23

In our recent research, it was demonstrated that the long-term facilitation (LTF) in CA1 neurons of guinea-pig hippocampal slices was induced by a 5 min perfusion with a conditioning solution (CS) containing glutamate (0.1mM), high-K^{+} (10-15mM) and no Mg^{++} and that the CS lacking one of these 3 factors failed to produce LTF. In the present study, the glutamate in the CS was replaced with its receptor agonists, N-methyl-D-aspartate (NMDA), quisqualate (QA) and kinate, to examine the receptor subtypes of glutamate involved in producing LTF.

Of the 3 receptor agonists, only high-concentration of QA (10μM) produced LTF which was blocked by simultaneous application with 2-amino-5-phosphonovalerate (APV, 50μM), a selective NMDA receptor antagonist, suggesting that both QA and NMDA receptors play a role in producing LTF. When both QA(1μM, the concentration not enough to induce LTP by itself) and NMDA (1μM) were applied in this order, LTF was induced with a mean amplitude increase of the population spike by 94% (n=6). However, the reversed order or simultaneous application of QA and NMDA failed to induce LTF. There results indicate that both QA and NMDA receptors play an essential role in the induction of LTP.

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MECHANISM OF THE LONG-TERM POTENTIATION OF TRANSMITTER RELEASE CAUSED BY TETANIC STIMULATION OF PRENERVE FIBRES IN BULLFROG SYMPATHETIC GANGLIA. MINOTA,S., KUBA,K. and KUMAMOTO,E. Dept. Physiol., Saga Med. Sch., Saga.

The mechanism of the long-term potentiation of transmitter release (pre.-ltp) in bullfrog sympathetic ganglia was examined by recording intracellularly the fast excitatory postsynaptic potentials (fast epsps). The frequency of miniature epsps increased for more than one hour after tetanic stimulation of the preganglionic nerves (33 Hz, 10-30 sec). The magnitude of a short-term facilitation of fast epsps induced by paired stimuli (100 ms interval) in a low Ca^{2+} and high Mg^{2+} solution was decreased during the generation of pre.-ltp. A calcium ionophore, A-23187, increased the amplitude and quantal content of fast epsps, but reduced the facilitation. A Ca^{2+}-chelating agent, quin 2/AM, reduced the amplitude and quantal content of fast epsps. Activators of protein kinase C, OAG and phorbol dibutyrate, increased the amplitude and quantal content of the fast epsps and the frequency of miniature epsps. The effect of phorbol ester was much greater than that of OAG.

These results suggest that the pre.-ltp is induced by a sustained rise in the basal level of free Ca^{2+} and also by possible activation of protein kinase C in the presynaptic nerve terminals.

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CHANGES OF NEUROTRANSMITTER RECEPTORS IN THE RAT BRAIN BY AGING. ASANUMA, A., HORIKOSHI, T., YANAGISAWA, K. AND GOTO, S.* Dept. of Physiol., Sch. of Dent. Med., Tsurumi Univ., 2-1-3 Tsurumi, Tsurumi-ku, Yokohama 230, *Dept. of Biochem., Sch. of Pharm. Sci., Toho Univ., 2-2-1 Miyama, Funabashi 274.

We used the Xenopus oocyte translation system of exogenous mRNA to examine the changes of the neurotransmitter receptors in the rat central nervous system (CNS) by aging. From young (3 months old) and aged (19 months old) rats, the CNS was cut out and separated into 4 parts; cerebrum, cerebellum, brain stem and spinal cord. Poly(A)$^+$-RNA from the cerebrum or the brain stem of each age rat was injected into Xenopus oocytes (stage IV or V). Two to three days after the injection of mRNA, current responses to 0.5 mM GABA, 5 mM glycine, 1 mM kainate, 0.5 mM NMDA with 3 μM glycine and 0.1 mM quisqualate were obtained under ordinary voltage clamp condition at holding potential of -60 mV. Saturation responses can be obtained with these concentrations of amino acids. The peak amplitude of these current responses in the young-rat-CNS-mRNA injected oocyte were compered with that in the aged-rat-CNS-mRNA injected oocytes. So far, we could not find any significant differences in the response between these oocytes. But this result might be obtained by rather low activity of exogenous mRNA.

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THE GLYCINE-GATED CHLORIDE CURRENT IN ACUTELY ISOLATED RAT HYPOTHALAMIC NEURONES. AKAIKE, N., OOMURA, Y., KANEDA, M. AND IKEMOTO, Y. Dept. Physiol., Fac. Med., Kyushu Univ., Fukuoka 812.

Electrical and pharmacological properties of glycine-induced currents were studied in single hypothalamic neurones acutely isolated from young and adult rats using a concentration-clamp technique. the glycine-induced current reversed at the Cl^- equilibrium potential. Glycine responses increased sigmoidally in a dose-dependent matter. The current desensitization occurred completely at all concentrations within 40 sec. The glycine-induced conductance exhibited a striking voltage-dependency at more negative membrane potentials than -50 mV, and reached to a steady-state value with hyperpolarization beyond -110 mV. Both the activation and inactivation phases of glycine-induced currents consisted of a double exponential with the concentrations used. The time constants of the two kinetic components in both phases decreased with increasing glycine concentration. The recovery process of glycine response was concentration-independent. The blockade of the glycine response by strychnine was mixed, both competitive and non-competitive while that by picrotoxin was non-competitive. Strychnine appears to act both at the agonist binding site and the chloride channel site.

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ENFLURANE DIFFERENTIALLY AFFECTS TRANSMITTER-INDUCED CHLORIDE CURRENTS IN ISOLATED APLYSIA NEURONS. IKEMOTO, Y., YOSHIDA, A. AND AKAIKE, N. Department of Physiology, Faculty of Medicine, Kyushu University, Fukuoka 812, Japan.

The mechanism of the action of volatile anesthetics on the central nervous system is unknown. The unitary hypothesis of anesthetic action is based on good correlation of lipid solubility and potency of anesthetics and on the chemical and structural diversity of the agents. We examined the effects of enflurane, a commonly used volatile anesthetic, on transmitter-induced chloride currents (I_{Cl}) of isolated Aplysia and rat neurons using the 'concentration clamp' technique. Clinical concentrations (0.4 to 2 mM) of enflurane increased the peak amplitude of the Glu-induced I_{Cl} and decreased that of the ACh-induced I_{Cl}. Desensitization of the Glu-I_{Cl} became faster, whereas that of the ACh-I_{Cl} was not affected. These differential effects of enflurane on the I_{Cl} in a single neuron suggest the existence of specific steps in the process of the activation and desensitization of channels, at which enflurane exerts differential effects on the postsynaptic currents. Similar results were obtained with isolated rat neurons.

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ADRENALINE INHIBITS CHOLINERGIC TRANSMISSION IN VESICAL PARASYMPATHETIC GANGLIA OF THE RABBIT. TSURUSAKI, M. AND AKASU, T., Dept. Physiol., Kurume Univ. Sch. Med., 67 Asahi-machi, Kurume 830

Intracellular recordings were made from neurons of vesical parasympathetic ganglia (VPG) isolated from the rabbit urinary bladder wall and maintained, in vitro. Adrenaline (Ad; 5 nM-10 μM) blocked the orthodromic action potentials elicited by preganglionic nerve stimulation. The fast excitatory postsynaptic potential (EPSP) mediated through nicotinic receptors was reduced by Ad and noradrenaline. Clonidine, an α_2-adrenoceptor agonists also inhibited the amplitude of fast EPSP. However, isoproterenol, a β-adrenoceptor agonist produced no inhibition of the fast EPSP. Yohimbine and idazoxan, α_2-adrenoceptor antagonists, selectively blocked the inhibitory action of Ad on the fast EPSP. Ad had no effects on the depolarization induced by iontophoretically applied acetylcholine (ACh), suggesting that Ad does not suppress the sensitivity of nicotinic receptors of the postsynaptic membrane. Ad decreased the quantal content of fast EPSPs. The inhibition of the fast EPSP by Ad may be due to a depression of the amount of ACh released from presynaptic nerve terminals. It is concluded that Ad inhibits ganglionic transmission in the rabbit VPG neurons acting on the presynaptic α_2-adrenoceptors.

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AFTERHYPERPOLARIZATION AND AFTERDEPOLARIZATION OF THE ACTION POTENTIAL IN NEURONS OF RABBIT VESICAL PARASYMPATHETIC GANGLIA. NISHIMURA, T., TOKIMASA, T. AND AKASU, T., Dept. Physiol., Kurume Univ. Sch. Med., 67 Asahi-machi, Kurume 830

Intracellular recordings were made from neurons of rabbit vesical parasympathetic ganglia (VPG). In a majority of VPG neurons, the action potential was followed by fast and slow afterhyperpolarizations (AHPs). Both fast and slow AHPs were nullified at equilibrium potential for potassium ions and were depressed by removal of extracellular calcium ions. Tetraethylammonium (TEA, 1-5 mM) depressed the fast AHP, while it augmented the slow AHP. Curare (100 μM) blocked only the slow AHP. In some cells, the single action potential had no detectable AHP. A repetitive firing of action potential evoked a depolarizing potential, the afterdepolarization (ADP), associated with a decreased input resistance. The ADP increased the amplitude by membrane hyperpolarization, while it decreased by depolarization. The estimated reversal potential of the ADP was -35 mV. The amplitude of the ADP was increased in low chloride solution and by intracellular injection of chloride ions. Removal of calcium ions from superfusing solution abolished the ADP. No sodium dependent properties were seen in the ADP. These results suggest that a calcium-dependent chloride conductance may underlie the generation of the ADP.

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α2-AGONISTS BLOCK INWARD CALCIUM-CURRENT IN PARASYMPATHETIC NEURONS OF THE RABBIT URINARY BLADDER. TOKIMASA, T., TSURUSAKI, M., NISHIMURA, T. AND AKASU, T., Dept. Physiol., Kurume Univ. Sch. Med., 67 Asahi-machi, Kurume 830

Intracellular recordings were made from vesical pelvic ganglion cells of the rabbit. Membrane currents were measured with a single-electrode voltage-clamp method in a Krebs solution containing tetrodotoxin (1 μM). An inward calcium current was separated from potassium currents by intracellular injection of cesium ions and by bath application of 20 mM tetraethylammonium. Inward rectification at potentials negative to -80 mV (presumably potassium current) was also blocked by extracellular cesium (2-4 mM). Brief (30-200 ms) depolarizing command pulses from the holding potential of about -50 mV to potentials less negative than -20 mV evoked the calcium current. The calcium current was followed by an inward tail current due to an efflux of chloride ions activated by the calcium current. UK-14304 (0.1-10 μM), a specific α_2-agonist, depressed both the calcium current and the chloride tail current in a dose-dependent manner (ED50 $\sim$ 1 μM). The depression of the calcium current by UK-14304 could explain the depression of the calcium spike by noradrenaline (1-30 μM) since noradrenaline action on the calcium spike was completely antagonized by a specific α_2-antagonist RK-781094 (1 μM) or yohimbine (1 μM).

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EFFECTS OF LOCAL ANESTHETICS AND ADENOSINE TRIPHOSPHATE ON THE CAFFEINE INDUCED RHYTHMIC HYPERPOLARIZATION IN THE SYMPATHETIC GANGLION CELLS. SOMEI, K., RIKER, W.K.*, SATO, T., SAWANO, H., AND SUZUKI, T.A.
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Blocking characteristics of local anesthetics on the caffeine-induced rhythmic membrane hyperpolarization(RMH) due to oscillatory increase in the Ca^{2+}-activated potassium conductance(G_{K^+}-Ca^{2+}) was investigated intracellularly in sympathetic ganglion cells of the bullfrog. Either one of 3 mM procaine, 3 mM cocaine, or 3.6 mM lidocaine depressed in amplitude and frequency of the RMH induced by 2 mM caffeine. The blocking potencies of these local anesthetics were in the order of procaine > cocaine > lidocaine.

1 mM ATP restoed in amplitude, but not in frequency, of the RMH which had been depressed by local anesthetics, although the same concentration of ATP alone caused neither reduction nor augmentation of the caffeine-induced RMH.

These results suggest that ATP might compensate G_{K^+}-Ca^{2+} reduction by local anesthetics.

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HEART EXCITATORY NEURONES IN THE AFRICAN GIANT SNAIL, *Achatina fulica* Férussac. KOBAYASHI, M. AND FURUKAWA, Y. Physiol. Lab., Fac. Integrated Arts and Sciences, Hiroshima Univ., Hiroshima 730.

Seven heart regulatory neurones were identified in the suboesophageal ganglion (SOG) of *Achatina fulica*. Among these neurones, a periodically oscillating neurone (PON) was the most effective heart excitor. Two identified cerebral ganglion (CG) neurones were found to have excitatory connections with some of the SOG neurones including PON. Firings of the CG neurones induced a slow depolarizing potential in PON. By the experiments of ionic substitution and of Cs^+-injection, this depolarization was found to be due mainly to the decrease of background K^+-conductance. Serotonin (5-HT) produced a similar slow depolarization in PON which was also mainly owing to the decrease of background K^+-conductance. Both depolarizations induced by the CG neurones and 5-HT were depressed by a 5-HT antagonist, methysergide. In some preparations, a transient increase of conductance was induced in PON by the firing of the CG neurones. This component was assumed to depend on Ca^{2+}-current, since it was augmented by EGTA injection. 5-HT also increased the voltage-dependent Ca^{2+}-conductance in PON. These results suggest that the neurotransmitter of the two CG neurones is 5-HT. Physiological meanings of this synaptic action were considered.

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ANALYSIS OF INHIBITORY EFFECTS OF N-β-PHENYLPROPIONYL-L-TYROSINE (BPLT) ON THE MEMBRANE POTENTIAL IN A SNAIL NEURONE. FUNASE, K., SUN, X. P.*, TAKEUCHI, H., [1]ARIYOSHI, Y.* 1st Dept. Physiol., Gifu University School of Medicine, Tsukasa-machi, Gifu 500; [1]Central Reaseach Laboratories, Ajinomoto Co., Suzuki-cho, Kawasaki 210.

The inhibitory effects of BPLT, a derivative of L-Phe-L-Tyr, on the membrane potential in a snail neurone was analysed under voltage clamp. A long-lasting outward current, with a membrane conductance increase, was induced by the compound at the holding voltage of -55 mV, but the current-voltage relationships affected by BPLT ($I\text{-}V_{BPLT}$) never intersected that of its control ($I\text{-}V_{cont}$) in a physiological state. The current induced by BPLT (I_{BPLT}), which is the difference between $I\text{-}V_{BPLT}$ and its $I\text{-}V_{cont}$, was shifted according to the extracelluler K^+ concentrations, but the reversal potential of I_{BPLT} was not concordant to the K^+ equilibium potential (E_K), indicating that I_{BPLT} is composed of a K^+ current ($I_{BPLT\text{-}K}$) and another one ($I_{BPLT\text{-}NK}$). I_{BPLT} contained no Cl^- current, and was hardly influenced by Na^+-, Ca^{2+}- or Mg^{2+}-free media. Under ouabain, $I\text{-}V_{BPLT}$ intersected its $I\text{-}V_{cont}$ near E_K, indicating that $I_{BPLT\text{-}NK}$ is brought about by electrogenic sodium pump activation ($I_{BPLT\text{-}pump}$). With TEA, the $I_{BPLT\text{-}pump}$ was isolated, being hardly voltage dependent.

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STRUCTURE-ACTIVITY RELATIONSHIPS OF JORO SPIDER TOXINS ON GLUTAMATE RECEPTORS. KAWAI, N., MIWA, A., SHIMAZAKI, K., NAKAJIMA, T.* Dept. Neurobiol. Tokyo Metropolitan Inst. Neurosci. 2-6, Musashidai, Fuchu, Tokyo 183 and Dept. Analytical Chem. Faculty Pharmaceut. Sci. Univ. Tokyo, 7, Hongo, Bunkyoku, Tokyo 113.

We have characterized the structure of spider toxin (JSTX) which blocks the glutamate receptors (Aramaki et al. 1986). According to the toxic principles, JSTX and the related compounds were chemically synthesized. Activities of these synthetic compounds were compared using lobster neuromuscular synapses. A synthetic analog, composed of 2,4-dihydroxyphenylacetyl-asparaginyl cadaverine (C1) had suppressive action on EPSPs. However, the effect was much less potent than JSTX and easily reversed by washing the preparation. Another analog (C2) containing 2,4-dihydroxyphenylacetyl-asparaginyl spermine gave more potent suppression on EPSPs than C1. Effect of C2 was slowly reversible by washing for long time. These results along with the data using other analogs suggest that among the structure of spider toxin, 2,4-dihydroxyphenylacetyl asparaginyl part may be essential for suppressive action, whereas the remaining part containing polyamine chains was related to the affinity of the toxin to the glutamate receptor.

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SYNAPTIC MODULATION OF DORSAL UNPAIRED MEDIAN (DUM) NEURONS IN THE THORACIC GANGLION OF THE COCKROACH. WASHIO, H., MARUYAMA, M. and TANAKA, Y., Dept. Neurosci. Mitsubishi-Kasei Inst. Life Sci., Machida, Tokyo 194, R & D Lab. Hoechst Japan Ltd. Kawagoe, Saitama 350.

On the dorsal surface of the metathoracic ganglion eight large somata of DUM neurons were stained with neutral red. Stimulation of one of these DUM neurons (DUM 3,5,6) intracellularly during production of tetanus on the coxal depressor muscle reduced the tetanus tension and induced a rise in the basal tension of this muscle. Our pharmacological study showed that the reduction in the amplitude of the tetanus tension might be mediated by octopamine.

On the other hand, the increase in the basal tension was elicited by the superfusion of proctolin at the concentration as low as 10^{-9} M similar to that produced by the DUM stimulation. The biological responsiveness to the cell extract is reduced by dilution in a way which parallels changes in the responsiveness to different concentrations of authentic proctolin. Also the single peak of proctolin like bioactive materials which were partially purified from the cell extract coincided with that of authentic proctolin. The results show the possible involvement of proctolin in the DUM neuron with the increase in the basal tension of the coxal muscle in the cockroach.

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Membrane holding potential-effect on ACh-binding force and separating energy with their receptors in frog sensory neurones.

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Acetylcholine (ACh)-induced clamp currents (Na^+) were measured at different holding potentials of membrane voltage clamped condition by "suction pipet method" in single sensory neurones of the frog, under Na^+ ions only permeable through cell membrane with (Na^+)-outside of 112 mM. ACh-induced Na^+-current increased linearly with log ACh concentrations,their magnitude. Constant concentration of ACh-induced clamp currents increased linearly with membrane holding potentials (V-H) from negative to posisitive during -20 to +20 mV, with reversal potential of about -7 mV. Their plateau like currents increased with holding potential raised, both in negative and positive. Caliculated values of the binding force for single receptor site at the plateau like current was almost the same the value at the current peak site. The calculated values of binding force per receptor increased in parabolic shape with increase of holding potentials both negative and positive directions. The valaues of binding force per receptor was 120×10^{-15} watts at V-H +50 mV and 90×10^{-15} watts at V-H -50 mV. The caliculated values of ACh-receptor separation energt per receptor was 60×10^{-15} J at V-H +50 mV and 45×10^{-15} J at V-H -50 mV.

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CHOLINE UPTAKE AND ITS METABOLISM IN EXCISED RAT SUPERIOR CERVICAL SYMPATHETIC GANGLIA.

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Choline uptake and its metabolism in excised rat superior cervical sympathetic ganglia (SCG), in which contains abundant cholinergic nerve terminals, were examined during aerobic incubation in standard bathing solution (SBS) containing ^{3}H-choline (Ch). ^{3}H-Ch, after taken up into the SCG through high affinity choline uptake (HAChU) system, was converted not only in acetylcholine (ACh) but also in phosphocholine (P-Ch) and phosphatidylcholine (Ptd-Ch, lecithin) at very rapid rate during incubation. Omission of $[Na^+]_o$ caused clear reduction of HAChU, ACh and Ptd-Ch synthesis in SCG. Hemicholinium-3 (HC-3), a specific inhibitor of HAChU, produced a strong inhibition of ^{3}H-incorporation not in Ptd-Ch but in ACh. Addition of high K^+ to the medium decreased ^{3}H-Ch uptake by HAChU and the incorporation into ACh, P-Ch and Ptd-Ch fractions in SCG during short period (30 min) incubation. However, when SCG was incubated in the SBS containing ^{3}H-Ch for much longer period (3 h), enormous ^{3}H-incorporation was found especially in Ptd-Ch fraction by high K^+-stimulation. These results strongly suggest that added Ch in the medium is actively taken up into the SCG, and is metabolized for the synthesis of the neurotransmitter, ACh, but also for the synthesis of Ptd-Ch, then it stored inside of the cell membranes.

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G PROTEINS REGULATE POTASSIUM CONDUCTANCE IN NEURONS OF SUBMUCOUS PLEXUS OF THE GUINEA-PIG CECUM.

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The effects of the agents, which affect the intramembrane and cytoplasmic messengers, on the slow synaptic potentials of submucous neurons were studied by intracellular recordings. Intracellular injection of GTP-γ-S produced irreversible changes in both the slow EPSP and slow IPSP, which were associated with a decrease and an increase in the potassium conductance, respectively. Repeated evocation of the slow EPSP during GTP-γ-S injection induced the membrane depolarization reaching the levels between -30 and -45 mV and the slow EPSP was almost eliminated. On the other hand, when the slow IPSP was repeatedly elicited during GTP-γ-S injection, the membrane progressively hyperpolarized and reached the level near the potassium equilibrium potential. Forskolin, cholera toxin, dibutyryl cyclic AMP and 3-isobutyl-1-methylxanthine all produced the membrane depolarization, and the slow EPSP and slow IPSP reduced and increased, respectively. It is concluded that the reduction in the potassium conductance underlying the slow EPSP is mediated by the activation of Gs and the corresponding cyclic AMP accumulation, while the increase in the potassium conductance underlying the slow IPSP is produced by the activation of Gi.

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QUANTAL NATURE OF INHIBITORY SYNAPTIC CURRENT RECORDED WITH PATCH CLAMP METHOD FROM MAMMALIAN SPINAL MOTONEURON IN SLICE. TOMOYUKI TAKAHASHI Dept. Physiol., Kyoto University, School of Medicine, Sakyo-ku Yoshida, Kyoto 606

Whole cell patch clamp recording was made from motoneurons of neonatal rat spinal cord. The motoneurons were viewed under Nomarski optics in thin slices and the membrane surface was cleaned with a jet stream of saline applied locally. Local stimulation of the neighboring internuncial neurons evoked the inhibitory postsynaptic currents(i.p.s.c.s) in motoneurons. The latency of the i.p.s.c.s was less than 1 msec at 37 ℃ and was costant in tetanic (50 Hz) stimulation indicating the monosynaptic nature of the i.p.s.c.s. The amplitude of the i.p.s.c.s showed all-or-none behaviour against graded stimulus intensities suggesting that single neuron was stimulated. When Ca/Mg ratio of the perfusing solution was changed from 2 to 0.5 by replacing Ca with Mg, failure of the i.p.s.c. was markedly increased and the mean amplitude of the i.p.s.c.s was decreased. In this condition,the amplitude histogram of the i.p.s.c. showed satisfactory fit to binomial statistics. It is concluded that the release of inhibitory transmitter occurs in quantal steps in mammalian central neurons.

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RELATIONSHIP BETWEEN FLUCTUATIONS OF EVOKED AND SPONTANEOUS TRANSMITTER RELEASES UNDER LOW CALCIUM CONDITION. TAKEUCHI, N., TAKIKAWA, Y., MINO, H. AND YANA, K. Dept.Physiol., Sch. Med., Juntendo Univ., Hongo, Tokyo 113

Relationships between evoked quantal release and spontaneous quantal release (m.e.p.p) were investigated at the frog neuromuscular junction. For exact measurement of the number of quanta evoked by each nerve stimulus, Ca ion concentration in the solution was lowered (0.15 - 0.27 mM) and Mg ions were added (0.1 - 1.0 mM). Under stationary condition in these solutions, correlation coefficients between the series of the evoked release (stimulus interval, 3 sec) and the spontaneous release for the preceeding 1 sec were mostly ranged within $\pm$ 0.2. Relative values of the mean quantal contents evoked by the second stimulus of double stimuli (interval, 0.06 - 1 sec) were statistically not correlated to the probabilities of the m.e.p.p. occurrence in the corresponding time.

When theophylline (1 mM) was applied, the spontaneous release was markedly increased, while significant change in the evoked quantal numbers was not observed with stimulus interval of 3 - 6 sec.

These results suggest that the release sites for the spontaneous and evoked transmitter release might be, at least a few part, different qualitatively or spatially at the nerve ending membrane.

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EFFECTS OF Ba IONS ON NEUROMUSCULAR TRANSMISSION. HARA, N.* AND MAENO, T. Centl. Res. Lab. and Dept. Physiol., Shimane Med. Univ., Izumo, Shimane 693

Ba ions have been known to exert differential effects on neuromuscular transmission; facilitatory on miniature endplate potentials (MEPPs) and inhibitory on endplate potentials (EPPs). The frequency of spontaneously occurring MEPPs is increased with application of Ba ions, which is augmented further by repetitive stimulation of the motor nerve. Although stimulation evoked EPPs are abolished after total replacement of Ca with Ba, addition of Ba in Mg-Ringer increases post-tetanic potentiation (PTP) and frequency augmentation of EPP. Using various electrophysiological techniques, these interesting actions of Ba ions on neuromuscular transmission were investigated to explain in terms of mobilization of transmitter quanta readily available for release. Specific actions of Ba ions found in the present experiments were: (1) increase in frequency dependent component of frequency augmentation, (2) increase in augmentation phase of PTP, (3) elevation of depressed plateau phase during tetanic stimulation, and (4) acceleration of the rate of recovery from depression. Since Ca ions have none of these actions, the above effects of Ba ions cannot be attributed to direct actions on Ca-depended processes.

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ACTIVATION OF PROTEIN KINASE C PROMOTES GLUTAMATE MEDIATED TRANSMISSION AT THE NEUROMUSCULAR JUNCTION OF THE MEALWORM, TENEBRIO MOLITOR. YAMAMOTO, D., Lab. Neurophysiol., Mitsubishi-Kasei Inst. Life Sci., Machida, Tokyo 194. Japan

Protein kinase C activators, 1,2-oleoylacetylglycerol (OAG) and 12-*O*-tetradecanoylphorbol 13-acetate (TPA) stimulate the evoked and spontaneous transmitter releases from the presynaptic terminal, evidenced by an increase in the quantum content estimated by the number of failures of extracellular excitatory postsynaptic potentials (EPSPs), and in the frequency of miniature EPSPs. OAG and TPA act on the postsynaptic membrane to enhance responses to the transmitter L-glutamate. They increased the apparent maximum of the ionophoretic dose-response curve for glutamate-induced depolarization, without affecting the reversal potential and the voltage-dependent decay rate for the excitatory postsynaptic current under voltage-clamp conditions. The postsynaptic effect of OAG and TPA is distinctly different from that of activators of cyclic nucleotide-dependent protein kinases, such as octopamine, forskolin, CPT-cyclic AMP (8-(4-chlorophenylthio)adenosine 3',5'-cyclic monophosphate), and 8-bromo-cyclic GMP (8-bromoguanosine 3',5'-cyclic monophosphate which decreased the postsynaptic sensitivity to L-glutamate. I suggest that the responsiveness of the receptor to L-glutamate is under the control of these counteracting enzyme systems in the insect neuromuscular junction.

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TRANSMITTER RELEASE AT FROG END-PLATE LOADED WITH A Ca-CHELATOR, BAPTA: SOME CONDITIONS AUGMENT THE RELEASE INDEPENDENTLY OF INTERNAL Ca ION. TANABE, N. & *KIJIMA, H. Dept. Biol., Daiichi College Pharm.Sci., Fukuoka 815 & *Dept. Biol., Fac.Sci., Kyushuu Uni., Fukuoka 812

Transmitter release from the nerve terminal is regulated by internal Ca ion. A number of conditions have been reported to augment transmitter release, most of which have been interpreted to be due to a change in internal Ca ion. However, the mechanisms of Ca regulation or the existence of other factors possibly regulating transmitter release remain to be elucidated. We loaded a Ca-chelator, 1-2-bis-(2-aminophenoxy) ethane-N,N,N',N'-tetraacetic acid (BAPTA) into the presynapse of frog end-plate, and found that the BAPTA-loaded preparation showed little facilitation. However, the facilitation reappeared upon addition of an ionophore, X-537A, supporting the view that the loss of facilitation was due to the Ca-buffering action of BAPTA. Hypertonicity, erythrosin B and trinitrobenzene sulfonic acid (TNBS), increased transmitter release without any recovery of facilitation at the BAPTA-loaded end-plate. This strongly suggested that transmitter release was increased by these conditions without any change in intracellular Ca ion concentration.

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TOPOGRAPHICAL ORGANIZATION OF CORTICORUBRAL PROJECTION IN THE KITTEN AND CONSEQUENCES AFTER HEMISPHERECTOMY. HIGASHI, S.*, YAMAZAKI, M.* AND MURAKAMI, F. Department of Biophysical Engineering, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka 560.

We studied whether aberrant corticorubral (CR) projections formed after unilateral cortical lesions in the kitten show topographic specificity, using a plant lectin, Phaseolus vulgaris-leucoagglutinin (PHA-L). Intact kittens aged 2 to 8 weeks and those with unilateral cortical lesion received injections of PHA-L. Lesions were made at 3 - 4 weeks of age and injections were made within 5 weeks after lesion. In normal animals, injections lateral to the cruciate sulcus resulted in extensive labellings of fibers in medial part, and those into the medial part of the postcruciate cortex resulted in extensive labellings in ventrolateral part of the ipsilateral red nucleus. Area 6 injections resulted in poor labelling of CR fibers. Similar topographic organization was seen for the crossed CR projections in lesioned animals. These observations suggest that the same molecular mechanisms which might operate to form specific synaptic connections during development also operate to form lesion-induced aberrant projections.

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EFFECT OF GABA ON THE NEUROTRANSMISSION IN THE GUINEA PIG INFERIOR COLLICULUS. YAMAUCHI,R., OKADA,Y., *AMATSU,M. Dep.Physiol.,*Otolaryngol. Kobe Univ. Sch. Med., Kobe 650

Slices(400-600um thick) of the inferior colliclulus(IC) from guinea pig were prepared by cutting parasagittaly and incubated in the standard medium. Postsynaptic potential(PSP) was recorded in the superficial layer of Pericentral nucleus(PN) by stimulating deep layer of PN. GABA and other drugs were applied in the perfusion medium. GABA(10^{-3}-10^{-2}M), muscimol(10^{-6}-10^{-4}M) and (-)baclofen(10^{-7}-10^{-5}M) inhibited the PSP dose dependently. Bicuculline methiodide(10^{-6}-10^{-5}M) enhanced the amplitude of PSP and evoked the seizure dischardge(SD). Methoxypyridoxine(10^{-4}M) and 3-mercaptopropionic acid(10^{-4}M) reduced the concentration of GABA in the slice. The incubation with these agents reduced the GABA level to 50% of initial value, when distinct SD was recorded. The application of GABA to this condition blocked the SD dramatically. Removal of Cl^- from the medium as well as the application of furosemide(10^{-4}M) elicited also the SD. Further GABA application in this state did not block the SD. In summery, GABA plays the inhibitory role in the IC and the reduction of GABA in the slice and blockade of GABA by its antagonists evoke the SD in IC.

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CLASSIFICATION OF β-HYDROXYGLUTAMIC ACID RECEPTORS. TAKEUCHI, H., WATANABE, K., NOVALES-LI, P., *SHIMAMOTO, K. AND *OHFUNE, Y. Dept. Physiol., Gifu Univ. Sch. Med., and *Suntory Inst. Bioorganic Res.

β-Hydroxy-L-glutamic acid (L-BHGA), not L-glutamic acid (L-Glu), had marked effects on Achatina neurones. We examined effects of four stereoisomers of the novel L-BHGA analogues conformationally fixed in extended or folded form, L-α-(carboxycyclopropyl)glycine (L-ACCG), on these neurones (PON, VIN, d-RPLN, RAPN and v-RCDN). L-BHGA receptors were classified under neurone level into BHG (L-BHGA receptor type) 1, 2 and 3. Further, these were also subclassified into Ex (extended), Fd (folded) and Un (undetermined) types. Taking together the two classifications, these were actually: BHG 1Ex, 1Fd, 2Un, 2Fd and 3Un. The BHG 1Ex and 1Fd (PON and VIN) are inhibited by L-BHGA. BHG 1Ex are activated by erythro-L- compounds in the extended form, whereas BHG 1Fd are by the threo-L- compounds in folded form. BHG 2Un and 2Fd (d-RPLN and RAPN) are excited by L-BHGA. BHG 2Un are activated by erythro-L-compounds, while BHG 2Fd are by threo-L- compounds in folded form. BHG 3Un (v-RCDN) are inhibited strictly by threo-L-BHGA; None of the compounds tested in this study showed marked effects.

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CLASSIFICATION OF GABA RECEPTORS IN SNAIL NEURONES. YONGSIRI, A., FUNASE, K., TAKEUCHI, H., *SHIMAMOTO, K. AND *OHFUNE, Y. Dept. Physiol., Gifu Univ. Sch. Med., and *Suntory Inst. Bioorganic Res.

We examined effects of GABA and its analogues, muscimol, baclofen, L-GABOB and those conformationally fixed in either extended or folded form, such as trans- and cis-isomers of 2-(aminomethyl)cyclopropane-1-carboxylic acid (cyclo-GABA-extended and cyclo-GABA-folded) and 4-aminocrotonic acid (GABA-extended) on Achatina identifiable neurones (TAN, d-LPeLN, v-VNAN, v-LCDN and RPeNLN). With the results, we classified GABA receptors into the muscimol A (MA), muscimol B (MB) and baclofen (BC) types. The MA (TAN and d-LPeLN) and MB (v-VNAN and v-LCDN) receptors were respectively inhibited and excited by GABA and muscimol, whereas these were insensitive to baclofen. Muscimol was more effective on the MB receptors than on the MA ones. GABA-extended was also more potent on the former receptors than the latter. GABA is effective on the two muscimol receptors in the extended form, since muscimol, conformationally fixed in this form, is quite effective. The baclofen receptors (RPeNLN) were inhibited by GABA and baclofen, but almost insensitive to all of the GABA analogues tested, including muscimol.

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IDENTIFICATION OF GIANT NEURONES IN A JAPANESE DOMESTIC SNAIL (EUHADRA CONGENITA HICKONIS). KIM, K. H., YONGSIRI, A., TAKEUCHI, H., *ONOZUKA, M., *KUBO, K. AND *DEURA, S. Dept. Physiol. and *Dept. Anat., Gifu Univ. Sch. Med.

We studied the pharmacological characteristics and axonal pathways of giant neurones identified in the suboesophageal ganglia of a Japanese domestic snail (Euhadra congenita hickonis Kobelt). These were d-RPLE (dorsal-right parietal large Euhadra neurone), d-LPLE (dorsal-left parietal large Euhadra neurone), d-RPINE (dorsal-right parietal intestinal nerve Euhadra neurone), d-VCCSE (dorsal-visceral cerebro-pleural connective superior Euhadra neurone) and d-VCCIE (dorsal-visceral cerebro-pleural connective inferior Euhadra neurone).

The amines and amino acids effective on the Euhadra neurones tested were comparable to those on the Achatina neurones; for example, the Euhadra neurones were insensitive to L-glutamic acid, but some of them were sensitive to β-hydroxy-L-glutamic acid, likewise the case of Achatina neurones. The Euhadra neurones were insensitive to the peptides tested, though some Achatina neurones were sensitive to oxytocin and FMRFamide.

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EFFLUX OF [^{3}H]GABA IN THE BULLFROG SYMPATHETIC CHAIN AND SCIATIC NERVE. SAKAI, S., TASAKA, J., TOSAKA, T., HASHIGUCHI, T. and YOSHIHAMA, I.[2]* Dept. Physiol. and [2]Dept. Pathol., Tokyo Medical College, Shinjuku-ku, Tokyo 160

The efflux of [^{3}H]GABA from the bullfrog lumbar sympathetic chain and spinal nerve was examined. The spontaneous efflux was apparently enhanced with reducing the extracellullar Na^+, possibly due to the decrease of Na^+-dependent reuptake. GABA (2 mM) and δ-aminovaleric acid (2 mM) induced marked release of [^{3}H]GABA, depending on their affinity to the carrier. Raising the extracellular K^+ concentration caused the release of [^{3}H]GABA. The increase in the release was sigmoidally related to K^+ concentration, corresponding to the linear relationship to the membrane potential less than -30 mV, estimated from the Nernst equation. The K^+ evoked release required Na^+ but not Ca^{2+} and was unaffected by tetrodotoxin (1 μM). Caffeine (10 mM), theophylline (10 mM), veratridine (50 μM) and monensin (3 μM) did not induce the release of [^{3}H]GABA. Electrical stimulation gave rise to remarkable release of [^{3}H]GABA Na^+-independently, which seemed to occur at the vicinity of the electrodes. Light microscopic autoradiography revealed that the grains were localized mainly in glial cells and unmyelinated nerve fibers. It is thus evident that there are at least four components involved in the efflux of [^{3}H]GABA : 1) simple diffusion 2) carrier-mediated exchange 3) K^+-depolarization and 4) electrical passing current.

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THE EFFECT OF TEMPERATURE ON THE TRANSMITTER-INDUCED K^+-CURRENT MEDIATED BY GTP-BINDING PROTEIN. HAKOZAKI, S., MATSUMOTO, M., TAKAHASHI, J., SASAKI, K., TAKASHIMA, K. AND SATO, M. Dept. Physiol., Sch. Med., Iwate Med. Univ., Morioka, Iwate 020

Either dopamine, histamine, or acetylcholine can produce slow outward current in each identified neuron of Aplysia. All these responses are caused by a permeability increase toward K^+ following the activation of G-protein coupled to each receptor. Lowering the temperature from 22 to 12°C induced a inward current associated with a decrease in K^+-conductance, while raising the temperature from 22 to 32 °C induced a marked outward current associated with an increase in K^+- conductance. All transmitter-induced responses described above were markedly depressed when the temperature was lowered to 12 °C or raised to 32 °C from 22 °C. Intracellularly injected GDPβS depressed the transmitter-induced K^+-current responses as well as the warming-induced K^+-current of the same cell. Intracellular application of GTPγS apparently depressed the transmitter-induced K^+-current as well as warming-induced K^+-current of the same cell. These results suggest that the receptor coupled G-protein can be activated thermally to open K^+-channels without receptor stimulation.

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PROTEIN KINASE C ACTIVATORS MIMIC THE M_2-MUSCARINIC EFFECTS ON THE ACTION POTENTIAL.
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Action potentials (APs) in the isolated superior cervical ganglionic neurones of rabbits were recorded by tight-seal whole-cell recording electrodes. Pressure-applied muscarinic agonist, ACh or muscarine at 0.1-1 μM, caused a depression of the calcium-dependent components in the AP; an acceleration of the repolarizing phases. 4-(m-Chlorophenyl-carbamoyloxy)-2-butynyltrimethyl ammonium chloride (McN-A-343, 0.1-1 μM) had a weak agonistic effect but a novel M_1-muscarinic agonist, 2-methylspiro-(1,3-oxathiolane-5,3') quinuclidine hydrochloride (AF102 B, 0.1-50 μM), had no effect on APs. A protein kinase C activator 1,2-oleoylacetylglycerol (OAG, 0.5-5 μM), a synthetic diacylglycerol analog, or phorbol-12,13-dibutyrate ($Pb(Bu)_2$, 0.016-1.6 μM) mimicked the M_2-muscarinic receptor-mediated alteration of the AP. They depressed calcium spikes in the presence of tetrodotoxin at 0.3 μM but had no effect on sodium spikes in the calcium-free medium or in the presence of ω-conotoxin at 1 μM. The ACh effects on AP were obscured after perfusion with a protein kinase C inhibitor, 1-(5-isoquinolinesulfonyl)-2-methylpiperazine (H-7, 50 μM). These results indicate that protein kinase C may be an intermediator between the M_2-receptors and calcium channels regulating the firing rate of the sympathetic neurones.

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EFFECT OF CHRONIC MUSCLE STRETCHING ON NEUROMUSCULAR TRANSMISSION OF RAT SOLEUS MUSCLE.
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The effect of chronic muscle stretching on neuromuscular transmission was investigated using tibial nerve-soleus muscle preparations, which were obtained from rats subjected to a leg-lengthening operation with dislocation of the knee joint. The mean quantal content (m) in stretched muscle was significantly higher than that in contralateral control until the 30th day after the stretching. The increase in m obtained until the 7th day and that also obtained on the 7th to the 30th day were due to the increase of the probability of quantal release (p) and that of the number of releasable quanta (n), respectively. On the 40th to the 90th day, m in the stretched muscle was not significantly different from that in the contralateral control. This is explained by the result that the increase in n cancels the decrease in p. It is known that n reflects the nerve terminal size. The frequency of nodal sprouting closely correlated with the frequency of complex e.p.p.s, which closely related with n. Thus, it is considered that the increase in n is attributed to the enlargement of the terminal size.

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EFFECTS OF RELEASE STIMULI ON THE FREQUENCY AND AMPLITUDE OF MINIATURE END-PLATE POTENTIALS AT THE FROG NEUROMUSCULAR JUNCTION.
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After tetanic stimulation (10 Hz, 5 min) of the sciatic nerve, the elevated frequency of miniature end-plate potentials recorded intracellularly from the sartorius muscle declined exponentially to the initial level, but the reduced amplitude did not return to the control level even after 45 min. The coefficient of variation (c.v.) of the amplitudes was either above or below the control depending upon whether the post-tetanic frequency was above or below the control. The distribution of the amplitudes shifted toward the left after tetanus. When the tonicity of the bathing soluiton was raised by adding 75 mM sucrose, the amplitude increased above the control after a slight initial decrease corresponding to the enhanced frequency with a rapid rise and a following plateau phase. On return to normal Ringer, the frequency and amplitude returned to the initial level with some exceptions in the latter. The c.v. of the amplitudes was increased by hypertonicity and remained elevated after returning to normal tonicity. The addition of 0.1 mM La^{3+} caused increases in frequency and amplitude, but no unidirectional changes in the c.v. of the amplitudes. Ten μM AH5183 applied with 75 mM sucrose did not affect the elevated frequency, but produced an overall decrease in amplitude, abolishing the usual increase caused by 75 mM sucrose.

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UPTAKE OF [3H]DOPAMINE IN ISOLATED CHROMAFFIN CELLS OF MICE; EFFECT OF GLUCOCORTICOID.
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Effect of glucocorticoids on the process of catecholamine uptake in mouse adrenal chromaffin cells was investigated. Isolated chromaffin cells were incubated in 140nM of [3H]dopamine (sp.act. 33.4Ci/mmol) for 30 min. Chromaffin cells accumulated approximately ten times more dopamine than those in vivo. Lower dose of reserpine (0.1-10uM) did not suppress the uptake while 100 uM of reserpine reduced it to 60% of control indicating that this uptake is through plasma membrane not by chromaffin vesicles. The uptake was inhibited to one fourth to one fifth of control in the presence of 2 uM of dopamine, noradrenaline, adrenaline and serotonin. Corticosterone and dexamethasone (1-100 uM) only slightly suppressed the uptake while ACTH had no effect. The present results showed that dopamine uptake in adrenal chromaffin cells in vivo is significantly lower than that in vitro. It may be due to release of newly accumulated catecholamines and also due to suppression by neural factors including acetylcholine or peptides. It is considerable that cortical glucocorticoids are necessary to maintain basal level of catecholamine uptake in vivo whilst in isolated cells, without neural and humoral environment, glucocorticoids are only slightly effective.

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NORADRENALINE-HYPERPOLARIZATION IN SUBMANDIBULAR GANGLION CELL.
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This study was made to investigate the electrogenesis mechanism of noradrenaline (NA)-hyperpolarization accompanied by increased R_m in hamster submandibular ganglion cells, which is mediated by α_2 adrenoceptors. NA and clonidine (100-200 mM) were applied to isolated ganglion cells from micropipettes by pressure ejection. Hyperpolarizations were recorded intracellularly by KCl- or K acetate-electrodes. Clonidine caused hyperpolarizations of cells alone. Clonidine-hyperpolarization induced by ejection 10 times was 9.1 $\pm$ 1.2 mV in amplitude and 2.3 $\pm$ 0.1 min in duration at E_m=-59.1 $\pm$ 2.4 mV. R_m increased by 22.8 $\pm$ 2.5% during the hyperpolarization. These were prevented by yohimbine. The hyperpolarizations possessed a reversal potential at E_m of about -10--15 mV. Ca^{2+} and K^+ ions were not involved in generation of the hyperpolarization. Cl^- and Na^+ ions might be involved in its generation. Decreased G_{Cl} might occur in early phase of the hyperpolarization. However, Cl^- conductance blocker, Cd^{2+} ion, bumetanide, penicillin -G, DIDS had no clear effect on the hyperpolarization.

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Tetrodotoxin delays the appearance of long lasting hyperpolarization in the otic ganglion neuron of rabbit.
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In the otic ganglion neuron of rabbit, tetrodotoxin (TTX) saline suppressed the action potential and increased the intensity of threshold current as much as twice in normal saline. Application of tetraethylammonium (TEA) added to TTX saline resulted in generation of the action potential with prolonged duration, and Co^{++} added to TEA+TTX saline blocked the action potential. In TTX saline, the spike generated by the outward current of intensity more than five times of the threshold current in normal saline was followed by an afterhyperpolarization (AHP) reduced in both its duration and amplitude. AHP was also followed by a long lasting hyperpolarization (LLH) but the appearance of LLH delayed from 0.5 to 1.5 s as compared with that in normal saline. LLH generation in control is probably due to a slow $g_{K,Ca}$ activated by an increase of intracellular free calcium ($[Ca^{++}]_i$) which is presumably released from the intracellular stored-Ca by the Ca^{++} influx. The mechanism of TTX delay of LLH is presumed as follows. TTX blocks Na channel and then the inward Ca^{++} flux through Ca channels activated concomitantly by the increase of g_{Na} is abolished. As Ca^{++} influx is only activated by the increase of g_{Ca}, it takes a time to reach the sufficient $[Ca^{++}]_i$ level to release Ca^{++} from the intracellular stored-Ca.

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EFFECT OF TRIGEMINAL STIMULATION ON THE DISCHARGE PATTERN OF THE NEURONS IN THE LATERAL HORN.

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We previously demonstrated the close relationship between trigeminal stimulation and firing patterns of neurons in the vagaus nucleus. To elucidate the relationship between trigeminal stimulation and sympathetic nervous system in the Reilly phenomenon in oral medicine, effects of trigeminal stimulation on the changes in firing pattern of neurons in the thoracic lateral horn.

Unit discharges from the thoracic lateral horn of cats were recorded using a glass micropipette containing fast green FCF, and the microelectrode position was assertained histologically after the experiment.

There were three types of neurons in the lateral horn neurons from the viewpoint of effect of trigeminal stimulation: neurons for which firing was accelerated by trigeminal stimulatin, neurons for which firing was decreased by trigeminal stimulation and neurons indifferent to trigeminal stimulation.

These findings suggest that trigeminal stimulation modified the neuronal firing pattern and consequently causes changes in sympathetic outflow, finally evoking the Reilly phenomenon in oral medicin.

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CONTROL OF POSTPRANDIAL GASTRIC MOTILITY BY ENDOGENOUS HISTAMINE IN THE GASTRIC WALL IN DOGS.

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In order to clarify the role of endogenous histamine in the control mechanism of postprandial gastric motility, the effects of famotidine, a histamine H_2-receptor antagonist and cepharanthine, a inhibitor of histamine release from histamine-secreting cells in the gastric wall, on postprandial gastric motility were investigated in dogs.

Postprandial gastric motility was significantly enhanced by intravenous administration of famotidine(0.3 mg/kg) and cepharanthine(2.0 mg/kg) previous to feeding. When, however, famotidine or cepharanthine was administrered during interdigestive state, no change occurred in gastric motility. On the other hand, postprandial gastric motility was unaffected by peroral administration of omeprazole(gastric proton pump inhibitor ; 1.6 mg/kg) previous to feeding.

These results suggest that the endogenous histamine plays an important role in the control mechanisms of postprandial gastric motility.

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EFFECT OF ENKEPHALIN ON THE INTRACELLULAR CALCIUM ION CONCENTRATION OF GUINEA-PIG ENTERIC NEURONS.

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Intracellular free calcium concentration was measured in enteric neurons of the guinea-pig by using the fluorescent calcium indicator, fura-2; at the same time, intracellular recordings were made from the neurons. Submucous or myenteric plexus preparations were made from the isolated caecum or ileum of the guinea-pig sacrificed by heavy stunning and bleeding from the neck. Fura-2 fluorescence emission was detected either by photomultiplier tube or by a SIT camera combined with an image processing device. [Met^5]enkephalin (30 nM-1 μM) caused a membrane hyperpolarization, and a biphasic change in intracellular calcium ion concentration; an initial transient increase was followed by a decrease. However, when the hyperpolarization was prevented by the voltage-clamp method, the decrease was largely recuded. This suggests that the transient increase in the calcium concentration may be due to receptor-mediated calcium release from calcium stores and the decrease due mostly to calcium-flux through voltage-dependent calcium channels. (Supported by the Nakatani Electronic Measuring Technology Association of Japan.)

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EFFECT OF GALANIN ON THE Ca^{2+} SPIKE OF MYENTERIC AH/TYPE 2 NEURON

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Galanin is a 29 amino acid gut-brain peptide and has been known as an inhibitory neuromodulator of myenteric neurons in guinea-pig small intestine. With conventional intracellular recording methods, precise ionic mechanisms of galanin were investigated in myenteric AH neurons. Galanin reversibly hyperpolarized the cell membrane and mimicked slow IPSP. Several lines of evidence indicated opening K^+ channel of the somal membrane for the ionic mechanism of membrane hyperpolarization. Unlike the other inhibitory substances, galanin showed direct inhibitory action on the somal action potential of AH/type 2 neuron. Simultaneous suppression of after-hyperpolarization (AH) occurred with the spike duration reduction indicated decrease of Ca^{2+} ion entry during an action potential. Ca^{2+} spike, enhanced by the intracellular injection of Cs^+ ion, was reversibly suppressed by galanin. It appears that galanin has two inhibitory mechanism on myenteric AH neuron. One is to open K^+ channel and the second is blokcade of voltage gated Ca^{2+} channel.

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AN INHIBITORY ACTION OF CAPSAICIN ON VAGALLY-EVOKED JEJUNAL CONTRACTION IN DOGS.

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The contractions sensitive to hexamethonium and atropine were induced by vagus nerve stimulation (10 Hz, 1 ms, 10 - 12 V) in the jejunal segments in dogs anesthetized with urethane and immobilized with gallamine. This response was largely reduced by i.a. infusion of capsaicin (10 - 100 μM, 0.07 ml/min, 5 - 10 min) not only in the segment infusing capsaicin but also in the segments infusing no drugs. An inhibition of vagally-induced contractions by capsaicin was abolished after sympathectomy and by i.a. infusion of phentolamine and yohimbine (1 mM, 0.07 ml/min, 15 min in both), but was not affected by propranolol (1 mM, 0.03 ml/min, 15 min). Spontaneous discharges of mesenteric efferents and afferents were markedly increased by capsaicin. An increase in efferent discharge rate by capsaicin was blocked after sympathectomy. These results suggested that capsaicin applied in the small intestine activates sympathetic adrenergic efferents through sympathetic afferents, resulting in an inhibition of vagally-evoked jejunal contractions through α_2-adrenoceptors presynaptically.

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THE RELATIONSHIP BETWEEN MOTILITY AND SECRETION IN THE GUINEA PIG COLON.

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The relationship between the motility and epithelial transport functions were examined in the isolated colon from guinea pig. The motility was measured manometrically and the intraluminal potential as referred to the bath was recorded to assess the change in epithelial ion transport. The peristaltic contraction occurred spontaneously at the rate of 0.6-1.5 cycle/min. The contraction was associated with a change in intraluminal potential, the lumen being more negatively charged. When bumetanide (10^{-4} M) was added to the bath, the change in luminal potential was markedly reduced while the magnitude and the frequency of the peristaltic contraction was essentially unchanged. The addition of tetrodotoxin ($3x10^{-7}$ M) abolished both the peristaltic contraction and the change in the intraluminal potential. These result suggest that the Cl^- secretion in the colon is stimulated in association with the contraction. The intramural enteric neurons are important for this association.

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EFFECT OF CEMOSENSITIVE MUCOSAL REFLEX ON COLONIC ION TRANSPORT IN THE RAT.

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The effects of luminal chemical stimuli such as short-chain fatty acids (SCFA)(T. Yajima, J. Physiol. 368, 667-678, 1985) and electrical field stimulation (EFS) on colonic ion transport were studied in vitro in the rat. The short-circuit current (Isc) was measured using an Ussing chamber. Mucosa-submucosa preparations (containing the submucosal nerve) from the distal colon were used. Mucosal application of SCFA (propionate, butyrate and valerate) caused increase in the PD (the mucosal side negative), Isc and conductance. The Isc-increase response to propionate was concentration dependent (ED_{50} 70μM). The increases in the Isc were probably due to Cl^- secretion, since serosal-to-mucosal Cl^- movement was increased by propionate. Pretreatment (2 min) with the luminal procaine (0.5mM) inhibited the propionate-evoked increase in Isc by 90% but not the Isc-response to EFS. TTX (1μM) inhibited the propionate- and EFS-evoked increase in Isc by 40% and more than 90%, respectively. Atropine (50μM) also inhibited the the Isc-increase response to propionate more than 90% and the Isc-response to EFS by 20%. The results suggest that luminal chemical stimuli by SCFA transiently stimulated the colonic chloride secretory response, probably via an enteric reflex involving mucosal sensory mechanism and submucosal nerve reflex in part.

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EFFECT OF TASTE STIMULATION ON THE RATE OF EFFERENT DISCHARGES IN THE AUTONOMIC NERVES INNERVATING VISCERAL ORGANS IN THE RAT.

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Effect of taste stimulation on the efferent discharges in the pancreatic and hepatic branch of the vagus nerve, and those in the adrenal, pancreatic and hepatic branch of the splanchnic nerve were observed in the anesthetized rat. Effect of taste stimulation on the efferent discharges in the sympathetic nerve innervating the interscapular brown adipose tissue was also studied. An increase in discharge rate following stimulation with 5% glucose or 10% sucrose over the tongue for 5 min, and a decrease of it following application of 5% NaCl for same duration were observed in the pancreatic and hepatic branch of the vagus nerve. However, the activity of the adrenal, pancreatic and hepatic branch of the splanchnic nerve as well as brown tissue nerve was suppressed by 10% sucrose or 5% glucose, and activated by 5% NaCl.

The results indicate that the existence of reflex pathway from taste receptors to the vagal and sympathetic nerves innervating pancreas, liver, adrenal gland and brown adipose tissue. This pathway may play a role on the regulation of the blood glucose following taste stimulation as an anticipatory response.

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EFFECT OF TASTE STIMULATION ON ELECTRICAL ACTIVITIES IN THE AUTONOMIC NERVES INNERVATING THE HEART IN RAT.

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In anesthetized rats we first examined the effect of chemical stimulation of oro-lingual mucosa on the cardiovascular function. Of 4 qualities of basic taste stimuli, HCl and NaCl but not quinine and sucrose were found effective in inducing change in the heart rate (HR) and arterial blood pressure (BP). HR was increased by 14 ± 4 (mean ± S.E.) and 40 ± 8 beats/min following application of 1 M NaCl and 30 mM HCl, respectively. BP was also increased by 8 ± 2 and 33 ± 6 mmHg due to application of 1 M NaCl and 30 mM HCl, respectively. These changes were based on a reciprocal change between efferent activities in two cardiac nerves; an increment of 29% in the sympathetic nerve activity was accompanied with a decrement of 34% in the vagal nerve by 1 M NaCl whereas, by 30 mM HCl, 48% increment in the former occurred with 34% decrement in the latter. Intracellular recording from the superior cervical ganglion cell revealed that taste stimuli increased the frequency of EPSPs so as to increase the rate of spike initiation.

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REGIONAL DIFFERENCES IN SYMPATHETIC RESPONSES TO BRAIN ISCHEMIA IN THE RABBIT.

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We studied the responses of sympathetic outflow to the brain ischemia in urethane anestetized rabbits. The activities of renal sympathetic nerve(RNA), cardiac sympathetic nerve(CNA), lumber sympathetic nerve(LNA), splenic sympathetic nerve(SNA) and mesenteric sympathetic nerve(MNA) were recorded during complete brain ischemia. Short term brain ischemia caused a marked increase in discharges of sympathetic nerve activities and reached to their maximum level. Thereafter, the depressed periods were observed in all measured sympathetic nerves after releasing brain ischemia. Some of CNA which is decreased in the early phase of both short term and long term brain ischemia showed different discharge pattern from the other nerve activities. These results suggest that sympathetic outflow to the different organs except the heart are uniform directionaly and/or qualitatively different in the response to the brain ischemia.

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The effects of sodium pentobarbital and halothane on baroreceptor reflex of heart rate and renal nerve activity in chronic cats.

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This experiment was studied to examine effects of sodium pentobarbital (PB, 4mg/kg, iv) and halothane (H, 0.75% and 1.5%) on baroreceptor reflex sensitivity (BRS) in conscious cats. PB caused a tachycardia (from 176 ± 5 to 191 ± 2 beats/min) without a hypotension, and an augmentation in renal nerve activity (RNA). PB elicited a significant depression of BRS of HR, but not of RNA. H produced a hypotension (from 120 ± 3 to 84 ± 5 at a concentration of 0.75% and 80 ± 8mmHg at 1.5%) and a bradycardia (from 180 ± 10 to 171 ± 8 at 0.75% and 165 ± 12 beats/min at 1.5%) with a reduction in RNA (from 100 to 75 ± 13 at 0.75% and 70 ± 8% at 1.5%). H caused a dose-dependent supression in BRS of both HR and RNA. These results indicate that 1) PB, even at the hypnotic doses, causes a depression of BRS of HR, probably resulting from the vagolytic effects of PB, and 2) H produces the dose-dependent deterioration in BRS of both HR and RNA.

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BLOOD PRESSURE AND RENAL NERVE RESPONSES TO INTRAVENOUSLY INJECTED CCK AND VIP IN DOGS

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We examined reflex responses of renal nerve activity (RNA) to intravenous injection of cholecystokinin (CCK) and vasoactive intestinal peptide (VIP) in dogs. Intravenous injection of VIP caused a significant fall of systemic blood pressure (SBP, +30 mmHg) and a significant increase (+60%) in RNA. This augmentation of RNA was abated after denervation of the carotid sinus nerves, indicating that RNA response to VIP is dependent on systemic baroreceptor reflexes. Following CCK injection, SBP fell significantly by -40 mmHg in the intact animal, with a significant decrease (-53%) in RNA. After cervical vagotomy, SBP reversed to increase significantly, but RNA did not show any significant alterations. CCK injection after denervation of the carotid sinus nerves caused significant increases in SBP and RNA. These results may indicate that CCK responses on sympathetic activity in the intact animal may be predominant in the vagal afferents from the abdominal viscera. Systemic baroreceptor system also minimize these enhanced responses to CCK after deafferentiation of the vagal nerves.

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REFLEX MECHANISMS FOR RENAL VASCULAR RESISTANCE DURING OCCLUSION OF SUPERIOR MESENTERIC ARTERY IN ANAESTHETIZED DOGS

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Ten adult mongrel dogs were used, and left kidney was perfused at a constant flow by using a roller pump. Renal perfusion pressure was measured simultaneously with arterial blood pressure and heart rate during occlusion of superior mesenteric artery (SMAO). Renal vascular resistance (RVR) was calculated by deviding renal perfusion pressure with flow. Experiment was performed in the following three groups: systemic baroreceptor intact (I group), vagotomy (V group), and combination of vagotomy and carotid sinus denervation (V+CS group). Following SMAO, mean arterial pressure (MBP) and RVR increased significantly in all three groups. RVR before SMAO in V group was higher than that in I group, and more significantly increased in V+CS group. To compare changes of RVR during SMAO between groups, RVR during SMAO were 119 $\pm$ 4%, 122 $\pm$ 5% and 179 $\pm$ 20% in I, V and V+CS group respectively. We concluded that SMAO elicites increases of arterial pressure and RVR. The reflex renal vasoconstrictor response to SMAO is modified and minimized by systemic baroreceptor reflexes.

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EFFECTS OF α- AND β-ADRENERGIC BLOCKING AGENTS ON MUSCLE SYMPATHETIC NERVE ACTIVITY AND HEMODYNAMICS IN MAN.

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To analyze the role of α_1- and β-adrenergic receptors in sympathetic nervous function in humans, especially orthostatic tolerance, 1mg of prazosin (PRZ), an α_1-blocker and 10mg of carteolol (CTL), a β-blocker were orally administered to healthy volunteers in order to observe the effects of these drugs on muscle sympathetic nerve activity (MSA) and hemodynamics. Subjects were healthy male students aged 19 to 25. MSA was recorded microneurographically from the tibial nerve, and was analyzed quantitatively as burst number per minute (burst rate). Electrocardiogram (ECG) for heart rate (HR), respiration, blood pressure (BP), leg volume (LV), impedance cardiogram for cardiac output (CO) and stroke volume (SV) were simultaneously monitored. A single dose of PRZ, CTL, or placebo was orally administered and the effects of these two drugs on MSA at supine position (BA), activity in standing (SA), responsiveness to head-up tilt (RO), as well as on HR, SV, CO, LV, were statistically analyzed. As the results, the spontaneous MSA were increased after 40 min of either PRZ or CTL, however, the increase was more marked in PRZ. HR and BP were not significantly changed after the drugs. PRZ enhanced the BA and SA, without changing the RO. CTL also elevated BA, but less than PRZ did, while not changing SA and RO. In total of 30 experiments, 9 out of 10 trials of PRZ, and 7 out of 10 trials of CTL suffered from fainting or near-fainting. PRZ increased the orthostatic intolerance index (sum of 1/[sine of fainted angle]) to 1.10, and CTL to 0.85 (placebo: 0.22). PRZ raised HR, LV and reduced CO in standing, whereas CTL reduced HR, SV, CO, LV in standing. It is concluded that an oral administration of α_1- and β-blockers enhances MSA BA. The former, which blocks the peripheral vasoconstriction, enhances MSA more than the latter, which suppresses CO. The orthostatic intolerance, induced more frequently by PRZ than CTL, is caused by blood pooling to the lower body, in spite of marked enhancement of MSA. It is suggested that the orthostatic tolerance in postural change in humans depends more on the increase of peripheral resistance mediated by α_1-receptor than on the increase of CO mediated by β-receptor.

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FUNCTIONAL SUBDIVISIONS OF THE LOWER BRAIN STEM OF THE CAT AS DETERMINED BY CIRCULATORY AND RESPIRATORY RESPONSES TO ELECTRICAL AND CHEMICAL MICROSTIMULATION.

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To make a topological map of sites of circulatory and respiratory responses, these responses were surveyed in the lower brain stem of the cat. Cats were anesthetized with chloralose. Natural breathing was maintained under normal end-expired CO_2 and O_2 concentrations. The lower brain stem was explored, using double barrel coaxial electrode; inner barrel filled with 3M NaCl and the outer one with 5 mM kainic acid and 6% WGA-HRP. Five sets of characteristic responses due to cellular excitation were observed: (1) a pressor-tachycardiac-hyperpneic response in the lateral parabrachial nucleus; (2) a pressor-hypopneic response in the reticular formation subjacent to the trigeminal motor nucleus; (3) a pressor-bradycardiac-apneic response in the regions ventrolateral to the retrofacial nucleus; (4) a pressor-bradycardiac-apneustic response in the regions ventrolateral to the ambiguus nucleus at the level behind the obex; (5) a depressor-bradycardiac-hypopneic response in the regions just medial to the solitary tract in the intermediate solitary tract nucleus and the commissure subnucleus. These data suggest a strong combination of the circulatory and respiratory response at several sites in the lower brain stem.

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FUNCTIONAL SUBDIVISIONS OF THE LOWER BRAIN STEM OF THE RAT AS DETERMINED BY CIRCULATORY AND RESPIRATORY RESPONSES TO ELECTRICAL AND CHEMICAL MICROSTIMULATION. SAJI,M., TAKAYAMA,K. AND MIURA,M., Dept. Physiol., 1st Div., Gunma Univ. Sch. Med., Maebashi 371

To make a topological map of sites of circulatory and respiratory responses, these responses were surveyed in the lower brain stem of the rat. Wister rats were anesthetized with urethane and chloralose, but natural breathing was maintained under normal blood gas. We examined the circulatory and respiratory responses to electrical stimulation and/or chemical stimulation (5 mM kainic acid). Characteristic responses due to cellular excitation were something different from those of the cat: (1) a pressor-tachycardiac response in the lateral parabrachial nucleus (Pbl) was associated with an apneustic response: (2) a pressor-apneustic response in a narrow zone corresponding to the C1 and A1 area of the ventrolateral medulla (VLM) was associated with a tachycardiac response; (3) a pressor-bradycardiac-apneustic response in the intermediate Pbl, a depressor response in the region medial to the ambiguus nucleus (AMB) at the level of the rostral VLM and a bradycardiac-hypopneic response in the intermediary zone between the solitary tract nucleus and the AMB were found only in the rat. These data suggest a strong combination of the circulatory and respiratory response at several sites in the lower brain stem of the rat.

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STIMULATORY EFFECT OF ALIPHATIC AMINES ON ELECTRICAL ACTIVITY OF SYMPATHETIC NERVES IN RAT. MATSUMOTO, A. AND YONEMURA, K. Dept. of Physiol., Miyazaki Medical College, Miyazaki 889-16

Some of the aliphatic amines are present at significantly raised concentrations in the plasma of uremic patients. The present study was carried out to clarify the effects of the aliphatic amines such as monomethylamine, dimethylamine, trimethylamine (TMA) and ethanolamine (ETA) on electrical activity of the cervical sympathetic nerves as well as on heart rate (HR) and arterial blood pressure (BP) in anesthetized rats. When injected into the femoral vein, these amines were found to induce enhancement of the electrical activity, resulting in elevations of HR and BP. Among the 4 kinds of aliphatic amines, TMA induced the greatest change in the electrical activity, HR and BP. ETA was found to induce little change in the electrical activity and HR but induce an elevation of BP, indicating that this amine would act directly on arterial smooth muscles and/or heart muscles. Thus, the present study suggests that the aliphatic amines may play a role in inducing some of the symptomes of uremic patients.

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EFFECTS OF THE INTRATHECAL ADMINISTRATION OF VIP TO THE MICTRITION REFLEX OF THE CAT. KAWATANI, M. and TAKESHIGE, C., Dept. Physiol., Sch. Med., Showa Univ., Tokyo, 142.

Previous studies indicated that Vasoactive intestinal polypeptide(VIP) was present 42% of the pelvic nerve afferent neurons in the cat. The present experiments were under taken to determine whether intrathecal(IT) administration of VIP modulate mictrition reflexs. Total 24 cats were used. Some animals were spinalized at T_{12} segments 1-3 months prior to experiments. IT administration of VIP(0.1-1 ug) in the sacral spinal cord produced weak(10%-20%) facilitation of spontaneous bladder constraction(SB-C) in 50% of the animals. The large dose of VIP(10-500ug) produced strong inhibition in all animals. The effects were dose-dependent and varied from a reduction in amplitude and frequency of bladder activity to complete supression. The inhibition persisted for 1-1.5 hrs. VIP (10-500ug) blocks reflex firing on the pelvic nerve or post ganglionic fibers, which respond to the stimulation of pelvic nerve afferents. However it did not block reflex firing on the hypogastric nerve. In contrast, when VIP was administrated at middle lumbar spinal cord reflex firing did not alter the mictrition. Spinal transaction made left-shift of the dose-response course of the VIP inhibitory effect to the mictrition reflex. These VIP effects were abolised by IT pre-perfusion of the VIP antiserum. These data indicate VIP which significantly located at the pelvic nerve afferent neurons may inhibit the mictrition reflex at the sacral spinal cord label.

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CORTICAL INTERRUPTION OF URINATION IN DOGS. FUKUDA, H. AND KOGA, T. Dept. of Physiol., Kawasaki Med. School, Kurashiki 701-01

Man can voluntary interrupt urination through an unknown pathway. The pathway was studied in chloralose anesthetized dogs. Stimulation of pelvic and pudendal afferents evoked first positive waves (P1) in each one area in the post- and precentral gyri of the cortex. Both areas seem to correspond to somatosensory (S1) and motor (M1) areas of the sacral segment. No difference was recognized between latencies (10-13 msec) of both P1 in the S1 and M1. Moreover, both P1 were not influenced by i.v. injection of nembutal (40 mg/kg). Stimulation of the M1, but not the S1, elicited discharges of motor fibers to the external urethral sphincter (EUS) (latency, 18-55 msec) and a concomitant interruption of reflex discharges of pelvic vesical branches (latency, 60-140 msec). The motor fiber discharges disappeared after a bulbar pyramidotomy ipsilateral to the M1 stimulated, but the interrupiton survived. The results suggest that corticospinal fibers of the M1 excite EUS motor neurons, but do not inhibit directly parasympathetic neurons to the bladder at the spinal level. The interruption of reflex discharges of the parasympathetic neurons may be performed at pontine micturition reflex center.

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EFFECTS OF AMYGDALOID STIMULATION ON THE EFFERENT ACTIVITIES OF THE VESICAL BRANCH OF THE PELVIC NERVE AND OF THE URETHRAL BRANCH OF THE PUDENDAL NERVE IN DOGS. KOYAMA, K. Dept. Physiol., Kawasaki Med. Sch., Kurashiki 701-01

In ketamine and chloralose anesthetized 38 dogs whose hypogastric nerves were divided, the bladder was filled with Tyrode's solution from a reservoir under 15-20 cm H_2O pressure. The outflows of the pelvic vesical branch (PV) and of the pudendal urethral branch (PU) were recorded, and effects of amygdaloid stimulation on them were studied. Stimulation (2-100 Hz, 3 msec, 0.2 mA) was applied through a unipolar glass electrode inserted into the amygdala from the ventral surface of the exposed pyriform lobe. When the bladder contraction was induced by amygdaloid stimulation, the increased PV and decreased PU appeared after latencies of about 115 msec and 110 msec, respectivley. When the bladder relaxation was, oppositely, elicited by stimulation, the decreased PV and enhanced PU occurred after latencies of about 110 msec and 90 msec, respectively. The PV excitation (bladder contraction) was elicited from medial parts of the intermediate principal nucleus, medial parts of the medial principal nucleus, a part of cortical nucleus and of pericortical nucleus. Inhibition of PV (bladder relaxation) was induced from lateral parts of the medial principal nucleus, medial nucleus, central nucleus and a part of pericortical nucleus.

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EFFECTS OF HYPOTHALAMIC STIMULATION ON REFLEX OUTFLOW OF PELVIC VESICAL AND RECTAL BRANCHES OF DOGS. YAMANE, M. Dept. Physiol., Kawasaki Med. Sch., Kurashiki 701-01

Effects of electrical stimulation of the hypothalamus on reflex outflow of vesical and rectal branches were simultaneously observed in urethane-chloralose anesthetized dogs. The urinary bladder and rectum were removed in all dogs after isolation of bilateral vesical and rectal branches of the pelvic nerve. Stimulation of the hypothalamus inhibited or excited reflex outflow of vesical and rectal branches. Both effects were observed at points scattered widely in the hypothalamus. While stimulation of the posterior hypothalamus only inhibited both pelvic outflows. Stimulation of the most points in the dorsal hypothalamus inhibited outflow of the vesical branch, but did not affect on outflow of the rectal branch. In the supraoptic and periventricular nuclei, the excitatory responses in both pelvic branches and the inhibitory response in the vesical branch were observed, but the inhibitory response in the rectal branch was not observed. In the lateral hypothalamus, the inhibitory responses in both pelvic branches and the excitatory response in the vesical branch were obtained, but the excitatory response in rectal branch was not induced. A partial incision in the rostral part of the midbrain abolished the inhibitory response in the vesical branch, but the inhibitory response in the rectal branch remained.

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MECHANOSENSITIVITY OF HYPOGASTRIC AND PELVIC AFFERENT FIBERS SUPPLYING FEMALE REPRODUCTIVE ORGANS IN THE RAT. BERKLEY, K. J.*, HOTTA, H., ROBBINS, A.* and SATO, Y. Dept. Physiol., Tokyo Metropol. Inst. of Gerontol., Tokyo 173.

Responses of hypogastric and pelvic single afferent nerve fibers supplying reproductive organs to mechanical stimulation of the uterus and vagina were studied in the anesthetized rat. 32% of single filaments of hypogastric afferent nerve had their receptive fields on the uterine horn, while 33% of single filaments of pelvic afferent nerve had their receptive fields on the vaginal wall. Distention of the uterine horn with a pressure higher than 100 mmHg could produce increases in hypogastric afferent activity while distention of vaginal wall with a pressure higher than 15 mmHg could produce increases in pelvic afferent activity.

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THE RESPONSE PATTERN OF SYMPATHETIC NERVOUS BRANCHES DURING PGE_2-FEVER SAIGUSA, T. AND IRIKI, M.
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We have compared the response patterns of skin and visceral sympathetic nerves during spinal cord cooling with those during fever caused by i.v. injection of LPS and i.c.v. injection of PGE2 in urethane-anaesthetized rabbits.

The spinal cord cooling induced an increase of the skin sympathetic nerve activity, but on the other hand it caused an inhibition of the major splanchnic nerve activity.

During LPS-fever, both the skin sympathetic and the splanchnic nerve activities increased.

During PGE2-fever, the skin sympathetic and splanchnic nerve activities increased. Cardiac sympathetic activity also increased, suggested by heart rate increase withstanding cervical vagotomy. The renal sympathetic activity decreased, but mainly due to barorelfex to blood pressure increase.

The skin sympathetic nerve responds to spinal cord cooling and to LPS-fever and PGE2-fever unimodally in such a way to conserve heat. However, the response patterns of the visceral sympathetic branches are different between spinal cord cooling and fever.

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NEURONAL CONTROL OF LIPID METABOLISM IN BROWN ADIPOSE TISSUE. MINOKOSHI, Y. AND SAITO, M. Dept. Med. Biochem., Sch. Med., Ehime Univ. Ehime 791-02

The role of the sympathetic nerves in regulating lipid synthesis in brown adipose tissue (BAT) was studied by measuring incorporation of ^3H from ^3H_2O into fatty acids and glyceride glycerol of lipids in interscapular BAT in anaesthetized rats. Direct electrical stimulation of the sympathetic nerves caused two different kinds of response, depending on stimulus parameters: when electrical stimuli, consisting of 20-sec train of monophasic square pulses, were applied at 1 min intervals (ordinary pattern) or norepinephrine was infused intravenously, ^3H incorporation into glyceride glycerol increased whereas ^3H incorporation into fatty acids did not change. However, when stimuli of much shorter duration, 2 sec, were applied at 3 min intervals (burst pattern), ^3H incorporation into both fatty acids and glyceride glycerol was enhanced. Pretreatment with both propranolol and phenoxybenzamine did not suppress activation of lipid synthesis by electrical stimulation of the burst pattern, but paradoxically increased ^3H incorporation into both fatty acids and glyceride glycerol by stimulation of the ordinary pattern. These results suggest that the sympathetic nerves control lipid synthesis in BAT probably by the action of a substance other than norepinephrine secreted from the nerve terminals.

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Effect of pancuronium and vecuronium on baroreflex responses of renal nerve activity (RNA) to changes in blood pressure in rabbits

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Refelex responses of RNA to acute hypertension and hypotension were studied for determining baroreceptor sensitivity, which was induced pharmacologically (phenylephrine = PN and sodium nitroprusside =SNP) respectively, before and after pancuronium (PANC, 0.5mg/Kg) and vecuronium (VEC, 0.5mg/Kg) in urethane anesthetized rabbits. Intravenous injection of PANC and VEC produced slight and temporal changes in systemic blood pressure, heart rate and RNA. After the recovery of these parameters to the baseline levels, then, we tested repeatedly changes in baroreceptor reflex sensitivities. No significant changes in baroreflex sensitivity were found between before and after these both agents of PANC and VEC. These results suggest that these muscle relaxants (pancuronium and vecuronium) have no effects on baroreceptor reflex response of renal nerve activity.

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THE EFFECT OF HEPATIC BRANCH VAGOTOMY ON FOOD AND WATER INTAKE IN FEMALE RATS.

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Food and water intake were examined after hepatic branch vagotomy in rats with various ovarian treatments. Hepatic branch vagotomy produced a reduction in food and water intake in the rats with sham ovariectomy, ovariectomy and ovariectomy plus estradiol supply. The decreases in food intake caused by the vagotomy were even in the three ovarian treated rats, whereas reduction in water intake by the vagotomy was most prominent in the ovariectomized animals. Moreover, a linear relation of water intake to plasma osmolality was obtained when the hepatic vagotomy was made at the day of estrus or diestrus, and it was noted that regression coefficients between the two lines were significantly different from each other. These results suggest that food intake by the hepatic vagus nerve occurs unrelated to the estrus cycle, while water intake by the nerve varies according to the cycle through a change in plasma osmolality.

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PROJECTION OF NUCLEUS TRACTUS SOLITARIUS NEURONS TO CAUDAL VENTROLATERAL MEDULLA INFLUENCED BY HEPATOPORTAL OSMORECEPTIVE AFFERENTS IN RATS.

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Effects of hepatoportal osmoreceptive afferents on neurons that projected to the caudal ventrolateral medulla (CVLM) were investigated within the nucleus tractus solitarius (NTS) in rats. One hundred and ten neurons that responded antidromically to electrical stimulation of the CVLM were identified within the NTS. Among them, 62 neurons showed excitation (excitatory neuron), 6 neurons showed inhibition (inhibitory neurons) and 3 neurons showed both in response to electrical stimulation of the hepatic branch of the vagus nerve. Further, 12 excitatory and 2 inhibitory neurons showed decrease in discharge rate and another excitatory one did increase in response to portal infusion of hypertonic saline. The NTS neurons that projected to the CVLM were predominantly decreased in discharge rate by portal infusion of hypertonic saline.

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THE EFFECT OF ACUPUNCTURE STIMULATION ON THE PERIPHERAL SYMPATHETIC ACTIVITIES SYNCHRONIZED WITH CARDIAC AND RESPIRATORY RHYTHMS IN MAN.
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We studied the effect of acupuncture stimulation at an ankle (TAI-KEI or KON-RON) on the action potentials of the vasomotor nerve to ipsilateral soleus muscle by applying a tungusten microelectrode to the tibial nerve in man. Tonic discharges were observed in muscle sympathetic activities (MSA). We calculated the auto-power spectrum of MSA (APS). There were three peaks in the APS. The respiratory component of APS was inhibited by acupuncture stimulation in 5 out of 6 cases. The fundamental cardiac component of APS was inhibited in 3 out of 6 cases. The second harmonics of cardiac component of APS was inhibited in 4 out of 6 cases.

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CAPSAICIN IS A SPECIFIC SUBSTANCE P RELEASER FROM SENSORY NERVE ENDINGS IN THE GUINEA-PIG ILEUM? TAKAKI,M. AND NAKAYAMA,S. Dept.Physiol.,Okayama Univ.Med.Sch.,Okayama 700

The effects of capsaicin on the electrical behavior of myenteric neurons were examined with intracellular electrical recording techniques to determine whether capsaicin acts mediated via a mechanism other than the release of substance P from primary sensory afferents in the guinea-pig ileum. Pressure microejection of capsaicin(0.1mM) evoked a marked long-lasting slow depolarization associated with an increased input resistance, an action of generating and/or increasing soma spike potentials without any changes of membrane potentials and conductance in myenteric neurons. Superfusion with capsaicin(1μM) had no effect on myenteric neurons which respond to substance P(0.1mM) microejected. However,superfusion with capsaicin(10μM) evoked the same excitatory effects as those by pressure microejection of capsaicin in the presence of elevated magnesium(12.5mM) and reduced calcium(1.25mM). It is,therefore,likely that higher concentration of capsaicin acts directly on myenteric neurons in addition to the well-known substance P-releasing action from sensory nerve endings which is exerted by lower concentration of capsaicin.

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Gastric ulcer formation by kainic acid injection into DMV in the rat.
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Cells of origin innervating stomach are located in the dorsal motor nucleus of the vagus nerve (DMV). In this study, we tried to stimulate these cells chemically by focal injection of kainic acid. A microcapillary filled with 0.1M kainic acid was stereotaxically inserted to the left DMV, and kainic acid was iontophoretically ejected there. After 24 hours survival time, rats were sacrified with ether anesthesia and the stomach was examined. In 8 out of 10 rats, gastric ulcerations were found in the glandular stomach and ulcer indices were 19.0±12.0 (mean±SD) mm. Histologically, the ulcerations were erosions and mucus in mucosa decreased remarkably. Since kainic acid is a long-acting neuronal excitant, it can be considered that gastric ulcer formation is due to long lasting excitability increase of DMV neurons. The decrease of mucus in mucosa may also facilitate the process of gastric ulcer formation .

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RESPONSES ON SUPERIOR SALIVATORY NEURONS TO STIMULATION OF HYPOTHALAMIC AREA IN THE CAT. ISHIZUKA, K., MURAKAMI, T. AND NAKAYAMA, K. Dept. of Oral Physiol., School of Dentistry at Niigata, The Nippon Dental Univ., Niigata 951

Responses on superior salivatory neurons to stimulation of hypothalamic area were studied in lightly anesthetized cat with ketamin hydrochloride. Eight superior salivatory neurons responded polysynaptically to stimulation of ipsilateral anterior hypothalamic area, paraventricular region, lateral hypothalamic area, dorsomedial hypothalamic area and ventromedial hypothalamic nucleus. The latency range of these responses were 10.2 - 45.4 msec. Many of them also responded to peripheral sensory stimulations. These results indicate that many superior salivatory neurons receive inputs from wide hypothalamic area and those from peripheral sensory nerves.

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ROLE OF THE PARASYMPATHETIC INNERVATION OF THE LIVER UPON HEPATOCYTE PROLIFERATION AFTER PARTIAL HEPATECTOMY IN RATS. KINO,S., MITO,M.* and MORI,S.# Second Department of Surgery and Second Department of Physiology#, Asahikawa Medical College, Asahikawa

Two groups of rats (vagotomy group; the hepatic branch of the vagus nerve (HBVN) was severed, control group; the HBVN was preserved) were partially (70%) hepatectomized. DNA content of hepatocyte nuclei was measured by flow cytometry. Hepatic DNA synthesis, cell cycle progression (changes in mean ploidy of nuclei) and nuclear chromatin structure (DNA content distribution) were assessed. 1) The time course of DNA synthesis was delayed by 3 hours in vagotomy group even at the first peak of DNA synthesis. The cell cycle progression was also delayed by 3 hours. 2) Mean ploidy of vagotomy group (4.32±0.01c) was significantly higher than that of control group (4.05±0.02c) at 168 hours after partial hepatectomy. 3) Nuclear chromatin structure was not uniform in vagotomy group as compared to that of control group on and after 48 hours after partial hepatectomy. It was concluded that the parasympathetic innervation of the liver contributed to the progression of hepatocyte proliferation at the cellular level by providing a suitable environment for DNA synthesis at early stage of liver regeneration and by controlling cell kinetics, especially in the mitosis phase.

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EFFECTS OF CALCITONIN ON INTRAGASTRIC PRESSURE IN ANESTHETIZED RATS. KUROSAWA,M.[1], MATSUO,Y.[*2], OHNO,H.[*3] and SATO,A.[1] 1; Dept. of Physiol. Tokyo Metropol. Inst. of Gerontol., Tokyo 173, 2; 3rd. Dept. of Internal Medicine, Nihon University, Tokyo 173, 3; Toyo Jozo Co.Ltd., Tokyo 108.

The effect of calcitonin on intrapyloric pressure was examined in urethane anesthetized rats. The intrapyloric pressure was decreased dose dependently by intravenous administrations of 0.002-20 U of calcitonin. The calcitonin-induced decreased response was abolished after the severance of bilateral vagal nerves at the cervical level. Ongoing efferent activity of vagal gastric nerve branches was decreased by intravenous administration of calcitonin. On the contrary, intravenous administration of calcitonin increased intrapyloric pressure via vagal nerves in atropinized or gallaminized animals. The contribution of the cholinergic excitatory and the non-cholinergic inhibitory vagal nerve fibers to the calcitonin-induced responses of intrapyloric pressure is discussed.

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GUIDANCE OF NERVE FIBERS FROM EMBRYONIC CHICK SENSORY NEURONES BY PARALLEL-ALIGNED COLLAGEN MICROFIBRILS. FUKUDA, J. and KEINO, K. Dept. Physiol., Fac. Med., Univ. Tokyo, Bunkyo-ku, Tokyo 113.

Dorsal root ganglion cells mechanically dissociated from embryonic chick embryos were cultured on glass plate surfaces on which various species of fibrous molecules of polypeptides were lined up in a parallel manner by means of a specific alignment technique, so as to examine the role of the fibrous structures of protein molecules in the extracellular matrix in guiding the growth of nerve fibers. Parallel-aligned collagen fibrils exhibited a unique capability of guiding the growth of the nerve fibers in the direction parallel to the axis of the fibrils; most of the nerve fibers (approximately 3/4) grown during 48 h of tissue culture were oriented within 30 degrees of the axis of the matrix. In addition, the total length of the nerve fibers grown from the individual sensory nerve cell on the parallel-aligned collagen fiber matrix was increased. The total length was approximately twice as long as that grown on the matrix in which collagen fibrils were oriented in a random manner. SDS-PAGE and immunoblot examinations indicated that the matrix contained no other species of extracellular matrix proteins, such as fibronectin, laminin or vitronectin, except for the collagen fibers. A similar orientation of the growth of nerve fibers were recognized by the parallelization of other fibrous molecules, such as poly-L-lysine.

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CHANGE OF CHOLINERGIC MARKERS IN THE DEVELOPING SPINAL CORD SEGMENTS OF THE MOUSE. HIGASHIOKA,Y., SUNAYASHIKI-KUSUZAKI,K., MITANI,A., MASUDA,S., SHIBATA,T. and KATAOKA,K. Dept. Orthop., Physiol. and Cen. Res. Lab. Ehime Univ. Sch. Med., Ehime 791-02

For elucidation of the cholinergic synaptogenesis and differences thereof among spinal cord segments, we analyzed the cervical, thoracic and lumbar cord for the postnatal development of acetylcholine content(ACh) and related enzymes. We also measured the segmental distribution of fractional rate constant of ACh formation. As the individual grew older, we found a remarkable and consistent increase of choline acetyltransferase activity(ChAT) in parallel with ACh. On the other hand, practically no change of choline content(Ch) was observed during developmental processes and among the spinal cord segments analyzed. Segmental distribution study showed the highest value of both ACh and ChAT in the lumbar and the lowest of both in the thoracic cord. A sharp increase in acetylcholinesterase activity(AChE) was depicted until 2 weeks of postnatal age followed by fairly little alteration in the subsequent period studied. Fractional rate constant of ACh formation at a mature level was significantly high in the thoracic cord segments than in the cervical and the lumbar cord segments. The parallel increase of ACh and ChAT will reflect the quantitative aspect of the cholinergic synaptogenesis whereas AChE will not be involved directly, and the segmental differences will indicate functional differences of motor neurones.

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TRANSIENT INCREASE IN MOTONEURON DENDRITIC RESPONSES FOLLOWING TETANIZATION OF AFFERENT NERVES IN PIGS AND CATS. FUJITA,Y., HARADA, H., FUJII, N., Dept. Physiol., Nippon Medical School, 1-1-5, Sendagi, Bunkyo-ku, Tokyo, 113 Japan.

It was reported that chronic stimulation of a dorsal root led to enhancement of dendritic spikes (D-spikes) and slow depolarizations of dendritic origin (D-waves) (Fujita et al., J. Physiol. (Lond.), 383: 171-190, 1987). This prompted us to study the effects of tetanization of afferent nerves on the dendritic responses in acute experiments. The experiments were made in decerebrate, nonanesthetized infant pigs and adult cats. Intracellular recordings were made in the lumbar enlargement. Following tetanization of the dorsal root (L7 or S1) or that of peripheral nerves (sciatic, biceps-semitendinosus & tibial nerve) at 500/s for 5 s, enhancement of the dendritic responses were observed which lasted for 0.5-3 min. Considering from the latency of these responses, it was thought that potentiation of polysynaptic pathways was involved. In order to know this, the effects of tetanization of the dorsal root were studied by recording compound action potentials (spikes) from the ventral root (L7 or S1) in cats. Whereas monosynaptic spikes were enhanced predominantly by 500/s tetanization, polysynaptic spikes were enhanced by 10-500/s tetanization. There were homosynaptic and heterosynaptic potentiation of polysynaptic spikes. These potentiations were reversibly abolished by Nembutal injection, while monosynaptic spikes were enhanced.

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SUPRASPINAL INVOLVEMENT IN SPINAL NEURONAL HYPERACTIVITY FOLLOWING PERIPHERAL NERVE SECTION IN THE RAT. ASADA, H., YASUMO, W. AND YAMAGUCHI, Y. Department of Health Sci., Coll.Integ.Arts & Sci., Univ. of Osaka Pref., Sakai,591

Abnormal spontaneous hyperactivities often occur in the rat spinal cord following peripheral nerve section. These hyperactivities are considered to be correlated with autotomy of the rat after nerve section. Experiments were performed on rats in an attempt to study the role of the supraspinal centers in the spinal hyperactivity.

Male wister rats were examined after the unilateral sciatic nerve section. Spinal unit activities were recorded under ketamine anesthesia, immobilized by pancuronium bromide. Spontaneously firing units increased in the spinal cord (L2-4), seen widely in the gray matter, at 18 hours to 220 days after the nerve section. The units with high frequency (30-200Hz) activities often showed rhythmic burst firing which was never seen in the intact rat. More than half of the hyperactive neurons presented decreased or increased activity during a reversible cold block of the spinal cord at segment T3. About half of hyperactive neurons showed decreased activity during and/or after repetitive electrical stimulation for 1 min. in the thalamus, chiefly the ventralis posterolateralis nucleus. These results suggest that spinal abnormal spontaneous hyperactivity is partly due to descending influences of higher centers including the inhibition from the thalamus.

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PREMOTOR INTERNEURONES MEDIATING SKIN REFLEXES IN THE FORELIMB OF THE CAT. HONGO, T., KITAZAWA, S., OHKI, Y. AND XI, M.C. Dept. Neurophysiol., Institute of Brain Res., School of Med., Univ. of Tokyo, Tokyo 113

Intracellular recording from cat's forelimb motoneurones showed that both the excitatory and inhibitory skin reflex pathways are di- and polysynaptic and are facilitated from the pyramidal tract. This study aimed at identifying interneurones of the reflex pathways using anesthetized cats. Neurones retrogradely HRP-labelled from the motor nuclei of T1 distributed in laminae IV-VII, most densely at C7-C8. Neurones excited mono- or polysynaptically from skin afferents were recorded in this region. Among them we found those descending in the lateral funiculus and terminating in the motor nuclei as indicated by threshold mapping for antidromic activation, and further those producing monosynaptic EPSPs or IPSPs in motoneurones at T1 as revealed by spike triggered averaging. Termination of such neurones in the motor nuclei was also shown by intracellular HRP staining of them. The excitatory and inhibitory neurones were located mixed in laminae V, VI and the dorsal part of lamina VII. Both the neurones were excited mono- or polysynaptically from skin afferents and also from the pyramidal tract. The input properties were as expected from the previous observations in motoneurones. To conclude, the last order interneurones of di- and polysynaptic skin reflex pathways, both excitatory and inhibitory, were identified in laminae V-VII.

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DORSAL COLUMN DYSFUNCTION IN EXPERIMENTAL NEUROPATHIES. KOYAMA,N., TERADA, M.※, YOKOTA, T., Dept. Physiol., Medical College of Shiga, Seta, Otsu 520-21

In chronic clioquinol, diabetic and 3,5-hexanedione cats, (1) surface potentials evoked by electrical stimulation of the sural nerve (SUR), (2) spike responses of relay neurons in the gracile nucleus to electrical stimulation of the SUR, (3) primary afferent depolarization within the gracile nucleus, (4) antidromic compound action potentials in the SUR evoked by electrical stimulation of the gracile nucleus, (5) dorsal root potentials evoked by electrical stimulation of the SUR, (6) primary afferent depolarization within the spinal cord and (7) antidromic compound action potentials in the SUR evoked by electrical stimulation of the dorsal root were recorded under urethan-chloralose anesthesia. In clioquinol cats, damage of primary cutaneous afferent neurons was demonstrated in and near the gracile nucleus, but nor at the level of the lumber spinal cord, nor in the SUR. In diabetic cats, conduction velocity of sural nerve fibers was reduced, but the gracile tract remained unaffected. In 3,5-hexanedione cats, primary cutaneous afferent neurons were damaged both in the gracile tract and in the SUR.

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CRAYFISH UROPOD POSTURE CONTROL SYSTEM: AN ANALYSIS OF UNDERLYING NEURAL CIRCUIT WITH LASER DESTRUCTION OF NEURITES.

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A laser apparatus was recently devised in our laboratory. This apparatus is basically a dissecting microscope combined with short wave-length laser (441.6nm, He-Cd) illumination. The system can be converted into either an epiilluminating fluorescence microscope or an intense microbeam irradiation apparatus with displacing a single lens. Combined with low level vital staining of neurons with Lucifer yellow dye through the recording electrode, the apparatus facilitates the identification of the penetrated neuron while the activity is recorded, and enables the in situ destruction and subsequent removal of the neuron or a part of it from the neural circuit. The extensor inhibitory motoneuron which had output effect to its contralateral homologue was irradiated its axon by the intense microbeam, and could no longer propagate its orthodromic action potential over the irradiated portion. The rest of the neuron in the ganglion, however, operated normally. Applying this method to the uropod motor system of crayfish, we could confirm that certain branches of nonspiking interneurons would operate as the input site while others act as the output region. The results support the possibility that each branch of nonspiking interneurons might function independently of each other. The device has proved to be extremely useful to the study of individual neurite function.

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DEVELOPMENT OF INHIBITORY PATHWAYS IN THE LUMBAR SPINAL CORD OF RATS

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Development of inhibitory pathways to the lumbar motoneurones was studied using isolated spinal cord and spinal cord-hind limb preparations of fetal (E16.5-20.5) and new-born (P4-6) rats. Intracellular recordings from motoneurones were performed with a glass microelectrode filled with 3M methyl potassium sulfate. Stimulation of dorsal roots and ventrolateral funiculus of the first cervical spinal cord evoked EPSPs in 70% and 35%, respectively, of motoneurones examined at E16.5. IPSPs were also evoked by stimulation of the dorsal roots at E16.5 (50%), while the descending IPSPs first appeared at E17.5 (44%). The IPSPs were always accompanied by EPSPs, and the descending IPSPs appeared exclusively in the motoneurones with IPSPs from the reflex pathways. EPSPs from both reflex and descending pathways were evoked in all motoneurones examined at E18.5, and IPSPs at E19.5. At E20.5 and P4-6, the input pattern to quadriceps (Q) motoneurones from the posterior biceps (PB) and sural nerve was examined. Stimulation of the PB nerve evoked only IPSPs in Q motoneurones at E20.5 and P4-6. Central latencies of the IPSPs were significantly shorter than those of the sural nerve at each age, suggesting that the inhibitory pathways, mediating the reciprocal inhibition, start functioning by E20.5, one day prior to birth.

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FACILITATION OF REFLEX PATHWAYS ONTO FORELIMB FLEXOR MOTONEURONS BY THE CENTRAL LOCOMOTOR PATTERN GENERATOR IN CATS

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We found that in elbow flexor motoneurons EPSPs evoked from forelimb nerves increased in amplitude during motoneuronal depolarization occurring at flexion phase of fictive locomotion induced by stimulation of midbrain in immobilized decerebrate cats with the lower thoracic cord transected. Present study further analyzed their synaptic mechanisms. It was revealed that EPSPs with short segmental latencies (about 3 ms) evoked from cutaneous afferents (superficial radial nerves) were rather small during extension phase of fictive locomotion (1.5±0.5 mV, n=8), but they increased twice or more during flexion phase. Similar amplitude modulation also appeared in EPSPs from muscle nerves with segmental delay of 1.2-1.8 ms. In contrast to such marked changes, both input resistance of motoneurons and amplitude of monosynaptic EPSPs from group I muscle afferents remained substantially constant during fictive locomotion, suggesting that amplitude modulation of those EPSPs does not occur at the motoneuron level. It was concluded that interneurons mediating those reflex pathways received excitation during flexion phase from the central locomotor pattern generator.

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MORPHOLOGICAL ANALYSIS OF INTERNEURONES MEDIATING REFLEXES FROM THE HINDLIMB FOOT PADS . KUDO, N ., OGUNI, E ., and YOSHIDA, K Dept. of Physiol., Inst. of Basic Med. Sci., Univ of. of Tsukuba , Tsukuba, Ibaraki 305 Japan

Pressure stimuli applied to the foot pads evoke particular reflex actions in toe extensors of the sole. In the present study, we attempted to elucidate morphological properties of premotor interneurones mediating these reflexes by means of intra-axonal staining with horseradish peroxidase (HRP). Recordings were made in the lateral funiculus of L6-S1 in Nembutal anaesthetized cats. HRP was injected into axons of interneurones responding to stimulation of the foot pads. Thirty-one stained axons which gave off their collaterals to the ventral horn were selected for analysis. Somata were also labelled in 15 cases. Medium-sized cell bodies (20-30μm), with 5-7 primary dendrites, were located in laminae VI-VII of L6-7. All stained axons ran in the medial part of the lateral funiculus and could be traced down to the sacral level and issued many collaterals into the gray matter. Each collateral arborized and terminated extensively in the dorsolateral part of the ventral horn. In preparations in which toe extensor motoneurones had been labelled with HRP transported retrogradely from the muscle, it was found that the terminals of injected interneurones were most densely distributed within and around the motor nucleus. These morphological findings are consistent with the fact that the skin reflex from foot pads appears specifically in toe extensors.

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LOCOMOTOR ACTIVITY OF HINDLIMBS IN CATS WITH CHRONIC LONGITUDINAL SEPARATION OF THE LUMBAR SPINAL CORD. KATO, M. Dept. Physiol., Hokkaido Univ. Sch. Med., Sapporo 060

The present study was undertaken to investigate which structures, spinal segmental or supraspinal, play more important roles in coordinated locomotor activities of the right and left hindlimbs of the cats whose spinal cord was sectioned longitudinally at the lumbar level. Lumbar cord was carefully sectioned from L_3 through L_7 or S_1 aseptically. The chronic cats were investigated for more than 3 months by recording EMG activities from triceps brachi, vastus lateralis and tibialis anterior muscles of both sides during locomotion. The cats were encouraged to walk on the floor after surface electrodes were attached on skin covering the appropriate muscles, following hairs were carefully removed by hair remover cream. Phase relationship between the two limbs was analysed by Wendler's method as used earlier. Coordination between two hindlimbs was well preserved in these chronic cats, suggesting that pathways from supraspinal and/or higher spinal structures play important roles in coordination of two hindlimbs during overground locomotion.

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COMPARISON OF THE MOTOR CORTEX-INDUCED FLEXOR MUSCLE ACTIVITY INHIBITION BY HARD PRESSURE OF THE BODY PARTS AND BY LIGHT PINCH OF THE ULCER SUFFERING ANIMAL ABDOMEN.

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The flexsor muscle electromyogram(EMG) of the upper extremities in response to the motor cortex stimulation was inhibited by hard hand pressure on base of the ear lobe and lumbar perivertebral region. Similar inhibition was produced by electrical stimulation around the brachium conjuctivum and locus coeruleus (BC-LC) and the reticulogigantocellular nucleus (NRGC). Inhibition of the flexor muscle EMG due to hard pressure on the body parts was abolished by electrical lesion of the BC-LC and NRGC. The light pinch with hand on the restricted abdominal region did not inhibit the flexor muscle EMG induced by the motor cortex stimulation in normal condition, while such stimulation inhibited the flexor muscle EMG in the ulcer suffering animals after treatment with cysteamine. This inhibition was not influenced by destruction of the NRGC. Therefore, it was suggested that this inhibitory mechanism was different from that of hard pressure of ear lobe and lumber region.

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THE MORPHOROGICAL STUDY ON THE SOMATO-VISCERAL REFLEXES. Kashiba,H. and Ueda,Y., Kansai College of Acupuncture Medicine, Ogaito 990, Kumatori-cho, Sennan, Osaka 590-04, Japan.

The soma size of dorsal root ganglion(DRG) cells projecting the skin and visceral organs were compared at the spinal level of T9-10 in the rat by retrograd tracing and immunocytochemical demonstration of calcitonine gene-related peptide(CGRP). Moreover, possibility of collateral project ions from the same DRG cells to both visceral and cutaneous regions, was examined by means of double fluorescence labeling.

The findings of the present study are as follows: 1) The cell size of visceral DRG neurons was larger than that of somatic ones. Visceral CGRP-like immunoreactivity(CGRP-IR) DRG neurons were also larger than somatic CGRP-IR ones. 2) The incidence of CGRP-IR neurons was higher in the visceral DRG cells than in the somatic ones. 55% of visceral DRG neurons displayed CGRP-IR, whereas only 21% of somatic DRG neurons were CGRP-IR. 3) Few DRG neurons dichotomized into visceral and somatic nerves.

These experiments were carried out in cooperation with Senba,E. and Tohyama,M.(2nd Anat.,Osaka univ.).

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THE RELATIONSHIP BETWEEN CUTANEOUS ELECTRICAL STIMULATION AND CHANGING THE RECRUITMENT LEVELS OF THE LOWER LEG MOTOR UNITS IN MAN. OKAND, K. HOKKAIDO UNIVERSITY, SCHOOL OF MEDICAL TECHNOLOGY, KITA 12 JO, NISHI 5 CHOME, KITA-KU, SAPPORO 060

The relationship between the electrical stimulation of the toe and changing the recruitment levels of the motor units in the lower leg muscles were studied by 8 experiments from the three subjects. Electrical stimulation was applied by the disc electrodes on the surface of the second toe at 3 times the threshold for perception (pulse width 50 us, 50 shocks second^{-1}, duration 15 min). 5 layered Isonel coated stainless steel wires were used for recording motor units and a storage scope was used for examinations of the motor units identification. The ankle joint was immobilised and the isometric contraction forces of either dorsiflexion or plantar flexion produced by the lower leg muscles were recorded for measuring the recruitment levels of the motor units. After cutaneous stimulation, 18 out of 28 motor units from the tibialis anterior muscles showed the decreases of the recruitment levels (mean = -9.9 % of the maximum voluntary contraction: MVC). 15 out of 16 motor units from the soleus muscles showed the increases of the recruitment levels (mean = +29.9 % of the MVC). Present results were obtained from the low threshold motor units. It was congruent with our previous results; flexor reflex pattern.

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REDUCTION IN NERVE CONDUCTION VELOCITY CAUSED BY REPETITIVE STIMULATION.
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The effect of repetitive stimulation on frog sciatic nerve fibers were examined. (1) Supramaximal pulses, having 0.05 msec duration and 9 V intensity, were used at 1 to 100 Hz for 60 min. Conduction velocity decreased exponentially to the increase of stimulus frequency. Conduction velocity decreased to about 60 % of the control in case of 100 Hz for 60 min stimulation. (2) Potassium concentration on the surface of isolated single fibers was examined with X-ray microanalyzer. The correlation coefficient of K/P ratio vs axonal diameter was -0.49. The K/P ratio increased at higher stimulus frequencies over 10 Hz. (3) Potassium concentration in the whole-nerve trunk was examined by flame photometry. Potassium concentration after 100 Hz stimulation became about three-fold greater than that of the control. The increase was significant at higher stimulus frequencies over 100Hz. The increase in sodium concentration was slight, and far less than that of potassium. It is suggested that repetitive stimulation caused a large increase in potassium efflux from intracellular space, and produced potassium ion accumulation at the circumferential extracellular space, including Schwann cells and mesoaxons. The increase in the extracellular potassium concentration is expected to decrease membrane irritability of nerve fibers.

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EFFECT OF DORSAL ROOT TRANSECTION AND HEAT COAGULATION OF DORSAL SPINAL ARTERY ON SOME NEUROTRANSMITTER CANDIDATE LEVELS IN RAT SPINAL CORD. FUJITA, K. and NAGATA, Y., Dept. of Physiol., Sch. of Med., Fujita-Gakuen Health Univ., Toyoake, Aichi 470-11

In order to search for neurotransmitter candidates of primary sensory neurons and interneurons in the spinal cord, changes of acetylcholine synthesizing and decomposing enzyme activities, and some amino acid contents in the tissue were examined 7 days after hemitransection of dorsal root or heat coagulation of unilateral dorsal spinal artery entering into the cord. By the surgical transection of unilateral dorsal root, reduction of acetylcholinesterase activity in the spinal cord on the same side, and the decrease of choline acetyltransferase activity in the dorsal half of the operated side were observed. These data suggest that cholinergic transmission system might be partly involved in the sensory transmission process. However, there was no appreciable changes in free amino acid levels in either operated or controlside of the cord. Unilateral heat coagulation of dorsal spinal artery branch caused a significant decrease in aspartate, glutamate and GABA levels, and increase in taurine in the dorsal part of the operated spinal cord. These results suggest that these amino acids may be operated as neurotransmitter candidates in the interneurons of the dorsal spinal cord.

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EFFECTS OF NUCL. RAPHE STIMULATION ON AFTERDISCHARGE OF SPINAL MOTONEURONS IN CATS. WADA, N., NAKAJIMA, Y., MITSUHASHI, T., MOCHIDA, A. & HOMMA, S., Dept. Physiol., Sch. Med., Chiba Univ., Chiba, 280

Experiments were performed on cats decerebrated under ether anesthesia. Afterdischarge of spinal motoneurons induced by peripheral nerve stimulation was depressed by spinalization or spinal lesions. These facts indicate the effects of supraspinal center on the afterdischarge. Housgaard et al(1984,85) reported that spinal motoneuron has an intrinsic behaviour such as repetitive discharge which occur even after cessation of synaptic inputs from the afferent nerve and that such a behaviour is induced by 5-HT. It has been reported that Nucl.Raphe contains serotonergic neurons. In this experiment, we investigated the effects of Nucl. Raphe stimulation on afterdischarge. The medial gastrocnemius nerve was electrically stimulated (1.3T, 100Hz). A single stimulation sequence was composed of a 1-second tetanic stimulation followed by a pause of 2-seconds. Tungusten micro-electrode was inserted into Nucl. Raphe and the stimulus intensity was adjusted at 30-50 uA. Alpha-motoneuronal activity was recorded as a single unit from finely dissected filaments of the L7 ventral root. Stimulation of the middle part of Raphe magnus(R.m.) and Raphe obscure(R.o.) increased the rate of after-discharge, while another parts of R.m. and R.o inhibited afterdischarge generation.

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MULTIPLE-SITE OPTICAL RECORDING OF ELECTRICAL ACTIVITY IN THE EMBRYONIC CHICK VAGUS/BRAIN STEM PREPARATION USING VOLTAGE-SENSITIVE DYES. KOMURO, H., KATOH, Y., SAKAI, T., SATO, K. and KAMINO, K. Dept. of Physiol., Tokyo Ika-Shika Dai., Sch. Med. Tokyo 113.

Electrical activity in the embryonic chick brain stem has been optically monitored. The vagus-brain stem preparations isolated from 7-day old chick embryos were stained with the voltage-sensitive merocyanine-rhodanine dyes. Voltage-related optical absorption signals evoked by vagus nerve stimulation with depolarizing and hyperpolarizing pulses using a suction electrode were recorded simultaneously from 127 adjacent loci in the brain stem using a 12x12-element photodiode array. The optical signals evoked by the stimulation appeared to be concentrated longitudinally in the central lateral regions, both in the stimulated side of the brain stem, and they did not spread to the opposite side. In addition, the evoked optical responses were detected from the small areas on the dorsal surface of the stimulated side, in the experiments using the brain stem slices. On the basis of the data obtained from these experiments, we depicted the spatial pattern of the vagus dorsal nucleus in the embryonic chick brain stem.

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SOME PHYSIOLOGICAL NATURES OF OPTICAL RESPONSE EVOKED BY VAGUS STIMULATION IN THE EMBRYONIC CHICK BRAIN STEM MONITORED BY VOLTAGE-SENSITIVE DYES. SATO, K., KOMURO, H., SAKAI, T., KATOH, Y. and KAMINO, K. Dept. of Physiol., Tokyo Ika-Shika Dai., Sch. Med. Tokyo 113.

Voltage-sensitive merocyanine-rhodanine dyes (NK2761; NK3225; dye XVII) together with a 12x12-element square multiple-site optical recording system of changes in membrane potential were used to reveal the electrical activity in the embryonic brain stem. The vagus-brain stem preparations isolated from 7-day old chick embryos were stained with the dyes. With the brief depolarizing stimulus, the optical signals conducted and were blocked completely by tetrodotoxin. These optical signals appeared to be concentrated longitudinally in the limited central zone in the stimulated side of the brain stem, and they did not spread to the opposite side. When 2uA/2ms hyperpolarizing impulses were applied, anode-break excitation signals appeared and they were also blocked by tetrodotoxin. The present study demonstrates the usefulness of voltage-sensitive dyes and the multiple-site optical recording method in the analysis of the organizing processes of neuronal functions in the central nervous system during the early stages of development.

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MULTIPLE-SITE OPTICAL RECORDING OF SPREADING ELECTRICAL ACTIVITY IN THE EMBRYONIC CERVICAL VAGUS NERVES USING A VOLTAGE-SENSITIVE DYE. KATOH, Y., KOMURO, H., SAKAI, T. and KAMINO, K. Dept. of Physiol., Tokyo Ika-Shika Dai., Sch. Med. Tokyo 113.

A multiple-site optical recording method using a 12x12-element photodiode array was used to study the spread of electrical activity in the cervical vagus nerves isolated from five- to twenty-one-day-old chick embryos. The preparation was stained with a voltage-sensitive merocyanine-rhodanine dye (NK2761). A brief stimulus, applied to the end of the bundle of the vagus nerve fibers by means of a suction electrode, evoked changes in light absorption related to action potential and the optical signals spread from the site of stimulation. We measured delays between the feet of the optical action signals. From the relationship between the delay and distance from the site of stimulation, we estimated conduction velocity of the action potential. The conduction velocity was about 0.1 m/sec in the five-day-old embryo and it increased to about 0.5 m/sec as development proceeded to the twenty-one-day. This increase in the conduction velocity was directly related to that in the diameter of the bundle of vagus nerve fibers.

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LOW-THRESHOLD CA-DEPENDENT RESPONSE IN NIGRAL PARS RETICULATA NEURONS OF THE GUINEA-PIG.
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Electrophysiological properties of the neurons in the substantia nigra pars reticulata (SNR) were studied in a slice preparation obtained from the guinea-pig. Many of the SNR neurons studied generated action potentials spontaneously (8-40 spikes/s) and the neurons were capable of producing a repetitive firing at relatively high rates (250-300 spikes/s) in response to injected depolarizing currents. The input resistance and membrane time constant of the neurons measured 68±28 MOhms (n=36) and 13±6 ms (n=11), respectively. A low-threshold Ca^{++}-dependent response was also noted as reported for rat SNR neurons. The response was elicited when the baseline level of the membrane potential was polarized by 10-20 mV from the control level (-53±8 mV) and it took the form of a slow depolarization with a burst of spikes on it. The low-threshold response could be demonstrated in approximately one third of the neurons which exhibited the firing pattern and passive electrical properties of a typical SNR neuron.

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DIFFERENCE IN MOTOR RECOVERY BY THE GRAFT OF NIGRAL AND ADRENAL MEDULLARY CELLS IN DOPAMINE DEPLETED CAUDATE IN THE RAT .
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Cell suspension of fetal rat substantia nigra or newborn rat adrenal medulla was grafted in unilaterally dopamine depleted caudate in the rat. By nigral graft Met-amphetamine circling disappeared completely after the 4th week. When tyrosine hydroxylase positive cells (grafted dopamine cells) survived more than 300 to 400 per animal, recovery from motor imbalance continued for more than 80 weeks. Dopamine and its metabolites (DOPAC, HVA), measured by in vivo dialysis, recovered to 30 to 50% of those in intact animals. By adrenal medullary graft the recovery from motor imbalance was poor (0 to 30%). Intravenous injection of horseradish peroxidase (HRP Sigma Type VI , 0.3 ml of a 5% solution per 100g body weight) revealed a small and massive HRP deposits around transplanted areas of nigral and adrenal grafts, respectively. Data suggest the extent of disturbance of the blood brain barrier following these 2 kinds of grafts differs, and this might be one of the mechanisms that control functional recovery.

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TURNING MOVEMENTS VIA DESCENDING PATH FROM SUBSTANTIA NIGRA PARS RETICULATA IS EVIDENT IN THE PREMAMMILLARY DECEREBRATE CATS.
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It has been proposed that descending path from pars reticulata (p. r.) of the substantia nigra (s. n.) acts to prevent turning movements of the rat and the cat. We have investigated this possibility and contribution of the superior colliculus using cats (d. c.) decerebrated at the precollicular and the premammillary level.

In the d. c., muscimol (2-3ug/2-3ul) was injected unilaterally through a microsyringe into p. r. of s. n. At once, lateroflexion of the head and the cervicothoracic vertebrate column, and turning movements appeared toward the contralateral side. Similar movements appeared when muscimol was given after destructing dopaminergic neurones by 6-OHDA, and also in the d. c. after destructing p. r. neurones in the area of about 1mm diameter by intranigral injection of ibotenic acid.

The muscimol-induced contraversive movements in the d. c. were attenuated partially when descending impulses from the ipsilateral superior colliculus were blocked by intrategmental injection of procaine (2%, 20ul). These results indicate that the descending path from p. r. of s. n. acts to prevent contraversive turning movements of the cat, and superior colliculus partially contributes to this action.

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ROLE OF PONTINE OMNIPAUSE NEURONS IN GENESIS OF VERTICAL EYE MOVEMENTS.
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Omnipause neurons (OPNs) in the midline pontine tegmentum exhibits a tonic firing ceasing prior to and during fast eye movements in all directions. A class of burst neurons (BNs) in the Forel's field H (FFH) emit bursts of firing during vertical fast eye movements and project to the oculomotor nucleus (ON). In the present study, extracellular spikes of the single OPNs and BNs were recorded from the respective regions of chronically prepared alert cats. The following results were obtained. (1) OPNs were antidromically activated by microstimulation at the recording sites of the BNs on both sides. (2) Systematic tracking with a stimulating microelectrode revealed that OPNs issued axonal branches within the BN area. (3) Antidromic spikes of the BNs evoked by ON stimulation were suppressed by microstimulation within the OPN area. These results suggest that OPNs make direct inhibitory synaptic connections with the BNs in the FFH. A cease of OPNs' firing (disinhibition) may play an important role in the genesis of vertical fast eye movements.

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THE FACILITATORY INPUTS FROM THE BULBAR RETICULAR FORMATION TO THE FACIAL MOTONEURONS OF THE CAT. ASAHARA, T. AND TANAKA, T., Dept. Physiol., Sch. Med., Mie Univ., Tsu, Mie 514

The afferent inputs from the bulbar reticular formation to the facial neurons were studied experimentally in Nembutal anesthetized cats by the aid of the intracellular recording technique. Stimulation of the dorsolateral part of the bulbar reticular formation on the ipsilateral side evoked EPSPs with latencies of 1.4-3.0 msec(mean 2.2±0.4 msec, 21 cells). This mean latency is longer by about 1.0 msec than that of monosynaptic EPSPs elicited by stimulation of the midbrain reticular formation. We have previously reported a direct excitatory connection between the midbrain reticular formation and the facial nucleus. Stimulation of the ventromedial part of the bulbar reticular formation produced monosynaptic EPSPs with latencies of 0.5-0.9 msec(mean 0.7±0.1 msec, 14 cells). The time to peak of the EPSPs ranged from 1.2 to 2.0 msec (mean 1.6±0.2 msec, 11 cells). Any hyperpolarizing potentials could not be evoked in the facial neurons after stimulation of both the dorsolateral and ventromedial parts of the bulbar reticular formation. Single volleys in the contralateral bulbar reticular formation also elicited EPSPs with a wide range of the latencies of 1.5-3.0 msec(mean 2.1±0.6 msec, 10 cells). These results suggest that the bulbar reticular formation projects to the facial nucleus in the cat directly or indirectly on both sides, and could have facilitatory effects on the facial motoneurons.

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CONVERGENCE OF CORTICAL AND PERIPHERAL INPUTS TO BRAIN STEM NEURONS IN THE RAT. INOUE, T., MASUDA, Y., SAITOU, O. AND MORIMOTO, T. Dept. Oral Physiol., Osaka Univ. Fac. Dent., 1-8 Yamadaoka, Suita, Osaka 565

Previous study showed that cortically induced jaw movements were modulated by intraoral stimulation. In order to identify the mechanisms underlying such modulation, neurons responding both to repetitive stimulation of cortical masticatory aera (CMA) and stimulation of trigeminal sensory branches were examined in the brain stem of the nembutal anesthetized rat. Thirty-three neurons were recorded in the reticular formation around trigeminal motor nucleus and in the parabrachial nucleus. Twelve of these neurons showed rhythmic modulation of the firing frequency during CMA stimulation (phasic type). Fifteen neurons increased the firing frequency tonically (tonic excitation type), while six decreased it tonically (tonic inhibition type) during CMA stimulations. Most of these phasic and tonic type neurons also responded either to stimulation of the trigeminal sonsory branches and/or to the passive jaw opening. The majority of phasic type neurons fired in the interburst phase of the digastric nerve. And they were located in the supratrigeminal area and the parabrachial nucleus. Similar results were obtained in the rabbit.

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INCISOR AND MOLAR CONTROL MECHANISM OF JAW MOVEMENT IN THE RAT.
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Periodontally controlling mechanism of the jaw movement was examined in lightly anaesthetized rats. The EMGs of the masseter and temporal muscles were recorded and pressure stimulation was applied on the upper incisor and the upper molar. Reflex responses were changed with background activity of the muscles. Stimulation of the incisor and the molar induced tonic excitatory reflexes of the both muscles in low background activity, but tonic inhibitory reflexes in high background activity. In medium background activity, the excitatory reflex of the masseter muscle and the inhibitory reflex of the temporal muscle were elicited from the incisor and reversed responses occured from the molar. Periodontal input regulates reciprocally activity of the masseter and temporal muscles in medium background activity.

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MODULATION OF MASTICATORY RHYTHM ACTIVITY BY CEREBELLAR NUCLEUS INTERPOSITUS.
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We reported that stimulation of the cerebellar nucleus interpositus (NI) of the guinea pig inhibited masseter motoneurons and excitated anterior digastric motoneurons after a short latency. In the present study we analyzed the effects of NI stimulation on the rhythmical masticatory activity (RMA) induced by repetitive stimulation of the cortical masticatory area of the ketamine-anesthetized, paralyzed guinea pig. The RMA was monitored by the rhythmical burst activity in the anterior digastric motoneuron pool. The cycle time (CT) was defined as the period from the onset of the burst phase to the end of the interburst phase. The following results were obtained: 1) The CT and the interburst phase tended to be prolonged in proportion to the period from the onset of the cycle to application of a short train-pulse to the NI. This effect was confined only to the cycle, during which the NI stimulation was applied. 2) A short train-pulse applied to the NI did not change the mean duration of the burst phase of the next cycle. 3) NI stimulation lagged the phase of the next cycle about the same length of time as that of stimulus application from the onset of masticatory cylce: NI stimulation tended to trigger the next burst after a constant latency of a CT. The results suggest that the output of the NI exerts its effect on the central masticatory rhythm generator.

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SYNAPTIC POTENTIALS IN JAW CLOSER AND JAW OPENER MOTONEURONS DURING SWALLOWING.
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Synaptic potentials in cat masseter and anterior digastric motoneurons (Mass- and Dig-Mns) during swallowing were studied. A Mass-Mn and Dig-Mn was identified by recording an antidromic spike and unitary muscle activity in the masseter muscle and anterior digastric muscle (Mass- and Dig-muscle) followed an induced spike of a motoneuron one-for-one. As a result, during swallowing, a depolarizing potential was evoked on a Dig-Mn and a depolarizing-hyperpolarizing potential sequence on a Mass-Mn. A hyperpolarizing potential in a Mass-Mn during swallowing was sensitive to membrane polarization. In immobilized cat, a depolarizing potential was evoked reproducibly on a Dig-Mn and a depolarizing-hyperpolarizing potential sequence on a Mass-Mn by repetitive electrical stimulation of the superior laryngeal nerve at optimal frequency and strength for elicitation of swallowing. A superior laryngeal-induced hyperpolarizing potential in a Mass-Mn was sensitive to intravenously administered strychnine and to membrane polarization. In addition, we found that discharge rates of afferent fibers from jaw closing muscle spindles were increased during jaw-closure associated with swallowing. The results suggested that jaw closing muscle fusimotoneurons were activated during jaw closure associated with swallowing.

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PROJECTION AND FIRING BEHAVIOR OF VERTICAL EYE POSITION-RELATED SECONDARY VESTIBULAR NEURONS IN THE CAT. IWAMOTO, Y., KITAMA, T.*, and YOSHIDA, K. Dept. of Physiol., Inst. of Basic Med. Sci., Univ. of Tsukuba, Ibaraki 305, and Dept. of Neurophysiol., Inst. of Brain Res., Sch. of Med., Univ. of Tokyo, Tokyo 113

It has been reported that the vertical eye position-related secondary vestibular (VPV) neurons make direct connection with ocular motoneurons. In the present study, their firing behavior was quantitatively analyzed. Recordings were made in the medial longitudinal fasciculus (MLF) just caudal to the trochlear nucleus from axons of VPV neurons and their descending projection was tested by stimulation of the caudal MLF at the level of the obex. The units were devided into two groups in terms of their discharge regularity. As compared with irregular ones, regular units had a firing rate which was higher and more closely related to vertical eye position. Analysis of change in firing rate during a sinusoidal head rotation suggested that regular units had a larger phase lag and a smaller gain with respect to head velocity than irregular ones. The units were also classified into three groups depending upon their axonal projection pattern: uncrossed ones without direct activation from the caudal MLF (ipsi-VO) and crossed ones with or without the direct activation (contra-VOC, contra-VO). Both ipsi- and contra-VO units fell in the regular category, whereas most units in contra-VOC group showed irregular discharge although this group contained some regular units.

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EFFECTS OF THE LESION OF FOREL'S FIELD H ON VISUALLY GUIDED ORIENTING MOVEMENTS OF THE HEAD IN THE CAT. ISA, T., ITOUJI, T. AND SASAKI, S. Dept. of Neurophysiol., Institute of Brain Res., School of Medicine, Univ. of Tokyo, Tokyo 113

We showed that neurones in Forel's field H (FFH) exert excitatory effects on neck motoneurones, chiefly those innervating head elevator muscles. Effects of lesion of FFH neurones by kainic acid injection (4μg) on orienting movements of the head were studied. Cats were trained to fixate eyes on one of the four LED lights aligned vertically in front and then to orient rapidly toward another target lighten immediately after the initial light was turned off. The movements of the head consisted of three components which were combined in varied degree, vertical rotation around the junction between neck and trunk and that between head and neck and parallel shifts by forelims. The maximum angular velocity was lineally related to the total angle of rotation of the head (10°/sec/deg). The saccade always preceded head movements by 10-50 ms. The bilateral lesion of FFH produced persistent lack of the saccade in the vertical direction. The vertical rotatory components of the head movement were severely impaired so that cats could not orient the head toward the target in most trials. When succeeded, the cat lifted or lowered the head mainly by aid of forelimb movements. Head movements and saccades in the horizontal direction were unaffected. These results suggested that FFH neurones are involved in the orienting movements in the vertical direction.

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COMPARISON OF STEPPING AND SBS REFLEXES IN THALAMIC CATS. SHIMAMURA, M., FUWA, T. and TANAKA, I. Dept. of Neurophysiol. Tokyo Metrop. Inst. for Neurosci. Fuchu-city Tokyo 183

Thalamic cats can perform stepping on a motor-driven treadmill, and stimulation of the mesencephalic locomotor region (MLR) can induce stepping. In this experiment, we attempt to analyze neural mechanisms of stepping from results of spinal and SBS reflexes in thalamic and low-spinal cats. Under ether anesthesia, tracheal cannulation, decerebration at the stereotaxic A12 level, and spinal transection at the Th10 segment were performed. The head was fixed in a stereotaxic device and cervical and lumbar regions were suspended by a hammok. EMGs were monitering of the forelimb movements. The spinal and SBS reflexes were recorded from the deep radial nerve of bilateral forelimb following stimulation of the superficial radial nerve. In the stepping of MLR stimulation, the SBS reflexes of bilateral forelimb and the supraspinal suppressions of extensor muscle activities were obtained. In contrast, these supraspinal reflex responses were not observed when non-stepping was obtained. These observations suggested that the stepping in the thalamic cat may be evoked at the stage of higher excitability of the brainstem, in relation to flexion reflex pathways involving supraspinal structures.

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SWALLOWING RELATED NEURONS IN THE MEDULLA OBLONGATA IN THE CAT.

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Swallowing is a complex centrally programmed motor sequence, involving the coordinated contraction of many buccopharyngeal and laryngeal muscles. Many experiments of brain stem lesion and stimulation have revealed that the neurons in the nucleus of the solitary tract and the adjacent reticular formation (NTS/RF) appear to play a cardinal role in the central programming of swallowing. We investigated the unit activity of medullary neurons during reflex swallowing induced by water pouring into the pharynx in the anesthetized cat. In the NTS/RF area (just ventrolateral to the NTS) and the nucleus ambiguus (NA) area, some neurons increased the firing rate around the beginning of an EMG activity of the thyrohyoid muscle during swallowing. Such neurons in both areas were found to receive oligosynaptic inputs from the ipsilateral superior laryngeal nerve. Some swallowing related neurons in the NA showed an antidromic response to electrical stimulation of the ipsilateral recurrent laryngeal nerve. Swallowing related activity in the NTS/RF area was preserved after the disapperance of swallowing movement induced by curarization. The results suggest that NTS/RF neurons which exhibited swallowing related activity are involved in the central programming of swallowing.

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CHEMICAL MODULATION OF RETICULOSPINAL EFFECTS UPON HINDLIMB ALPHA-MOTONEURONS IN DECEREBRATE CATS.

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In this study, carbachol (long-acting cholinomimetic agent) and noradrenaline were focally injected into the medial pontine reticular formation (injection site; P 2 - 4, L 0.5 - 2, H -3 - -5, dose; 100 mM, 0.1 - 0.25 ul) of the decerebrate cats. Then the stimulus effects of the pontine and medullary reticular formation upon hindlimb alpha-motoneurons (MNs) were studied with intracellular recording. Before injections of these substances, excitatory and inhibitory postsynaptic potentials (PSPs) with short (5-20 ms) and long (30-70 ms) latencies were evoked in the alpha-MNs. Focal injections of carbachol and noradrenaline resulted in the modifications of these PSPs recorded before chemical activation of pontine structures. These results indicate that the stimulus effects of the brainstem changes dependent on the activation level of the populational activities of the ponto-medullary reticular formation. Role of the cholinergically and noradrenergically activated reticulospinal effects originating from the pontine reticular formation was discussed.

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ANATOMICAL ANALYSES OF DESCENDING PROJECTIONS OF THE MEDIAL PONTO-MEDULLARY RETICULAR FORMATION

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Descending projections of the nucleus reticularis pontis oralis (NRPo), the nucleus reticularis gigantocellularis (NRGc) and the nucleus reticularis magnocellularis (NRMc) were studied in the cat by anterograde tracer, Phaseolus vulgaris leucoagglutinin (PHA-L), suvival period of the cat being 4 weeks. Descending axons were traced as far caudally as the upper thoracic cord. Descending axons from the NRPo mainly coursed through the ipsilateral ventral funiculus of the cervical cord and gave off terminal fibers mainly in the laminae VI to VIII, while those from the NRGc coursed bilaterally through the ventral and ventrolateral funiculi and gave off terminal fibers mainly in the laminae VII and VIII. In addition, some terminal fibers were observed in the medial part of the lamina IX. Descending fibers from the NRMc coursed ipsilaterally through the ventral, ventrolateral and dorsolateral funiculi and gave off terminal fibers in the laminae V to IX. There were also commissural fibers entering from the PHA-L injection side of the gray matter to the contralateral gray matter. It was noteworthy that the NRPo projected abundantly to the bilateral NRGc but not to the NRMc.

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INTRACELLULARLY RECORDED MEMBRANE POTENTIAL CHANGES OF ONUF'S NEURONS DURING REFLEX MICTURITION IN A REFLEXIVELY-STANDING DECEREBRATE CAT. SHIMODA, N., TAKAKUSAKI, K., SAKAMOTO, T. and MORI, S. Dept. Physiol., Asahikawa Med. Col., Asahikawa, 078, JAPAN

During reflex micturition in a reflexively-standing decerebrate cat, the urinary bladder pressure increases and the discharge of the external urethral sphincter muscle (EUS) is supressed. Since the cells of origin innervating the EUS are located in the Onuf's nucleus, intracellular recording of cells in Onuf's nucleus was performed during reflex micturition. Corresponding to the phase of bladder pressure increase, the membrane potentials of all the recorded cells (n=14) were hyperpolarized (mean hyperpolarization; 4.8±2.1mV). The beginning of membrane hyperpolarization varied across cells. During the period of augumented EUS activity after reflex micturition, the membrane potentials of these cells were depolarized. From these results, the neuronal mechanisms contributing to the reflex micturition will be discussed.

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MEMBRANE POTENTIAL CHANGES IN THE HINDLIMB MOTONEURONS EVOKED BY STIMULATION OF THE NUCLEUS RAPHE MAGNUS IN CATS. EDAMURA, M. AND AOKI, M. Department of Physiology, Sapporo Medical College, S.1, W.17, Chuo-ku, Sapporo 060 Japan.

We previously reported that the stimulation in the nucleus raphe magnus (RM) produced the biphasic, facilitatory and subsequent inhibitory effects on lumbar monosynaptic reflexes (MSRs) in cats anesthetized with α-chloralose and urethane. In this study, to analyze the mechanisms underlying the effects, intracellular recordings were performed from α-motoneurons (MNs) of the common peroneal nerve (CP) and the tibial nerve (TN). RM stimulation produced postsynaptic potentials (PSPs) coinciding with the time courses of the facilitation of MSRs. In 22 TN-MNs, excitatory PSPs (EPSPs) and inhibitory PSPs (IPSPs) were evoked in 10 and 9 MNs, respectively. On the other hand, in 29 CP-MNs, EPSPs and IPSPs were evoked in 26 and 2 MNs, respectively. The mean onset latencies of EPSPs (3.5 ms) were significantly shorter than those of IPSPs (4.5 ms). Furthermore, RM stimulation inhibited EPSPs evoked by stimulating the group I afferents without apparent membrane potential changes of MNs. This inhibition continued until about 200 ms coinciding with the time courses of the inhibition of MSRs. These results demonstrate that RM-evoked biphasic effects on MSRs consist of the combination of the early facilitation on MNs, due to the EPSP, and the late inhibition on group I afferents, possibly due to the presynaptic inhibition.

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THE HABENULA INVOLVED IN A NEURONAL FEEDBACK PATHWAY REGULATING THE ACTIVITY OF DOPAMINE NEURONS IN THE SUBSTANTIA NIGRA OF RATS. SASAKI, K.[1], SUDA, H.[2*], WATANABE, H.[2*] and ONO, T.[3] [1]Scientific Instrument Center, [2]Research Institute for Wakan-Yaku, and [3]Department of Physiology, Toyama Med. & Pharmaceu. Univ., Sugitani, Toyama 930-01.

In the present study, the possibility that the activity of mesencephalic DA systems is regulated by a feedback pathway via the habenula was investigated by examining the inhibitory effects of methamphetamine (MAP) on the activity of SNC DA neurons in urethane anesthetized rats. When the habenular nuclei were completely destroyed by bilateral electrolytic lesions, the depressant effect of intravenous MAP on the activity of SNC DA neurons was markedly attenuated as compared to the sham-lesined or unlesioned controls. The attenuation of MAP-induced inhibition of SNC DA neurons in habenular lesioned rats caused an upward shift of the cumulative dose-response curve. Transections of the stria medullaris or kainic acid lesions of the entopeduncular nucleus elicited an attenuation of the MAP-induced inhibition of SNC DA neurons similar to that of the habenular lesioned rats. The sensitivity of DA autoreceptors on cell bodies or dendrites of SNC DA neurons does not change between habenular-lesioned and unlesioned rats. These results indicate possibly that the habenula, perhaps the lateral habenula, is involved in a neuronal feedback pathway from the striatum to the substantia nigra and regulates the activity of the SNC DA neurons.

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NECK EMG RESPONSES AND HEAD MOVEMENTS EVOKED BY STIMULATION OF MOTOR CORTEX, DEEP SUPERIOR COLLICULUS AND PONTOMEDULLARY RETICULAR FORMATION IN AWAKE CATS. SUZUKI, S. Sepulveda V.A. Medical Center, CA 91343 and UCLA Dept. of Psychiatry, Los Angeles, CA 90024, USA

Cats were implanted with (1) microelectrodes into the motor cortex (MC), deep superior colliculus (SC) or pontomedullary reticular formation (PMRF), and (2) EMG wires in neck muscles. Neck EMG responses and head movements (HMs) evoked by electrical stimulation were recorded. The averaged EMG response evoked by MC stimulation showed a bilateral excitation with an onset latency (OL) of 4-8 ms. MC stimulation did not evoke natural-looking, lateralized HMs. In most cases SC stimulation evoked contraversive HMs accompanying a contralateral excitation and an ipsilateral inhibition with a similar OL (3-7 ms). Depending on the stimulation sites and parameters, SC stimulation induced either fixed amplitude HMs independent of an initial head position (HP) or goal-directed HMs where a final HP was attained by HMs with different amplitudes and velocities. PMRF stimulation elicited ipsiversive and mostly fixed-amplitude HMs accompanying an ipsilateral excitation (OL, 2-5 ms) and a contralateral inhibition (OL, 2.5-6 ms).

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CENTRAL PATHWAY EVOKING SYNAPTIC POTENTIALS OF HYPOGLOSSAL MOTONEURONS BY TEMPORAL MUSCLE AFFERENTS. ISHIWATA, Y., ONO, T., KURODA, T. AND NAKAMURA, Y* Depts. Orthod. II. and Physiol*, Fac. Dent., Tokyo Med. Dent. Univ., Bunkyo-ku, Tokyo 113

It is known that jaw-tongue reflex (JTR) is evoked by the temporal muscle afferents. We reported that 1) JTR was evoked by the temporal muscle spindle afferents originating from the secondary ending, and 2) stimulation of the ipsilateral temporal muscle nerve (iTN) evoked EPSPs or IPSPs in hypoglossal motoneurons (XII MNs). In this study we analyzed the central pathway of JTR in chloralose-anesthetized cats, by recording the tongue muscle EMG activity, the hypoglossal neurogram and the intracellular potential of XII MNs. Perihypoglossal neurons were recorded intra- or extracellularly; spikes of these units were used as the trigger for averaging intracellular potentials of XII MNs. The following results were obtained: 1) A lesion of the Probst's tract abolished JTR and remarkably depressed the IPSP of XII MNs as well as the hypoglossal nerve volley evoked by stimulation of iTN. 2) Neurons were found in the ventral and lateral perihypoglossal region, which discharged repetitively following stimulation of iTN and mechanical stimulation of the temporal muscle. 3) Averaging of the intracellular potential of XII MNs by spikes of perihypoglossal neurons revealed an IPSP. We conclude that 1) Probst's tract is responsible for evoking JTR and the perihypoglossal neurons which fired repetitively following stimulation of iTN are inhibitory premotor neurons projecting to XII MNs.

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REPETITIVE STIMULUS EFFECT ON THALAMIC VB UNITARY DISCHARGE OF CAT.

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Unitary discharges were recorded extracellularly using single or multi-microelectrode technique in the thalamic ventrobasal complex in the immobilized cats. In so-called spontaneous unitary discharges,some synchronized to heart beats(HB). These HB discharges were inhibited by the electrical stimuli to the receptive fields which were distributed on most part of contralateral body surface, when the electric evoked discharges preceded the HB' with a given period. The HB discharges were inhibited much more by discontinuous pulse stimuli than single one. To continuous repetitive stimuli, HB discharges were little inhibited with low frequent stimulation, but wholly with high frequent. However, to some stimulus condition, such as weak stimulation, HB discharges were not inhibited perfectly even if with high frequent stimulation, suggesting the disinhibition which presumably resulting from fatigue of synaptic transmission in the somatosensory afferent pathway.

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ARCUATE NUCLEUS HYPOTHALAMUS ACTIVATED BY ENDOGENOUS OPIOID AS DESCENDING PAIN INHIBITORY SYSTEM

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Hypothalamic arcuate nucleus stimulation-produced-analgesia(ARN-SPA) estimated by tail flick test was divided into three types depending upon the stimulated ARN sites in the acupuncture responder rats. Type I: analgesia lasted after termination of stimulation (after effect) and was completely blocked by naloxone (1mg/kg, i.p.) Type II: analgesia showed after effect but was partially blocked by naloxone . Type III: analgesia had no after effect and was not affected by naloxone. Evoked potential induced by tsusanli stimulation was recorded from the sites of type I analgesia and was not from the sites of type III analgesia. Microinjection of β-endorphine and morphine into the sites of type III caused analgesia which was not affected by adrenalectomy. These results indicate the possibility that β-endorphine may activate the site which belonges to acupuncture efferent descending pain inhibitory pathway in the ARN.

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RELATION BETWEEN MORPHINE TOLERANCE AND PROGLUMIDE, AN ANTAGONIST OF CHOLECYSTOKININ.

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It was reported that proglumide, an antagonist of cholecystokinin, antagonized morphine tolerance. We found previously that destruction of the analgesia inhibitory system (AIS) antagonized morphine tolerance. In present experiment, the possibility that proglumide inhibits the AIS antagonizing morphine tolerance was examined.

Wistar rats were used. Pain threshold was measured by tail flick test. Morphine tolerance was made by 50 mg/kg 1st day and 100 mg/kg for 5 days morphine application. 20 mg/kg proglumide enhanced acupuncture analgesia caused by 1 Hz Tsusanli point stimulation and 0.5 mg/kg i.p. morphine analgesia, and produced non-acupuncture point stimulation-produced analgesia (NAA) which was antagonized by dexamethasone. Microinjection of 5 ng proglumide to the lateral centromedian nucleus of the thalamus (LCM) which is one of the sites of AIS, produced NAA. Morphine tolerance was antagonized by lesion of the LCM or proglumide.

From these results, it was concluded that proglumide acts on the AIS antagonizing the morphine tolerance.

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DISTRIBUTION OF NOCICEPTIVE NEURONS IN THE NUCLEUS VENTRALIS POSTERO-LATERALIS. YOKOTA, T., KOYAMA, N., MASUDA, T., ASATO, F.※, Dept. Physiol. Medical College of Shiga, Seta, Otsu 520-21

Recently we found that nociceptive specific (NS) and wide dynamic range (WDR) neurons are located in the shell region of the ventrobasal (VB) complex. In the present study, somatotopic organization of these two classes of nociceptive neurons were studied in the nucleus ventralis posterolateralis (VPL) of the VB complex. NS neurons were located in the shell region of the caudal VPL, whereas WDR neurons were located in a narrow zone of the shell region just rostral to the NS zone. NS neurons in the dorsal shell region had a receptive field on the dorsal integument, whereas NS neurons in the ventral shell region had their receptive field on the ventral aspect. In the dorsal shell region, the field for the upper cervical dermatome was found in the most medial part. Successively more caudal dermatomes were represented in a serial order more laterally. In the ventral shell region, NS neurons having a receptive field in the paw pads were intermingled with those having a receptive field in the rest of the body which was represented in an orderly sequence. A similar somatotopic pattern was also found in the WDR zone.

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RESPONSES OF PARAVENTRICULAR NEUROSECRETORY CELLS TO STIMULATION OF THE SUBFORNICAL ORGAN (SFO) AND THE PERIVENTRICULAR REGIONS OF THE ANTEROVENTRAL THIRD VENTRICLE (AV3V). YAMASHITA, H., OSAKA, T. and KOIZUIMI, K., Dept. of Physiol., Univ. of Occup. & Environ. Health, Kitakyushu 807, Japan, and Dept. of Physiol., State Univ. of New York, Health Science Center at Brooklyn, New York 11203, U.S.A.

It has been suggested that the AV3V and the SFO are sensors for circulating angiotensin II or osmotic pressure, and that these regions send excitatory information to paraventricular (PVN) neurosecretory cells. The main components of the AV3V are the organum vasculosum of the lamina terminalis (OVLT) and the nucleus of preopticus medianus (POMn). We examined separately the effects of electrical stimulation of OVLT, POMn and SFO on neurosecretory cells in Nembutal-anesthetized (35 mg/kg) hemispherectomized cats. Of 106 neurosecretory cells tested, 16-46% were inhibited, 5-20% were excited, and the remaining were unaffected. Injection of 50-100 nl of glutamate solution (0.5 M) into the POMn and SFO also inhibited 16 of 38 PVN cells; the remaining neurons were unaffected. These results suggest that activation of POMn, OVLT and SFO neurons mainly inhibits the PVN neurons in the cat.

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INCREASE IN BLOOD PRESSURE AND RENAL SYMPATHETIC OUTFLOW BY STIMULATION OF THE HYPOTHALAMIC PARAVENTRICULAR NUCLEUS IN CONSCIOUS RATS. KANNAN, H.[1], HAYASHIDA, Y.[2]. AND YAMASHITA, H.[1] Dept. of Physiol.[1], and Dept. of Systems Physiol.[2], Univ. of Occup. Environ. Health, Sch. of Med., Kitakyushu 807.

The paraventricular nucleus (PVN) of the hypothalamus has been suggested to participate in control of autonomic nerve activity. Our previous studies demonstrated in anesthetized rats that PVN stimulation resulted in depressor responses accompanied with decreases in sympathetic outflow. Because anesthesia may alter sympathetic responses and cardiovascular reflexs, we decided to examine the effects of PVN stimulation on blood pressure and renal sympathetic nerve activity in conscious rats. Electrical stimulation through chronically implanted electrode evoked increases in blood pressure and renal sympathetic nerve activity with a slight decrease in heart rate. These responses were dependent upon the frequency and the intensity of the stimulus. Latency of the excitatory response of the renal sympathetic nerve activity was approximately 70 ms. Microinjection of L-glutamate (0.5M, 200nl) into the PVN also elicited increases in blood pressure and renal sympathetic nerve activity. The result suggests that activation of PVN neurons in conscious rats leads to pressor responses due to increasing sympathetic outflow, which contrast with those obtained previously in anesthetized rats.

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KAPPA-AGONISTS INHIBIT SUPRAOPTIC NEURONS IN RAT HYPOTHALAMIC SLICE PREPARATIONS
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Opioid peptides richly exist in the supraoptic nucleus(SON), implying certain functions on the neural activities of the SON. Recently we observed that injection of κ-agonist, leumorphin (LM) into the cerebroventricle clearly inhibited vasopressin release from the posterior pituitary gland. However, there is no evidence on this inhibitory mechanism. To clarify the mechanism, extra and intracellular recordings were made from SON neurons in the rat hypothalmic slice preparations. LM dose-dependently inhibited a half of both phasic and non-phasic SON neurons. The threshold concentration of LM to produce the inhibition was approximately 10^{-8}M. The inhibition was abolished or suppressed by κ-antagonist MR2266. Another κ-agonist, dynorphin, had similar inhibitory effects on SON neurons to that of LM. On the other hand, μ- (morphine) and δ-(DADLE) agonists inhibited non-phasic neurons more preferentially than phasic neurons. Intracellular recordings showed that LM slightly hyperpolarized membrane potentials with decrease of excitatory postsynaptic potentials and membrane conductances. From these results, we suggest that κ-agonists inhibit presynaptically the neural activities of both vasopressin and oxytocin neurons in the rat SON.

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EFFECTS OF OSMOTIC STIMULATION ON PARAVENTRICULAR NEURONS IN SLICES OF THE PEKIN DUCK.
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Perfusion of the duck's third ventricle (3V) with hypertonic NaCl or LiCl solution and not with sucrose solution causes antidiuresis. This periventricular osmo- or ion-sensitivity might be established by dendritic processes of neurons of the paraventricular nucleus (PVN) which extended into the ependyma of the 3V (Korf et al., 1983). To test this possibility, we investigated activities of neurons in the magnocellular region (MC) and the periventricular layer (PL) of the PVN during osmotic stimulations. We made 400 μm thick slices of the duck's brain containing the anterior commissure and the optic chiasma. The slices were superfused with the standard 295 mOsm/kg medium. For osmotic stimulation the osmolality of the medium was increased 20 to 40 mOsm/kg by adding test solutes. Out of 41 MC neurons only three responded to the osmotic stimulation. In contrast, 19 out of 40 PL neurons changed their activities during osmotic stimulation. The responses were observed only when the medium was made hypertonic with NaCl or LiCl and not with sucrose. This response corresponds well to the antidiuretic responses to 3V perfusion. It therefore appeares that the PL neurons might be specifically involved in detecting changes in the ionic composition of the CSF in ducks.

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RELATIONS BETWEEN NEURONAL FIRING PATTERN OF HYPOTHALAMIC PARAVENTRICULAR NUCLEUS (PVN) AND BEHAVIOR IN THE FREELY BEHAVING RAT.
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Long-term single neuron activity of 67 PVN neurons was recorded in freely behaving rats (male), and relations between neuronal firing pattern and behavior were analyzed. PVN neurons were classified into two main groups: a nonburst firing group (43, group 1) and a burst firing group (24, group 2). Of 43 group 1 neurons tested activity of 29 increased during EEG arousal and decreased during SWS, responded to feeding acts and episodes, and decreased during intraventricular (i.c.v.) infusion of noradrenaline (NA) or clonidine. Activity of 3 changed with the light-dark cycle, and did not respond to feeding, but was decreased by i.c.v. NA and increased by i.c.v. glucose. Other group 1 neurons responded to mouth movement or posture. Activity of 24 group 2 neurons varied in response to NA or NaCl; most patterns showed burst. Feeding or drinking did not, but i.c.v. NA and NaCl and stress did change activity of 11, and 3 were suppressed by light flash. Some group 2 neurons responded to drinking. Data suggest that most group 1 neurons are related to feeding and internal rhythmicity, and group 2 neurons are related to drinking, emergency situations (stress), and response to light.

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ODOR AND TASTE RESPONSES OF LATERAL HYPOTHALAMIC GLUCOSE-SENSITIVE AND INSENSITIVE NEURONS DURING BAR PRESS FEEDING IN THE MONKEY. OOMURA,Y., NISHINO,H., KARADI,Z., LENARD,L. AND SCOTT,T.R. Dept. Biol. Cont. Syst., Natl. Inst. for Physiol. Sci., Okazaki 444

Single neuron activities in the lateral hypothalamic area (LHA) were recorded during bar press feeding task in the monkey. First, neurons were sorted into 2 groups, glucose-sensitive (GS) and glucose-insensitive (GIS). Then firing variations to feeding, electrophoretically applied catecholamines and opiate, and to odor and taste stimuli were investigated. GS neurons responded to dopamine, noradrenaline and morphine more often than GIS neurons. In feeding task GS neurons responded during bar press (BP) and reward (RW) periods with long lasting firing inhibition and at cue tone (CT) with transient inhibition, while GIS neurons responded during BP and RW periods mainly with excitation and at cue light (CL) with excitation. Majority of GS neurons responded to both odor and taste stimuli more often than GIS neurons. GS neurons responded to two or more while GIS neurons usually for one odor or taste quality. Data suggest that these 2 kinds of neurons in the LHA may be involved in different functional aspects of feeding.

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TRANSPLANTED FETAL HYPOTHALAMUS DISPLAYS CHARACTERISTIC CHEMOSENSITIVITY IN THE HOST BRAIN. ITO, C., PLATA-SALAMÁN, C.R., OOMURA, Y., ONO, K.* AND KAWAMURA, K.* Dept. Physiol., Fac. Med., Kyushu Univ. 60, Fukuoka 812 and *Dept. Anat., Fac. Med., Okayama Univ., Okayama 700

Bilateral lesion of the ventromedial hypothalamus (VMH) produces hyperphagia and obesity. We transplanted fetal hypothalamus to the VMH lesioned rats and examined whether fetal grafts could reverse hyperphagia. Immunohistochemistry revealed that grafted tissue contained substance-P and ß-endorphin which normally located only in the VMH and adjacent area to VMH. Serotonin immunoreactive fiber, which was thought to be projected from brain stem, was also found in the grafted tissue. Since normal VMH neuron has specific glucose responsiveness to control food intake, we checked it electrophysiologically in the grafted tissue. The result was that 10% of the examined neurons were glucoreceptor neurons. Though it was not statistically significant, recovery of food intake was observed in transplanted animals. These data suggest that transplanted fetal hypothalamus can display characteristic properties of the VMH neuron and has possibility to recover from hyperphagia.

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ROLE OF NEURONAL HISTAMINE IN THE HYPOTHALAMUS ON CIRCADIAN RHYTHM IN FEEDING BEHAVIOR. FUKAGAWA, K., OOKUMA, K., FUJIMOTO, K., YOSHIMATSU, H., SAKATA, T., *YAMATODANI, A. AND *WADA, H. 1st Dept. Intern. Med., Kyushu Univ., Fukuoka 812, *Pharmacol. II, Osaka Univ., Osaka 530.

In order to clarify physiological role of neuronal histamine on feeding behavior, histamine H_1- and H_2-receptor antagonists were infused into rat third cerebroventricle and ingestive behavior was observed. H_1-antagonists elicited feeding without periprandial drinking in dose responsive manner after infusion during the light when histamine level in the hypothalamus was high, but H_2-antagonists could not. Infusion of H_1-antagonist just before the dark when histamine level was low could not affect feeding behavior. Infusion of α-fluoromethylhistidine, histidine decarboxylase inhibitor, during the light decreased histamine content in the hypothalamus and elicited feeding in dose responsive manner. These results suggest that neuronal histamine in the hypothalamus suppresses feeding behavior through H_1 receptor and the daily fluctuation of neuronal histamine may modulate the circadian rhythm in feeding behavior.

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FEEDING ELICITATION BY H_1-ANTIHISTAMINES AND ITS ACTING SITES IN THE RAT HYPOTHALAMUS. OOKUMA, K., YOSHIMATSU, H., FUKAGAWA, K., FUJIMOTO, K., SAKATA, T. First Dept. of Internal Med., Faculty of Med., Kyushu Univ., Maidashi 3-1-1, Higashi-Ku, Fukuoka 812, Japan.

Neuronal histamine was found to suppress food intake through H_1-receptors in the rat brain (Sakata, et al. 1988). Chlorpheniramine was bilaterally microinfused into various loci in the hypothalamus. A test solution was infused at the light period, 1100 h. Bilateral infusion of chlorpheniramine into the ventromedial nucleus (VMH) elicited feeding dose-dependently. Rats with bilateral infusion of a 26 nmol dose into the anterior hypothalamus also initiated feeding. Bilateral infusions into the lateral hypothalamus and the dorsomedial hypothalamus had no effect on feeding. Bilateral infusion into the paraventricular nucleus elicited feeding at a dose of 52 μmol, but not at 26 nmol. Feeding after the VMH infusion was completely abolished when neuronal histamine was decreased with pretreatment of α-fluoromethylhistidine, a suicide inhibitor of histidine decarboxylase. These findings suggest that neuronal histamine may tonically suppress food intake through H_1-receptors, at least in part, in the VMH.

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STRUCURAL EVALUATION OF ANOREXIA INDUCED BY AMINO-SUGARS. Fujimoto, K., Sakata, T., and Shiraishi, T. Dept. of Intern. Med. I., Faculty of Med. Kyushu Uni., Fukuoka 812, and Dept. of Physiol., Tokai Uni., School of Med., Kanagawa 259-11, Japan.

It was demonstrated that 1-deoxyglucosamine reduced food intake after infusion into rat third cerebroventricle, and that it activated glucose-receptor neuron in ventromedial hypothalamus. Relationship between anorectic action and structural characteristics was investigated. Steric hindering group at carbon 2 of 1-deoxyglucose analogues was introduced by epimerization, deoxidation, and substitution of a hydroxyl group with either an acetamido or a fluoro group. Injection of this analogue into the rat third cerebroventricle attenuated feeding suppression produced by 1-deoxyglucosamine. In contrast, the magnitude of anorexia produced by 1-deoxyglucosamine was same as that produced by 1-deoxyglucose, but it reduced food intake longer than 1-deoxyglucose. The amination at carbon 2 was more potent than that at carbon 3, 4 or 6. These results indicate that an amino group at carbon 2 of the glucose molecule is important to reinforce feeding suppression caused by 1-deoxyglucose analogues.

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CHARACTERISTICS OF SENSORY RESPONSES OF MONKEY HIPPOCAMPAL AND ENTORHINAL NEURONS. TAMURA, R., ONO, T., NISHIJO, H., NAKAMURA, K. AND TABUCHI, E., Dept. Physiol., Fac. Med., Toyama Med. and Pharmaceu. Univ., Sugitani, Toyama 930-01, Japan

Neuronal activity in the hippocampus and entorhinal cortex of the monkey was recorded during operant feeding, drinking and shock avoidance behavior in a delayed matching to sample with response-delay task, and in a clinical test where the monkey was presented visual, auditory and tactile stimuli from various directions. We report here, the selective neuronal responses to direction in the clinical test. Of 399 neurons tested, 164 (41.1%) responded in some task or to the clinical test. Of these neurons, 40 (10.0%) had direction selectivity. Of these 45 neurons, 27 responded only during visual stimulus presentation (left anterior, 4; right anterior, 22; more than one direction, 1), 8 responded only to auditory stimulus presentation (anterior, 1; right posterior, 2; posterior, 3) and 5 responded to both visual and auditory stimulus presentation (right anterior, 1; more than one direction, 4). These direction-selective neurons tended to respond to visual stimulation when it was presented from the right anterior direction and to auditory stimulation when it was presented from the posterior direction.

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HIPPOCAMPAL MULTIPLE UNIT ACTIVITY IN THE CROSS-CIRCULATED BRAIN OF THE RAT.
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In an attempt to assess the role of signal inputs from the body trunk in information processing in the brain, multiple unit activity (MUA) of the hippocampal CA1 region was recorded before and after the rat brain was maintained by cross-circulation while the body trunk was functionally isolated by disconnecting its circulation. In most experiments the hippocampal MUA increased in the absence of inputs from the body trunk. However, any change was not detectable in the pattern of distribution of inter-spike intervals or of successive neuronal firings. In some experiments MUA correlation which was calculated by counting number of spikes within successive time-bins after each firing, was detectable in the hippocampus of the intact brain. After isolation, the MUA correlation was abolished or markedly reduced. The MUA temporal correlation in the intact brain ranged from 0.1 to 2.4 sec. Power spectral analysis of the hippocampal EEG showed that the frequency of EEG tended to increase after isolation and in some experiments theta wave was produced. These findings suggest that inputs from the body trunk participate in organizing the temporal correlation among the hippocampal multiple unit firings which are not necessarily associated with theta waves.

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RELATIONSHIP BETWEEN PYRAMIDAL AND NONPYRAMIDAL CELLS DURING ELECTRICALLY INDUCED PAROXYSMAL DISCHARGES.
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To reveal the relationship between pyramidal (P) and nonpyramidal (NP) cells during electrically induced paroxysmal discharges (PaDs), P cells were intracellularly studied in the hippocampus CA1 of anesthetized and immobilized rabbits. A single shock stimulation of the contralateral hippocampus generated in the P cell a brief EPSP with an action potential and a large IPSP. With the tetanus (20 Hz), the IPSPs decreased, while the EPSPs increased slightly with a sustained depolarizing shift of the membrane. The decrease in the IPSPs coincided with the response decrement of TYPE I NP cells whereas the increase in the EPSPs with the response enhancement of TYPE II NP cells. PaD followed the tetanus. During the early phase of PaD, the depolarizing shift was maintained and transient depolarizing oscillations with abortive spikes were superimposed on the shift. During the late phase, the oscillations gradually decreased in frequency, the membrane was repolarized, full spikes were generated and then a period of slight hyperpolarization occurred. TYPE II seemed to be involved partially in generating the depolarizing potentials, because it exhibited burstic discharges in synchrony with each paroxysmal wave. TYPE I seemed to participate in generating the late hyperpolarization because it refired during the late phase of PaD.

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TIME DISCRETE MODEL OF HIPPOCAMPAL RECURRENT INHIBITION.
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A time discrete model of recurrent inhibition in the hippocampal dentate gyrus was made and analysed. This model assumes that (1) each granule cell can generate only one action potential in response to a single stimulation of perforant path, (2) each interneuron receives synaptic inputs from many granule cells, and (3) an output of the interneuron works on granule cells inhibitory. Although each granule cell generates an action potential in the all-or-none fashion, the population spike can be approximated to increase linearly with an increase in the population EPSP when the population EPSP exceeds a certain value which can be regarded as macroscopic threshold. The proportional rate has relation to only variance of the threshold and EPSP of the cells, while this macroscopic threshold relates to both average and variance of them. The model shows that there are six patterns of the paired-pulse depression (recurrent inhibition). These patterns are composed of the four broken sticks. Their slopes and the positions of their crossing points express values of the macroscopic thresholds and the proportional rates. The analysis by this model indicates that some changes in the paired-pulse depression following an induction of long-term potentiation by tetanic stimulations could be due to an increase in only macroscopic threshold of the interneurons.

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A NEUROCHEMICAL SUBSTRATE INVOLVED IN CUE TONE LEARNING BY LATERAL HYPOTHALAMIC NEURONS IN THE RAT. NAKAMURA, K., ONO, T., NISHIJO, H. AND TAMURA, R., Dept. Physiol., Fac. Med., Toyama Med. and Pharmaceu. Univ., Sugitani, Toyama 930-01

Unit activity in the rat lateral hypothalamus (LHA) was recorded during discrimination learning of a cue tone stimulus predicting reward (CTS^+) (glucose or ICSS) or aversion (CTS^-) (electric shock or tail pinch). The catecholaminergic and cholinergic systems in the LHA were investigated by electrophoretic application of noradrenaline (NE), dopamine (DA), ACh, and their antagonists. Of 264 LHA neurons analyzed, 234 responded during CTS learning in one or more phases. Effects of DA were tested in 138, NE in 134 and ACh in 73. DA inhibited 40 and excited 14. NE inhibited 74 and excited 10. ACh inhibited 3 and excited 35. DA or ACh sensitive neurons responded to both reward and aversion and their CTSs more often than DA or ACh insensitive neurons. Usually, the DA effects were similar to those of reward and CTS^+, but opposite to the effects of aversion and CTS^-. Conversely, effects of ACh were similar to those of aversion and CTS^-. Neural responses to CTS^+ were blocked by spiperone, and those to CTS^- were blocked by atropine. Data suggest involvement of multiple afferent inputs from DA and ACh systems to the same LHA neuron in CTS learning of positive and negative reinforcement.

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RESPONSES OF NEURONS IN THE SUBFORNICAL ORGAN TO STIMULATION OF THE NEIGHBORING PERIVENTRICULAR TISSUES. OSAKA, T. and KOIZUIMI, K., Dept. of Physiol., State University of New York, Health Science Center at Brooklyn, New York 11203, U.S.A.

The subfornical organ (SFO) and the periventricular tissue of the anteroventral third ventricle (AV3V) have been implicated to play a cardinal role in the central control of water balance. The nucleus of preopticus medianus (POMn) and organum vasculosum of the lamina terminalis (OVLT) are the main components of the AV3V. In the present experiments, responses of SFO neurons to electrical stimulation of POMn, OVLT, fornix, and ventral and dorsal stalks of the SFO were studied. Experiments were done in 10 cats under Nembutal anesthesia (35 mg/kg). The SFO and AV3V were exposed by hemispherectomy, and all recording and stimulating procedures were made under direct visual control. Of the 239 neurons in the SFO tested, altogether 91 neurons were antidromically activated. On the other hand, orthodromic responses were observed more frequently than antidromic ones: 13-47% of the SFO neurons were inhibited and 13-32% were excited. Thus, mutual information exchange was revealed between the SFO and the AV3V.

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EFFECTS OF ADRENOCORTICOTROPIC HORMONE ON NEURONS IN THE HYPOTHALAMIC PARAVENTRICULAR NUCLEUS. KASAI, M., KANNAN, H., INENAGA, K. AND YAMASHITA, H. Dept. of Physiol., Univ. of Occup. Environ. Health, Sch. of Med., Kitakyushu 807.

It has been demonstrated that immunoreactive terminals and fibers of adrenocorticotropic hormone (ACTH), which may be derived from the arcuate nucleus, are present in the hypothalamic paraventricular nucleus (PVN). However, the functions of ACTH on the PVN are unknown. In the present experiment, the effects of ACTH on single PVN neurons were investigated in in vivo and in vitro. In urethane anesthetized Wistar rats, iontophoretically applied ACTH (5×10^{-4} M) excited 4 of 22 tuberoinfundibular neurons tested and 4 of 18 neurosecretory neurons tested in the PVN. Only one neurosecretory neurons was inhibited by ACTH. Whereas, 5 of 10 neurons in the cortex were inhibited by ACTH. In rat brain slice preparations, extracellular recordings were obtained from 29 neurons (PC-neurons) in the parvocellular division and 64 neurons (MC-neurons) in the magnocellular division of the PVN. A bath application of ACTH at a concentration of 10^{-7} M excited 4 of 29 PC-neurons tested and 15 of 64 MC neurons tested. ACTH inhibited one PC-neuron and 10 MC-neurons. The results suggest the possibility that ACTH acts as a neurotransmitter or neuromodulator in the rat PVN.

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SYNAPTIC INPUTS FROM THE STOMACH TO NEUROSECRETORY NEURONS IN THE HYPOTHALAMIC PARAVENTRICULAR NUCLEUS OF RATS. UETA, Y., KANNAN, H. AND YAMASHITA, H. Dept. of Physiol., Univ. of Occup. Environ. Health, Sch. of Med., Kitakyushu 807.

Extracellular recordings were made in rats anesthetized with α-chloralose(60mg/kg) and urethane(600mg/kg) to investigate the effects of electrical stimulation of the gastric branches of the vagus nerves on the neural activity of neurosecretory neurons in the paraventricular nucleus(PVN) of the hypothalamus. Electrical stimulation with a single shock of the gastric branches of the vagus nerves inhibited 5 and excited 10 of 32 phasically firing neurosecretory neurons. By contrast, of 70 continuously firing neurosecretory neurons, 43 were excited by electrical stimulation with a single shock. Remainning 27 neurons showed no change in firing rate. Repetitive stimuli produced same effects as a single shock stimulation on either types of neurosecretory neurons. There were no significant differences in the onset latency(140-300ms) and threshold(100-200μA) of the excitatory and inhibitory responses between phasically and continuously firing neurons. We conclude that putative AVP-secreting neurons in the PVN were excited and inhibited by the afferent inputs originating from the stomach and transmitted by the gastric branches of the vagus nerves, while presumed OXT-secreting neurons in the PVN were excited.

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2-BUTEN-4-OLIDE (2-B-4-O), A PUTATIVE ENDOGENOUS SATIETY FACTOR, EXCITES NEURONS IN THE VENTROMEDIAL HYPOTHALAMIC NUCLEUS (VMH) IN VITRO. FUKUDA, A., PLATA-SALAMÁN, C.R., ITO, C. AND OOMURA, Y. Dept. Physiol., Fac. Med., Kyushu Univ. 60, Fukuoka 812

2-B-4-O has been identified in the serum of fasted rats and proved as a feeding suppressant, these have led to postulation that 2-B-4-O may act as an endogenous satiety substance. The effect of 2-B-4-O on neurons in the VMH, known to be important in the regulation of feeding as a satiety center, was investigated with intracellular recordings in brain slice preparations of rats. 2-B-4-O, applied by perfusion (0.1 mM - 10 mM) or drops, dose-dependently depolarized 30% of the VMH neurons tested. The depolarization by 2-B-4-O persisted after complete elimination of synaptic inputs during perfusion with Ca^{2+}-free/high-Mg^{2+} solution. The depolarization was accompanied by a decrease in membrane conductance and reversed polarity around -95 mV, and the amplitude of the depolarization was dependent on $[K^+]_o$. The VMH neurons depolarized by 2-B-4-O had some specific electrophysiological properties: a relatively low input-resistance, a presence of I_A, and an EPSP-IPSP complex evoked by stimulation on the lateral edge of the VMH, which correspond with those of glucoreceptor neurons. The results suggest that 2-B-4-O directly excites VMH neurons, presumed to be glucoreceptor neurons, by decreasing K^+ conductance, and this effect may participate in the feeding suppressive action of 2-B-4-O.

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TUMOR NECROSIS FACTOR AND INTERLEUKIN-1ß: SUPPRESSION OF FOOD INTAKE BY DIRECT ACTION IN THE CENTRAL NERVOUS SYSTEM. KAI, Y. AND OOMURA, Y. Dept. Physiol., Fac. Med., Kyushu Univ., Fukuoka 812

Intracerebroventricular microinfusion of recombinant human tumor necrosis factor (rhTNF) and recombinant human interleukin-1ß (rhIL-1ß) suppressed food intake in rats. Central infusion of heat-inactivated rhTNF and rhIL-1ß, bovine serum albumin, heparin or transforming growth factor-ß had no such effect. Central infusion of rhIL-1ß did not affect the dipsogenic response to central administration of angiotensin II. Peripheral administration of rhTNF and rhIL-1ß in doses equivalent to or higher than those administered centrally had no effect. Electrophoretically applied rhTNF and rhIL-1ß specifically suppressed the activity of glucose-sensitive neurons in the lateral hypothalamic area. Glucose-insensitive neurons were little affected. The results suggest that TNF and IL-1ß act directly in the central nervous system to suppress feeding, and this effect may be operative during acute and chronic disease.

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THE ROLE OF LIMBIC HYPOTHALAMIC SYSTEM IN METABOLIC RESPONSE TO IMMOBILIZATION STRESS.

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The effects of lesions of the limbic hypothalamic system on the citrate metabolic responses to daily repeated immobilization stress in the liver slices of rabbits have been investigated. The experimental results were as follows; (1) The citrate metabolic responses to the 1st exposure of immobilization stress (exposure on the 1st day) were altered by lesions of arcuate nucleus (ARC), ventromedial hypothalamus (VMH), stria terminalis (ST) and dorsal fornix (FX). (2) The citrate metabolic responses to immobilization stress were completely abolished by seven times repetition of exposures of immobilization stress in rabbits with lesions of ARC and VMH, they were similar to sham-operated groups. (3) In rabbits with lesions of ST and FX, the citrate metabolic responses to the 7th exposures of immobilization stress (exposure on the 7th day) were similar to those after the 1st exposure of immobilization stress, but these metabolic responses were completely abolished by seven times repetition of exposures of immobilization stress in sham-operated animals.

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DAMAGE OF HIPPOCAMPAL NEURONS CAUSED BY COBALT FOCUS IN THE CEREBRAL CORTEX OF RATS.

YUZURIHARA,M., ISHIGE,A., SEKIGUCHI,K., IIZUKA,S., SUGIMOTO,A., ITOH,K., ABURADA,M., HOSOYA,E. AND SUGAYA,E.* Tsumura Res. Inst. for Pharmacology, Ami, Ibaraki, 300-11 and *Dept. of Physiol., Kanagawa Dental Col., Yokosuka, Kanagawa, 238

In the epilepsy patients, hippocampal neuron loss is frequently observed and this change is considered to be due to frequent generalized convulsions. To elucidate the relationship between the cobalt-induced epileptic focus and hippocampal neurons, morphological changes of the neurons in the CA1 area of the hippocampus were observed. Cobalt powder was applied to the left frontal cortex of the rats. Hippocampal neuron loss was observed from the early stage without generalized convulsions after cobalt application. The reduced threshold of pentylenetetrazol-induced convulsions followed by the provocation of EEG seizure pattern was observed. By the histochemical examinations, anti-GFAP possitive cells gradually increased. These findings suggest that the epilepsy model animals produced by the cobalt application in the cerebral cortex show hippocampal neuron loss without generalized convulsions accompanied with the histochemical changes of grial cells.

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EYE MOVEMENT CONTROL BY CEREBELLAR FLOCCULUS IN CATS.

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Extracellular unitary activities of 288 neurons were recorded in the medial vestibular nucleus in anesthetized cats. In 19 of 288 neurons, middle-zone stimulation resulted in cessation of spontaneous activities. In 16 of 19 neurons, axonal projections were studied by systematic microstimulation. These target neurons of middle zone inhibition project to the ipsilateral abducens nucleus, and not to the contralateral abducens nucleus nor the oculomotor nucleus. Target neurons were located in the fairly locarized region in the rostral part of the medial vestibular nucleus adjacent to the stria acustica. In additional experiments, secondary vestibular neurons projecting to the ipsilateral abducens nucleus were recorded. In only 7 of 36 recorded neurons, middle zone stimulation depressed activities of these neurons. There is a possibility that the interaction of relay neurons of the vestibulo-ocular reflex (VOR) and target neurons of floccular middle zone inhibition takes place at the ipsilateral abducens nucleus and cancel the VOR.

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DIRECTION SELECTIVITY OF COMPLEX SPIKES OF NODULUS PURKINJE CELLS TO OPTOKINETIC STIMULATION IN PIGMENTED RABBIT.

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Response properties of complex spikes of nodulus Purkinje cells (n=131) to optokinetic stimulation (OKS) were studied in gas-anesthetized (70 % N_2O plus 2-4 % halothane), immobilized pigmented rabbits (n=16). A whole field random dot pattern (60° x 60°) was moved to and fro in front of one eye at a constant velocity (0.1°--4.0°/s) along an axis of 0°, 45°, 90° or 135° to the horizontal plane of the eye. Cells responsive to OKS were mainly localized in the ventral lamella, but were rare in the dorsal lamella. The optimum velocity was within 0.1-2.0 °/s for all cells. Four medio-laterally aligned parts were demonstrated in terms of preferred directions of the responses to OKS. In the most medial part (0-0.75 mm, from the midline), the majority of cells were not responsive to OKS. In the second part (0.75-1.50 mm), most cells (76 %) were excited with forward movement to ipsilateral eye and/or were not responsive to contralateral eye (F/N type). In the third part (1.50-2.25 mm), most cells (77 %) were excited with ipsi-upward and/or contra-downward movements (U/D type). In the most lateral part (2.25-3.50 mm), most cells (71 %) responded to ipsi-forward and/or contra-backward movements (F/B type). These findings indicate that the ventral lamella of the nodulus consists of four functionally different zones.

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SIGNAL CONTENTS OF MOSSY FIBER INPUTS TO RABBIT FLOCCULAR PURKINJE CELLS OF THE HORIZONTAL EYE MOVEMENT FIELD (H-ZONE).

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The vestibular or visual responsiveness of floccular H-zone Purkinje cells (P-cells) were examined in chronically prepared pigmented rabbits. Single unit activities of P-cells were recorded during sinusoidal turntable oscillation (±2.5 deg., 0.1Hz) in darkness or screen oscillation (±1.25 deg, 0.33Hz) with glass microelectrode containing Fast Green or Pontamine Blue solution. Recording sites were marked with microinjection of dyes via the electrode and later identified histologically. The simple spike activities of H-zone P-cells were usually modulated outphase to turntable velocity or inphase to screen velocity and the amplitude of modulation was significantly greater than that of non-H-zone P-cells. The complex spike activities of H-zone P-cells were usually modulated inphase to screen velocity. Based on the previously reported mean eye velocity sensitivity of H-zone P-cells, the eye velocity inputs during turntable or screen oscillation was estimated to constitute less than 20% of total responses. Therefore, the major mossy fiber inputs to the H-zone are sensory signals and not eye movement signals.

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ELECTRICAL CORRELATES OF CEREBELLAR CORTICAL ACTIVITY IN CATS. TAKAHIRA, H. Dept. of Physiol. 1., Tokai Univ. School Med., Isehara, 259-11.

The compound action potential, evoked by peripheral stimulation and recorded at cerebellar cortical surface, was one of fashionable subjects during 40's and 50's. It was generally agreement on that the evoked potentials in anesthetized preparations consisted of two components; early small waves and late spiky deflections. Morin et al (1957) first presented the 'causality' hypothesis that the early wave (x) was a sign of incoming volley to the cortex and the late spike (y) was an index of cerebellar neuronal activation. By advent of microelectrode recordings from 60's onward, the two components were ascribed entirely to the activation of separate cortical inputs; i.e. mossy and climbing fibers (Eccles et al., 1967). In the present experiments, following the extra- and intra-dendritic recordings from Purkinje cells, extra- and intra-somatic recordings from Purkinje cells and Golgi cells with simultaneous recordings of surface potentials, it is again concluded in agreement with Morin's hypothesis that the potential-x is due to arrival of mossy fiber impulses and that the potential-y is due to 'slow spike' firing of soma-dendritic region of Purkinje cells. Further, it is found that the electrical activity could be detected only from Purkinje cells, Golgi cells and mossy fibers, not only with capillary microelectrodes at depth but also with wick electrodes at surface.

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STUDIES ON THE IMMUNOLOGICAL REJECTION AND VASCULARIZATION IN ZENOGENEIC NEURAL TRANSPLANTATION. NAKANO, T.[2], KOHSAKA, S.[1], SHINOZAKI, T.[2], INOUE, H.[2], TOYA, S.[2], and TSUKADA, Y.[1], [1]Dept. Physiol., and [2]Dept. Neurosurg., Sch. Med. Keio Univ., Shinjuku-ku, Tokyo 160.

The expression of Ia antigen on mouse brain xenografts was immunohistochemically investigated. Tissue from newborn mouse cerebral cortex was grafted into the third ventricle of adult rat brain. The Ia antigen was detected on the grafted tissue from 7 days after the transplantation. Investigations combined with laminin immunohistochemistry and India Ink perfusion test revealed that the Ia antigen was expressed on the vascular endothelial cells in the grafted tissue. India ink perfusion experiments showed that the recirculation was established from 5-6 days after the transplantation. These results suggested that the expression of Ia antigen on the vascular endothelial cells is regulated by certain factors in the blood stream and is closely associated with the immunological rejection in the xenogeneic neural transplantation.

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ACTIVITY OF CYCLIC AMP GENERATION IN THE CEREBRAL CORTEX OF RATS AFTER A POLARIZATION. MORIWAKI, A., HATTORI, Y., HAYASHI, Y., ASAKI, H. AND HORI, Y. Dept. of Physiol., Okayama Univ. Med. Sch., Okayama 700

In rats, 0.3, 3.0 or 30 μA of anodal direct current was continuously applied for 30 min or 3 h to the surface of the left anterior cortex (anodal polarization). One day after the polarization, rats were killed by decapitation and the cerebral cortex was dissected into four parts and sliced. The polarized point was in the left anterior cortical area. The slices of each cortical area were incubated for 10 min in Krebs-Ringer bicarbonate-glucose buffer with or without 0.1 mM norepinephrine after a preincubation for 60 min, and then cyclic AMP contents were determined and compared among four cortical areas. In 30 min-polarized rats, the cyclic AMP content in norepinephrine-treated slices was greater in the left anterior than in the right anterior cortical area when 3.0 μA was applied, and the regional differences were not observed when 0.3 or 30 μA was applied. In 3 h-polarized rats, no regional differences of cyclic AMP content in norepinephrine-treated slices were observed at these three intensities of current.

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CORTICAL EEG IN THE ACALLOSAL MICE. NEGI,T., TOYOSHIMA,Y., OKADA, Y. MURAKAMI,T.H. AND HORI.Y.. Dept. Biol., Kagawa Med. Sch., Miki-cho, Kagawa, 761-07, and Dept. Physiol., Okayama Univ. Med. Sch., Okayama, 700.

Morphologically, agenesis of corpus callosum (CC) in ddN strain mice was classified into two types. One was complete agenesis of CC, and the other revealed partial agenesis. In this work the differences of cortical EEG spectral characteristics were studied on the normal, hypogenesis and acallosal mice. A total of 75 male and female adult mice were used. Five stainless steel electrodes were implanted stereotaxically in the bilateral cerebral cortex and the cerebellum at a depth of 1.0 mm. After a one-week recovery period, the correlations of EEG on five combinations, such as homotopic anterior vs posterior, ipsilateral, crossed contralateral, and homotopic anterior and posterior to the reference electrode, were analysed with a signal processor. In the complete acallosal mice (n=11), the coeffcient of correlations were significantly lower ($p<0.05$) in the crossed contralateral, ipsilateral and homotopic posterior to reference. However, in the hypogenesis of CC (n=7) there were not significant differences in the correlation compared with normal mice (n=57).

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ELECTROPHYSIOLOGICAL PROPERTIES OF THE PREFRONTAL NEURONS IN VITRO. TANAKA, E., HIGASHI, H. and NISHI, S. Dept. Physiol., Kurume Univ. Sch. Med., Kurume 830

Intracellular recordings were made from neurons in the Vth layer of prefrontal cortex in tissue slices of the guinea-pig brain. Focal stimulation elicited a depolarizing synaptic potential and a slow IPSP. The depolarizing potential was depressed by DL-amino-phosphonovaleric acid and γ-D-glutamylglycine, while it was increased by L-aspartic acid β-hydroxamate and picrotoxin. The slow IPSP was suppressed by baclofen. These results suggest that the depolarizing synaptic potential consists of a fast EPSP and a fast IPSP which are likely mediated by glutamate and GABA, respectively. The fast EPSP, fast IPSP and slow IPSP were reversed at about -1 mV, -53 mV and -86 mV, respectively. Applied by pressure ejection, glutamate or GABA caused a depolarization, and baclofen induced a hyperpolarization. The glutamate-depolarization, GABA-depolarization and baclofen-hyperpolarization were reversed at about -6 mV, -56 mV and -92 mV, respectively. These results suggest that the fast EPSP, fast IPSP and slow IPSP may be mediated, respectively, by glutamate acting at glutamate receptors, by GABA acting at GABA-A receptors, and by GABA acting at GABA-B receptors. Dopamine applied by superfusion elicited a hyperpolarization associated with a decrease in membrane resistance. The dopamine-induced hyperpolarization was followed by a depolarization associated with an increase in membrane resistance. Either response was abolished by haloperidol.

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EFFECT OF REVERSIBLE BLOCKADE OF CORTICOSTRIATE TRANSMISSION ON VOLUNTARY MOVEMENT AND ITS FUNCTIONAL IMPLICATION OF BASAL GANGLIA. KATO, M. AND KIMURA, M., Dept. Physiol., Fac.of Med., Univ. of Tokyo, Tokyo 113 and Dept. Physiol., Jichi Med. Sch., Minamikawachi-machi, Tochigi, 329-04

A monkey(macaca fuscata) was trained to make a visually guided step tracking arm movement around the elbow joint(size 20 deg, movement time 300ms). In order to block corticostriate transmission, a glutamate antagonist, kynurenate(0.1M, 2 ul), was injected through a cannula(27G) into the arm area of the contralateral putamen identified by microstimulation. The effects on the movement appeared from one to several hours after the injection. They were : 1) The first step of an arm movement undershot and the deceleration markedly increased during the last half of movement and therefore multiple steps of movement were required to reach the target. 2) The burst activity of agonist muscle slightly decreased while that of antagonist muscle increased strongly. The latter positively correlated to the peak acceleration. The sequence of reciprocal activation of agonist-antagonist muscles was preserved. 3) The early surface-positive component of premovement field potentials was decreased in the arm area of the motor cortex. 4) The reaction time was not significantly changed. 5) The monkey made no tremorous movement to adjust and hold the arm onto the target. These results suggest that cortical inputs to the putamen play a role to suppress unexpected stretch reflex and to control the command to antagonist adequately during fast step movement to enable fast straightforward movements.

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THE EFFECT OF CHRONIC ABLATION OF THE ENTOPEDUNCULAR NUCLEUS ON THE HEAD-TURNING INDUCED BY ELECTRICAL STIMULATION OF THE CAUDATE NUCLEUS IN CATS. AKAIKE, N.※ OHNO, T., and TSUBOKAWA, H. Department of Physiology, Institute of Basic Medical Sciences, University of Tsukuba, Tsukuba, Ibaraki 305

Electrical stimulation of the caudate nucleus (Cd) induces contraversive head-turning (HT). On the basis of neuronal connections, several pathways can be considered as candidates for a pathway which is responsible for the induction of HT. In the present study, we investigated the contribution of a pathway from Cd to the spinal cord through the entopeduncular nucleus(ENT) and the mesencephalic tegmentum, by examining the effect of chronic ablation of ENT on the Cd- induced HT. Experiments were carried out with awake unrestrained cats of which frontal cortex had been suctioned out and ENT on one side had been ablated by kainic acid. Various points in Cd were stimulated systematically with trains of current pulses. Cats with ENT lesion did not show persistent postural asymmetry and stimulation of Cd on the side of ENT lesion did induce similar HT as in control cats. Furthermore, the distribution of effective stimulation points within Cd in inducing HT, the distribution of latencies of HT and patterns of EMG activities of related neck muscles were not significantly different from those in control cats. Therefore, it was concluded that this pathway did not play an important role in the generation of the Cd-induced HT.

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NEURAL ACTIVITY IN THE MONKEY CAUDATE NUCLEUS RELATED TO REWARD-OBTAINING BEHAVIOR. HIKOSAKA,O., SAKAMOTO, M. and USUI, S. Dept. Physiol. Toho University School of Medicine, 5-21-16 Omori-Nishi, Ota-ku, Tokyo 143.

A large portion of caudate neurons showed activities that were considered to be related to cognitive functions. Such activities were typically revealed in the delayed saccade task in which memory and anticipation are required. These activities preceded some of the task-specific events which were predictable. In this paper we report caudate neural activity related to expectation of reward. It was a tonic discharge which started with the appearance of the final target and ended with a reward; the reward was given if the monkey released his hand from the lever by detecting the dimming of the target. In most cases, however, the activity was non-selective for how the monkey obtained the reward; by visual fixation only, by a saccade, or by a hand movement. The activity was partly dependent on visual fixation, which, however, was not a necessary condition.

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MOVEMENT-RELATED ACTIVITY OF THALAMIC NEURONS WITH INPUT FROM PALLIDUM AND PROJECTION ONTO MOTOR CORTEX IN MONKEYS
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Thalamic neurons projecting on the forelimb area in the motor cortex were identified by antidromic response to stimulation of that area in two awake monkeys, and inputs from the cerebellar nuclei (CN) and the internal segment of the globus pallidus (GPi) were verified by recording responses to stimulation of CN and GPi. In reaction-time hand movement task, most (33/34) of thalamic neurons intermediating in cerebello-thalamo-motor cortical projection (CTM) and about half (10/18) of those in pallido-thalamo-motor cortical projection (PTM) changed their firing rate on the lever lifting movement. In one monkey, some neurons of both groups (CTM : 15/24, PTM : 3/8) changed their firing rate prior to the onset of the earliest EMG. These findings suggest that the pallidal neurons send the information for motor control to the motor cortex through the thalamus in the similar manner to the cerebellum.

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UNIT ACTIVITIES OF FRONTO-OPERCULAR CORTEX IN MACAQUE MONKEYS PERFORMING A GUSTATORY GO/NOGO TASK. ITO, S., AND OGAWA, H., Dept. Physiol., Kumamoto Univ. Med. Sch., Kumamoto 860 and Dept. Neurophysiol., Primate Res. Inst., Kyoto Univ., Inuyama, Aichi 484

We trained two Japanese monkeys to perform Go/NoGo task for discrimination between NaCl (Go) and water (NoGo) with sucrose as reward (Rw) and quinine-HCl as punishment (Pn). After a ratio of correct responses exceeded 80% we recorded unit activities from the fronto-opercular cortex of these monkeys during the task. Non-specific units, which constituted the major group, responded to all fluid in a similar fashion so that were regarded as representing somatosensory aspects of the fluid onset. Cue-nonspecific units, respond similarly to both cues but not to Rw/Pn, may relate to the animal's internal or psychological state concerning performing the task. Cue-differential units,selectively responding to one of the cue only, could code the choice of behavioral reaction between Go and NoGo. Another type of units responded to Rw/Pn. The latter two type units, which seems to include gustatory units, were recorded from so-called the masticatory area as well as from the gustatory area. It is suggested that not only the pure gustatory area but also the neighboring area in the fronto-opercular cortex are involved in taste discrimination.

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MOVEMENT-RELATED ACTIVITIES PRIOR TO SELF-INITIATED LEVER PRESS IN THE MACAQUE SUPPLEMENTARY MOTOR AREA

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Single neuron activities were recorded from the supplementary motor area (SMA), hand premotor area and hand motor area while macaque monkeys were performing a visually guided GO/NO-GO task (symmetrical). The task was self-initiated by lever press and the lever was released or withheld according to the GO cue or NO-GO cue. Out of the 213 task-related SMA neurons, 145 neurons showed activities before the lever press. Of these, 22 neurons, designated as Type I, responded with a gradually developing increase up to 1 s, before lever press. These neurons showed similar changes before lever release. Remaining 26 SMA neurons, designated as Type II, were activated, up to 3 s, before lever press. Neurons with these changes were not observed in the hand premotor and motor areas. The results indicate that the SMA participates in a neural mechanism for self-initiated movements.

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MAPPING OF MUSCLE ACTIVATION PATTERNS OF DORSOLATERAL PREFRONTAL AND PREMOTOR CORTEX BY LOCAL INJECTION OF BICUCULLINE.

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In two macaque monkeys, bicuculline (10-0.075 ug) was injected intracortically into areas 8, 6 and 4 and modes of movement activation patterns were observed. Immediately after an injection, neuronal burst activity was induced at the injected site and became gradually larger in magnitude and frequency. In area 8, 20-60 m after injection, movements of contralateral hand, arm and face, and eye movements to the contralateral side were induced. No clear topological relations were found. In area 6, 10-60 m after injection, movements were induced in face, hand, arm, shoulder and leg contralateral to the injection side. Effective sites for face tended to be lateral and those for leg to be medial along the caudal bank of the arcuate sulcus. In both areas 8 and 6, induced movements were reciprocal, contrasting to co-contraction of antagonistic muscles of area 4. These data indicate that areas 8 and 6 represent forelimb and face movements.

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NEURONAL ACTIVITIES AND THEIR MODULATION BY BICUCULLINE IONTOPHORESIS IN THE MACAQUE PREMOTOR AND MOTOR CORTEX DURING A GO/NO-GO TASK PERFORMANCE

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Single neuronal activities were recorded from the hand areas of premotor and motor cortex while monkeys were performing GO/NO-GO task. The task was initiated by lever press, and GO cue required monkeys to release the lever within 0.8 s and NO-GO cue to withhold it for 1 s. One hundred and six task-related premotor neurons and 47 motor neurons were recorded. Bicuculline (GABA antagonist) was iontophoretically applied to the task-related neurons during the task performance. More than 20% of the premotor neurons showed activity changes during NO-GO period. Additional 18% of premotor neurons with no changes during NO-GO period showed activity changes by Bicuculline application. None of the neurons in the motor cortex showed any changes during NO-GO period. These results suggest that GABA inhibition in the premotor cortex participates in a neuronal mechanism for the selection and performance of GO/NO-GO behavior.

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CORTICAL MECHANISM OF CNV (CONTINGENT NEGATIVE VARIATION) AND CPV (CONTINGENT POSITIVE VARIATION). GEMBA, H., SASAKI, K., TSUJIMOTO, T. AND MATSUZAKI, R. Dept. Physiol., Inst. for Brain Res., Fac. Med., Kyoto Univ., 606 Kyoto

Monkeys were trained to move the hand in response to imperative stimulus (I.S.) given at 1 s after go warning stimulus (W.S.), but not after no-go W.S.. Cortical field potentials on such a visual discrimination task were recorded with implanted electrodes in various cortical areas. The go W.S. induced surface-negative, depth-positive (s-N, d-P) slow potentials (CNV) after visual evoked potentials in many frontal areas, whereas the no-go W.S. elicited slow s-P, d-N potentials (CPV) in some frontal parts. 17 normal human subjects (20-50 years of age) were asked to perform the same task as the monkey. Potentials on the task were recorded from positions F7, Fz, F8, C3, Cz, C4, O1 and O2 (International EEG 10-20 system). The go W.S. induced marked CNV at F7, Fz, C3 and Cz but not at O1 and O2. The no-go W.S. elicited CPV at some electrode positions. Comparison of the findings in humans and monkeys led us to conclude as follows: 1. CNV in man also appears to reflect activities in the frontal cortices of both hemispheres. 2. CNV is considered to be produced by electrical dipoles due to EPSP currents in superficial parts of apical dendrites of pyramidal neurones in the frontal cortices. 3. CPV is likely produced by electrical dipoles in the prefrontal and premotor cortices caused by disfacilitation of background EPSPs in the superficial parts of the apical dendrites.

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SUPPRESSION OF VISUALLY-INITIATED HAND MOVEMENT BY STIMULATION OF THE PREFRONTAL CORTEX IN THE MONKEY. SASAKI, K., GEMBA, H. AND TSUJIMOTO, T. Dept. Physiol., Inst. for Brain Res., Fac. Med., Kyoto Univ., 606 Kyoto

Effects of stimulation of the prefrontal areas, in which 'no-go potential' (1) is recorded on the go/no-go reaction-time hand movement task with colour discrimination, were observed upon the go reaction-time movement in the monkey in order to study functional significances of the no-go potential. The surface and depth (2.0-3.0 mm) electrodes chronically implanted in various cortical areas of both hemispheres, originally for recording cortical field potentials, were used for bipolar stimulation of respective cortical areas. A train of brief electrical pulses was delivered to the prefrontal areas producible of the no-go potential, i.e. , the dorsal bank of the principal sulcus and/or the rostrolateral edge of the prefrontal cortices, of both hemispheres. The stimulation given at about a time of the no-go potential (100-150 ms after the onset of visual stimulus) suppressed the reaction-time movement which was otherwise performed on the visual stimulus, cancelling and delaying the movement. The suppressor effect was found to be considerably unique in those areas of the no-go potential. The result suggests that the no-go potential represents the suppressor action of the prefrontal areas and exerts revoking and deferring effects upon the motor command initiated by the visual stimulus. (1) Exp. Brain Res. 64: 603-606 (1986)

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LEARNING FORMS NEURAL REPRESENTATION OF PICTORIAL LONG-TERM MEMORY IN THE PRIMATE TEMPORAL CORTEX. MIYASHITA,Y. & MORI,K* Dept.Physiol., Sch.Med., Univ.Tokyo, Tokyo 113.

Long-term memory of visual experience has been proposed to be stored in the neural network of temporal cortex in humans. Recently, we have found shape-selective working memory neurons in monkey temporal cortex. We report here evidence suggesting that these working memory neurons also code the long-term memory of pictures. Two monkeys (Macaca fuscata) were trained to perform a modified delayed matching-to-sample task; sample and match stimuli are presented successively on a video monitor, each for 0.2s at a 16s delay interval. The stimuli were selected randomly among 100 computer-generated colored fractal patterns. In the training session, 100 fixed patterns were used for each monkey(learnt stimuli). When extracellular discharge of a neuron was recorded from the temporal cortex of these monkeys, the working memory responses of the neuron were tested not only by 100 learnt stimuli but also by 100 patterns which were newly generated for each neuron(new stimuli). In all of 15 neurons, the maximum delay discharge among those induced by 100 learnt stimuli was much stronger than that among those induced by 100 new stimuli. The stimulus-selectivity was also much higher in the learnt stimuli than in the new stimuli. These observations suggests that the responsiveness of these working memory neurons was formed through learning of the task, and that the network of these neurons represents long-term memory of the learnt pictures.

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LONG-TERM POTENTIATION IN THE MOTOR CORTEX IN CATS. SAKAMOTO, T., PORTER L.L.*[1] and ASANUMA, H.[1] Dept. of Physiol., ASAHIKAWA MEDICAL COLLEGE, ASAHIKAWA 078, and [1]THE ROCKEFELLER UNIVERSITY, 1230 York Ave, New York, N Y 10021, U.S.A.

The motor cortex (area 4) receives the topographically organized input from the sensory cortex (area 2). To examine the possibility that this projection participates in motor learning, we have investigated the effects of tetanic intracortical microstimulation of the sensory cortex on the EPSP recorded from motor cortical neurons.

Immediately after tetanic stimulation, the amplitude of the EPSP decreased for about 1 to 2 minutes. Then amplitude started to increase and reached a peak about 5 minutes after the tetanic stimulation. This increase lasted for more than 20 minutes, as long as membrane potential was kept at original level. These effects were restricted to the input arising from the tetanically stimulating site. When a cell received inputs from 2 sites in area 2 or area 2 and the thalamus, tetanic stimulation at one site of area 2 did not potentiate EPSPs elicited by the other site or the thalamus.

It is possible that this long term potentiation we have found modulates the activity of paticular motor cortical column and that the motor cortex itself is involved in motor learning.

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SELECTIVITY FOR STIMULUS SPEED AND DIRECTION OF CELLS IN THE MEDIAL SUPERIOR TEMPORAL AREA IN THE MACAQUE MONKEY. HIKOSAKA, K. AND IWAI, E. Dept. of Behavioral Physiology, Tokyo Metropolitan Inst. for Neurosci., Fuchu, Tokyo 183.

Using monkeys (M. fuscata) anesthetized with a gas mixture of N_2O:O_2 (3:1) and immobilized with gallamine triethiodide, single unit recordings were made in the medial superior temporal area (MST) in the caudal superior temporal sulcus (STS). A total of 115 MST cells which responded to unidirectional straight movement of visual stimuli in the frontoparallel plane were isolated. The selectivity for stimulus speed was examined moving the stimuli through the receptive field at 9 stimulus speeds ranging 2 to 512°/s along the preferred direction. The selectivity for stimulus direction was examined moving the stimuli in 12 directions separated by 30° at the optimal speed. Most cells showed highly directional selectivity. About half of cells showed inhibitatory responses in the null direction, and had directionality index (DI) values of greater than 1. The distribution of DIs ranged from 0.40 to 1.68. Most cells (80/115) were tuned for stimulus speed; on average, responses were greater than half-maximal over a 8.3-fold range of speed. About a third of cells showed optimal responses at 64°/s. The distribution of optimal speeds ranged from 4 to 512°/s. The full-widths of direction-tuning curves at half-maximal response ranged from 42° to 159°, and the mean full-width of 46 tuned MST cells was 97°.

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OCULAR FOLLOWING EYE MOVEMENT RELATED NEURONAL ACTIVITY IN THE POSTERIOR PARIETAL CORTEX OF ALERT MONKEY. KENJI KAWANO, YOSHIHIRO WATANABE* AND SHIGERU YAMANE Bionics Section, Electrotechnical Lab., Umezono, Tsukuba-shi, Ibaraki 305, JAPAN

Previous studies showed that a group of neurons in the posterior parietal cortex of the monkey are activated by movements of the entire visual field. In this study, experiments were concerned with their relation to the ocular following eye movement, which is always elicited by movements of the visual field in alert monkeys. A monkey faced a tangent screen onto which a random dot pattern was projected, and its eye movements were recorded with the magnetic search coil technique. Single unit activity was recorded in the posterior parietal cortex (area PG) of the monkey. One hundred and sixty-six neurons were activated by the movements of the visual scene. Most of them showed a high degree of direction selectivity and preferred high stimulus velocity. Their latencies were unexpectedly short. Eighty percent of the neurons were activated less than 50ms after the onset of the stimulus, and about half of them started their increase of firing rate more than 10ms before the onset of the eye movement. Spatial filtering of the moving images, by interposing a sheet of ground glass between the animal and the scene, delayed the onset of ocular following and the latency of neuronal response simultaneously. These data suggest that the neurons in the posterior parietal cortex of the monkey may play an important role in the initiation of ocular following.

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TOPOGRAPHIC STUDIES ON ELECTRICALLY ELICITED SACCADES IN THE MONKEY FRONTAL EYE FIELD. AZUMA, M. and SUZUKI, H. Dept. of Physiol., Hirosaki Univ. Sch. of Medicine, Hirosaki 036

The frontal eye field (FEF) is a part of the prefrontal cortex where electrical stimulation elicits saccadic eye movements. We tried to localize the extent of the FEF in macaque monkeys and further to examine whether or not the saccade is topographically organized in the area. We inserted the Elgiloy microelectrode into the prefrontal cortex of the alert monkey and applied a train of 10 negative pulses with a current of 70 μA or less (1-ms width, 200 Hz). We found in six hemispheres that a large extent of the FEF was localized in the anterior bank of the arcuate sulcus, and a part was in the exposed cortex anterior to the sulcus. When the stimulation was applied at each layer of of a given locus in the FEF, we obtained saccades with similar amplitude and direction. When a stimulating locus was gradually changed, saccade vector properties were also changed. A small saccade was elicited in the lateral and postero-lateral portions in the FEF, and a large one was in the medial portion. From the results, we postulated that the function of the FEF regarding the saccade is topographically differentiated.

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EFFECTS OF INTRACORTICAL MICROSTIMULATION IN THE PRIMATE FACE MOTOR CORTEX AND MASTICATORY CORTEX. HIRABA,H.,HUANG,C.-S.* and SESSLE,B.J.* Nihon Univ.Sch.Dent., 1-8-13 Kanda-surugadai, Chiyoda-ku, Tokyo 101. *Fac.Dent., Univ.of Toronto, Toronto, Canada.

This study was undertaken to characterize facial representations both of the facial motor cortex (M1) and the masticatory cortex (MA). In M1, the representation of the face, jaw and tongue was determined in unanesthetized monkeys by examining the twitch movements and EMG responses evoked by ICMS (≤30μA, 12train, 0.2ms duration, 333Hz). It was characterized as a representation of the facial musculature which partially enclosed and overlapped the rostral, medial and caudal borders of the more laterally located cortical regions representing the jaw and tongue musculatures. In MA, the topographic organization and the patterns of evoked rhythmic jaw movements (RJMs) were defined with the use of ICMS (≤60μA, 0.2ms, 50Hz). The RJMs could be differented into three basic patterns:vertical movement but with jaw deviation laterally to the side contralateral to ICMS (RJMc), vertical movement but with jaw deviation laterally to the side ipsilateral to ICMS (RJMi), and vertical movement with little lateral deviation (RJMv). Topographically, the RJMs were well represented in M1 and SI as well as the classical MA, but RJMi sites predominanted over RJMc sites in all areas except SI. Also in each of these cortical areas, most of the RJMi sites were located anterolaterally to the RJMc sites, and the RJMv sites were scattered throughout the cortical area.

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SI NEURONS RESPONDING TO HEATING OF FACIAL SKIN AND ORAL MUCOSA IN CATS. TSUBOI,Y.,IWATA,K.,MURAMATSU,H. AND SUMINO,R. Department of Physiology, School of Dentistry, Nihon University, 1-8-13 Kandasurugadai,Chiyoda-Ku, Tokyo 101, Japan

Cortical neurons responding to heating of the facial skin and oral mucosa were studied by recording single neuronal activities from SI region in the cat anesthetized with Ketamine-HCl and immobilized with pancuronium bromide. A total of 59 SI neurons responding to mechanical or heat stimulation of the orofacial regions were analyzed and 23 neurons were heat sensitive (Hs neurons) and 36 were heat insensitive. 7 Hs neurons responded to tactile stimulation of the facial skin, oral mucosa and the tooth and 13 of Hs neurons responded not only to touch stimulation but also to pinching of the facial skin, oral mucosa and the tooth (N-N Hs neurons). Only 3 Hs neurons received exclusively noxious cutaneous and mucosal inputs from orofacial regions (NS neurons). All Hs neurons located in cytoarchitectonic area 3b. The N-N Hs neurons showed graded responses to increasing stimulus temperature, while the NS neurons did not alter their response frequency until very high temperature (48-50°C) following heating of the facial skin and oral mucosa.

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SIMULTANEOUS STAINING OF VIBRISSAE BARRELS AND HRP-INJECTED NEURONS IN THE RAT SOMATOSENSORY CORTEX. ITO, M. Department of Physiology, Aichi Prefectural Colony, Kasugai 480-03.

A unique feature of the rodent somatosensory cortex is the presence, in layer IV, of the so-called barrels that correspond to each vibrissa on the contralateral face in a one-to-one fashion. The barrels are most clearly visualized by cytochrome oxidase histochemistry that uses diaminobenzidine as a chromogen. Since this chromogen is also used for identification of HRP-injected neurons in the CNS, it should be possible to examine the location of these neurons with respect to the barrels. More specifically, it was asked whether the vibrissae-sensitive neurons are in register with the barrels or not. Those vibrissae-sensitive neurons that could be injected with HRP were transient-type neurons and located below lauer IV. The apical dendrite of thus injected neurons was found to pass, in layer IV ,through the periphery of a barrel. The basal dendrites were found to extend the branches in various directions regardless of which barrel the parent soma belonged to.

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TWO TYPES OF INHIBITORY INTERNEURONS PROJECTING TO PYRAMIDAL TRACT CELLS IN THE CAT MOTOR CORTEX. ENDO, K., KANG, Y., KAYANO, F. AND ARAKI, T. Dept. Physiol., Fac. Med., Kyoto Univ., Kyoto 606

Cats were anesthetized with sodium pentobarbital and simultaneous recordings from pyramidal tract (PT) cells and neighboring interneurons were made in the cortical area 4. Unitary IPSPs produced in fast PT cells by the activity of single interneurons were recorded by spike-triggered signal averaging. Twenty six inhibitory interneurons, which produced unitary IPSPs in PT cells with latencies of monosynaptic range (0.5 - 0.9 ms), were identified. Inhibitory interneurons located in the cortical lamina II and upper lamina III (type S) produced IPSPs with relatively slow rise time (range; 2.60 - 5.50 ms), whereas those located in lower lamina III to lamina V (type D) produced IPSPs with faster one (range; 0.70 - 1.95 ms). IPSPs evoked by type D interneurons were easily reversed by hyperpolarizing current, while those produced by type S interneurons were not. Type D interneurons were synaptically fired by stimulation of the thalamic ventrolateral nucleus and the pyramidal tract, while type S interneurons were activated from the thalamic ventrolateral nucleus alone. It may be suggested that type S interneurons synapse at more distal dendrites of PT cells than type D interneurons.

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RECORDED AREAS OF EVOKED POTENTIALS IN CAT CORTEX AFTER STIMULATION OF THE CORPUS CALLOSUM. KAWASHIMA, T., UEKI, S., AND MATSUNAMI, K., Dept. Neurophysiol., Inst. Equilibrium Res., Gifu Univ. School of Medicine, Tsukasamachi 40, Gifu City, 500.

Recorded areas on the cortical surface were determined after stimulation of the corpus callosum in cat. The cat was anesthetized with alpha chloralose. A stimulating electrode, consisted of 5 acupuncture needles, separated by 1mm, was inserted into the anterior or posterior portion of the corpus callosum. Recordings were made simultaneously from 8 cortical points, 2 mm apart one another, with 8 recording needles. Thus we could record evoked potentials from more than 20-30 cortical points in relatively short period. The callosally activated areas were smaller at near threshold (1T) stimulation, but such areas spread larger with increasing stimulus strength (1.5, 2 and 10T). However, there were several types in spreading pattern of callosally activated areas.

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MULTIPLE CORTICAL CONTROL IN EYE MOVEMENTS.

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The "oculomotor" cortices responsible for eye movements in the cat are located in the medial wall of the hemisphere under the cruciate sulcus, the medial and lateral bank of the presylvian sulcus, the fundus of the coronal sulcus and the ventral bank of the anterior ectosylvian sulcus. In the present study, we examined the possibility of an independent control of the eye movement from these cortices located in the different portion of the cerebral cortex. Experiments were carried out using nonanesthetized cats with chronic microelectrodes implanted in the cortices. The possibility of the independent control of the eye movement among these cortices was suggested by the following reasons: 1) Eye movements were evoked by the intracortical microstimulation of each cortex. 2) Corticofugal fibers from these cortices terminate commonly in the subcortical structures related to the eye movement. 3) Presaccadic neurons were obtained from all these cortices during visually guided saccades. These results suggested that there are a multiple and parallel control of the cerebral cortex in eye movements.

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DESCENDING PATHWAY FROM CAT'S OCULOMOTOR CORTICES.

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Descending pathways from "oculomotor" cortices related to eye movements in the cat, which consist of five different parts of cerebral cortex, were examined with WGA-HRP tracing method under chloralose anesthesia (60 mg/kg). The WGA-HRP was iontophoretically injected into the cortex where eye movements were evoked by electrical stimulation. The labelled cell body and terminals were found ipsilaterally in the thalamus. The labelled terminals were found bilaterally in the superior colliculus, the pontine nucleus, the pontine tegmental reticular nucleus, and the brainstem reticular formation. These results indicate that the "oculomotor" cortices in the cat innervate the subcortical structures in a parallel fashion. The parallel innervation might contribute to a parallel control of the cerebral cortex in the eye movement.

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MODULATION OF EVOKED MUSCLE POTENTIALS IN RAT GASTROCNEMIUS MUSCLES INDUCED BY NEOSTIGMINE METHYLSULFATE. URAMOTO, I., TOTSUKA, T. Dept. Physiol., Inst. Develop. Res., Aichi Prefect. Colony, Kasugai, Aichi, 480-03

Experiments were carried out using male Wistar rats about 60 days old. They were anesthetized with pentobarbital sodium (60 - 75 mg/kg). Spontaneous activities and muscle potentials evoked by the stimulation of sciatic nerves were recorded from exposed medial gastrocnemius muscles using concentric electrodes. The stimuli were square pulses of 0.05 msec in duration and supramaximal intensity was used. Neostigmine methylsulfate (VAGOSTIGMIN, Shionogi) was applied intramuscularly (0.1 - 0.15 mg/kg). Muscle potentials in the gastrocnemius muscles were generally of a biphasic wave before the application of the drug. A few minutes after the injection of the drug, spontaneous electrical activities were observed to occur frequently in a burst and they seemed to be the discharge of motor units accompanied with vigorous spontaneous contractions. The injection had also an effect on the pattern of evoked potentials: One or more oscillations followed such a main biphasic wave as observed before the drug treatment.

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DEVELOPMENTAL CHANGES OF OCCIPITAL EEGS THROUGH THE FOLLOW -UP STUDY KOIKE,T.[1], KATADA,A.[1], OZAKI,H.[2] AND SUZUKI,H.[2] [1]Tokyo Gakugei Univ., Koganei 184, [2]Ibaraki Univ., Mito 310.

The present study investigated the developmental changes of occipital EEGs through follow-up recordings. Subjects were 23 normal children The first EEG recording was made within an age range of 3-9 years and the follow-up recordings were done during about 3-5 years. About occipital EEGs, spectra which showed multiple peaks in theta and alpha bands as well as spectra with a single component were recognized. Components which appeared at low frequencies within multiple peaks diminished in power and disappeared with increasing age. Components of the highest frequency within multiple peaks and a single component showed gradual increase of peak frequency. It may be pointed out that children's occipital EEGs include components which undergoes different developmental changes and that different maturational processes are inferred about these changes.

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EFFECT OF TRH ON THE ELECTRICAL PHENOMENA IN THE CENTRAL NERVOUS SYSTEM. NAITO, H., TAKEMURA, K., HORI, A., YAMAMOTO, T. AND YASUHARA, M. Dept. Physiol., Kansai Med. Univ., Osaka 570

The effect of TRH on central nervous system activity was investigated electrophysiologically.

TRH(0.05-1.0mg/kg) was injected intravenously in rabbits and the following observed. 1) The threshold of arousal reaction and evoked muscular discharge due to stimulation of the brain stem reticular formation declined. 2) The frequency of spontaneous unit discharge of the brain stem reticular formation increased markedly. 3) The threshold of the evoked muscular discharge declined on stimulation of the cerebral cortex but rose on stimulation of the hippocampus. 4) The amplitude of the photo-evoked eyelid microvibration increased. 5) The amplitude of the M- H wave and the nociceptive reflex muscular discharge increased.

The findings suggest that TRH has a consciousness-arousing effect, a facilitatory effect on the pyramidal system and the spinal reflex, and an inhibitory effect on the extrapyramidal system.

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AN ELECTROPHYSIOLOGICAL STUDY ON EXPERIMENTAL CERVICAL SYNDROME.
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In order to elucidate the mechanism of the cervical syndrome, electrophysiological studies were conducted in rabbits. The greater occipital nerve(GON), cervical sympathetic nerve(CSN) or both GON and CSN was stimulated electrically and the following observed. 1) The threshold of arousal reaction and evoked muscular discharge due to stimulation of the brain stem reticular formation increased. 2) The threshold of evoked muscular discharge due to stimulation of the cerebral cortex rose but those due to stimulation of the hippocampus declined. 3) The amplitude of the recruiting response, due to stimulation of the VA, increased. 4) The amplitude of the sciatic evoked eyelid microvibration(SMV) increased. 5) The blood flow volume of subclavicular and carotid arteries decreased by CSN stimulation but those by GON stimulation remained almost unchanged. 6) The above changes were inhibited following administration of diazepam(2-5mg/kg) but those following administration of pentazocine(3-6mg/kg) were not inhibited.

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CONDUCTED AND NONCONDUCTED COMPONENTS IN SPIKE POTENTIALS OF HUMAN SINGLE MOTOR UNITS
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Ordinary spike potentials, recorded by means of monopolar recording method, consisted three phases. The first and third phases could be due to the current flowing into the excited part from the front/behind of the excited part. When the electrode fixed just above the motor end plate, the first phase disappeared and the second phase showed the steeply rising form. This second phase of spike potentials showed the characteristics of the electro-tonic potential. When moving the electrode to distal and proximal from the end plate within 15 mm, the peak of second phase did not shifted in the time and the amplitude decreased. There was a time lag between the onset of the steeply rising phase and that of the first phase of ordinary spike, and the time lag was 0.23 ms. The muscular temperature decreased from 30°C to 15°C with applying the ice. During this process, there was a negative correlation between the muscular temperature and the time lag, and Q_{10} was about 3.

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MEASUREMENT OF CONDUCTION VELOCITY OF ACTION POTENTIAL IN HUMAN MUSCLES BY UNIDIMENSIONAL LATENCY-TOPOGRAPHY.
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The conduction profile of an action potential elicited by weak voluntary contraction of the m. biceps brachii was graphically displayed by unidimensional latency-topography, UDLT. The end-plate location and conduction velocity (CV) were determined by UDLT. The end-plate location of the m. biceps brachii was measured as 12-15 cm proximal to the epicondylus medialis and remained at the same region independently of the elbow angle. The CV of the action potential of various muscles was also measured in five subjects to reveal inter-muscular variation. The variation in the CV among various muscles in the same subject and that among subjects was not statistically significant. The CV measured ranged from 3.4 to 3.8 m/s.

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RELATION OF DECREASED CNV AMPLITUDE TO MOTOR READINESS POTENTIALS AND REACTION TIMES. TOMITA SAYURI, HAYASHIDA, Y. AND IKEMI, A.* Dept. Systems Physiol., Univ. Occup. Environ. Hlth., Kitakyushu 807.

Self Regulation Method(SRM) has shown to induce amplitude decrease of contingent negative variation(CNV) in our previous report. In this study, the effects of motor readiness potentials with key pressing and reaction times on CNV amplitudes were examined. EEG was recorded between Cz or Pz and both auricles. Twelve responses were separately averaged for obtaining CNVs responding to imperative stimulus(S2) with key pressing or without key pressing. Twelve responses were also averaged for CNVs with shorter or longer reaction times separately.

During SRM condition, there was also decrease in CNV amplitude obtained in response to the imperative stimulus without key pressing. Further, there was decrease in amplitude of CNVs with both shorter and longer reaction times. The results demonstrated that decrease in CNV amplitudes during SRM was attributed to changes in neither the motor readiness potentials nor reaction times influencing CNV components.

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ELECTROPHYSIOLOGICAL EVENTS INVOLVED IN THE INITIATION OF AFTERDISCHARGES (AD) IN THE ENTORHINAL CORTEX AND ACQUISITION OF BEHAVIORAL SEIZURES TO AMYGDALA KINDLING STIMULATIONS IN RATS. MATSUURA,S., KAWAWAKI,H., MORICKA,H., Dept. Physiol., Osaka City Univ. Med. Sch. Asahi-machi, Abeno-ku, Osaka 545

Interrelation of the events in the entorhinal responses to amygdala stimulation with AD requisite for the acquisition of generalized kindling seizure was studied by recording entorhinal field potential (EFP) to amygdala stimulations in awake rats. A bipolar stimulating and a fine tungsten wire electrodes were inserted in rats anesthetized with pentobarbitone. Input-output curve for FEP and AD threshold were determined before kindling stimulations. Generalized seizure was obtained with a lengthening of AD duration and the development of long-term potentiation (LTP) in EFP, even when kindling stimulations with intensities lower than the AD threshold were principally or intermittently applied. In the early kindling acquisition processs, a decrease in stimulus intensity failed to evoke AD in association with a decrease in EFP size. When AD was produced, a marked short-term potentiation (STP) as well as facilitation in EFP during the stimulation was usually evident. In the rats acquired generalized seizure, stimulations with a short (1-3 min) interval frequently failed to evoke AD and behavioral seizure in association with a decrease in EFP size, especially in the later wave component of EFP. The facilitation, STP and LTP interrelate with the initiation of AD.

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Location of generator and distribution of SEP elicited by selective stimulation of skin afferents in man. TOMA,S.,NAKAJIMA,Y. and HOMMA,S. Dept. of Physiol.,Sch.of Med.,Chiba Univ., Chiba 280.

A tungsten microelectrode was percutaneously inserted into the left median nerve at the wrist in 6 human subjects. The afferent activities from the grabrous skin of hand area were recorded and identified. Then an electric shock was delivered through the recording electrode tip to stimulate the fascicle of skin afferent. SEP were recorded on the right central area of scalp from the 21 needle electrodes arranged by checking equal intervals of 2cm, the center electrode being in coincidence with 2cm posterior to C4 of the international 10-20 system. The indifferent electrode was placed on Fpz point. Each peak latency was measured and processed for an isopotential topography and estimated electric equivalent dipole by dipole tracing method. These results were compared with those obtained from the mixed nerve stimulation. N20 potential distributed as positive in the antero-medial to C4 and as negative in postero-lateral to C4. The dipole vector moment orientated up ward and anterior direction. Tangential surface of this vector coincident with 0 potential level of topography, which seems to be along by the central sulci. Generator of N20 may be located in the primary sensory cortex probably in 3b area. N30 potential distributed as negative-positive revasal of N20 and dipole vector moment orientated opposite direction. N30 potential may generate in area 4 motor cortex.

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DIPOLE-TRACING OF EARLY COMPONENTS OF HUMAN SOMATOSENSORY EVOKED POTENTIALS ELICITED BY DOUBLE STIMULI OR AFFECTED BY VOLUNTARY ACTION. NAKAJIMA, Y., HOMMA, S. and KAWASHIMA, Y. Dept. Physiol., Sch. Med., Chiba Univ., Chiba 280.

Somatosensory evoked potentials (SEP) elicited by electrical stimulation of the median nerve were simultaneously recorded in humans using twenty-one surface electrodes positioned on the scalp. Double shock stimulation at an interval of less than 30 ms failed to elicit a discriminative sense of two stimuli. In this stimulus condition, the component at 40 ms elicited by the second stimulus of the double shock did not show positivity. On the other hand, after voluntary action of the thumb flexion, the amplitude of P22 was suppressed. By subtracting SEP elicited by single shock (control SEP) from either that elicited by double shock or that during voluntary action, the equivalent dipoles of the potentials corresponding to P40 of the second stimulus or P22 after the voluntary action were calculated, respectively. In either condition, the resulting dipole was located in the same region, but the vector was in the inverse direction of that of the dipole calculated from the control SEP. It seems that the generation of these inverse potentials in the cortex, which suppress P40 or P22, are closely related to loss of discriminative sense of the double shock, or a voluntary action or the subject's awareness that stimulation will be given after the voluntary action, respectively.

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AUDITORY BRAIN-STEM RESPONSE (ABR) AND SOMATOSENSORY EVOKED POTENTIAL (SEP) DURING HYPOPERFUSION OF THE BRAIN IN DOGS. MOTOCHIGAWA,H., KAJIMOTO,S., NISHIDA,Y., MORITA,H., MATSUSHITA,K., KAWADA,M., NAMEKATA,K., NAKAYAMA,S. and HOSOMI,H. Dept. of Physiol., Kagawa Medical School, Miki, Kita, Kagawa 761-07

The goal of this study was to determine the regional differences in resistance to hypoperfusion of the brain. Under computer control, simultaneous and continuous measurements of auditory brain-stem response (ABR) and somatosensory evoked potential (SEP) were taken at rates of 80 / 10 sec and 20 / 10 sec, respectively. After the control period, the brain perfusion pressure was reduced from a control level (122 $\pm$12 mmHg) to about 40 mmHg for 3 min. The peak latency and the peak amplitude of the I, II, III and IV waves of ABR and the P1, N1, P2 and N2 waves of SEP (latency 15, 19, 22 and 35 msec, respectively) were measured. Also the I-II, II-III and III-IV interpeak latency (IPL) of ABR and P1-P2 and N1-N2 IPL of SEP were calculated. For ABR, the changes in peak latency, IPL and peak amplitude of all waves were not significant. For SEP, peak latency and IPL of all waves did not change significantly, but the peak amplitude of P1 and N1 decreased significantly at 2 min after the start of hypoperfusion and that of P2 and N2 decreased significantly at 1.5 min. These results indicate that during hypoperfusion the brain stem can preserve its function better than the cortex.

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CHANGES IN THE AMPLITUDE OF THE PHOTICALLY EVOKED LID POTENTIALS DURING WAKEFULNESS AND AT EACH STAGE OF SLEEP. HOSHINA, Y., SAKUMA, Y., TANNO, T., AKITSU, H., HASEGAWA, N., CHIBA, Y. AND *NIKARA, T. Dept. Physiol. I, Sch. Med. and *Physiol. Lab., Sch. Allied Med. Sci., Hirosaki Univ., Hirosaki 036

Effects of wakefulness and sleep on the photically evoked orbicularis oculi reflex was studied in 4 healthy subjects. EMG activity of the muscle, which we termed the eye lid potential (ELP), was recorded from the eyelid using nonpolarizable electrodes. Eye movements were monitored via an electrode below the eye. Trials contaminated with eye movements were excluded from the average. Scalp EEG recordings were made from the parietal and occipital locations in the right hemisphere. Standard full-field flash was used as the photic stimulus. Data from all channels were stored on FM tape for off-line singal averaging with a signal processor. A 400 ms epoch of eye lid potential date beginning at each stimulus was analyzed. The ELP appeared with the largest amplitude at the shortest latency in the awake subjects when they were making mental arithmetic with their eyes closed. The amplitude decreased and the latency lengthened when the subjects terminated the arithmetic and as their sleep deepened: the ELP diminished at stage 2 and was absent at stage 3. Thus, the ELP is closely associated with the over all activity of the central nervous system.

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BRAIN LATERALITY DURING THINKING AND EEG TOPOGRAPHICAL ANALYSIS.

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EEG was measured with eyes closed on a several kinds of thinking process and also during listning music as the comparison. Signals were digitized, analyzed through FFT and topographically mapped. When subjects are listning music, α_1 waves activity is increased. Mental calculation decreases α on the left hemisphere and increases β_1 and β_2. Imaginary tasks, e.g. "imaging some poster" or "thinking the way to the station", suppress α_1 but increase α_2 waves; the integral of whole α(8-13Hz) dose not change statistically. By thought, α waves become faster significantly than those at the resting condition (the frequency of peak-α during imaging a poster; 10.21±0.08Hz: While, at the resting state; 9.83±0.07Hz (mean value of 55 examples ± S.E.)). Hemispheric difference in the peak-α change was not found.

Beta waves are increased on just the area of working in the cerebrum for the actual image.

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INFLUENCE OF THE HIPPOCAMPAL SEIZURE ON THE CENTRAL NERVOUS SYSTEM (II).

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The effect of hippocampal seizure on the CNS was investigated in rabbits. When the seizure discharge was induced by hippocampal stimulation, the following was observed. 1) The threshold of arousal reaction and evoked muscular discharge due to stimulation of the brain stem reticular formation(RF) increased. 2) The threshold of evoked muscular discharge of the fore- and hindlimbs, due to stimulation of the cerebral cortex or the hippocampus(HPC), increased. 3) Late components(N_4-N_7) of the average evoked potential, appearing in the cerebral cortex were inhibited. 4) Components(HN_1, HN_2, HN_6) of the average evoked potential, appearing in the HPC(AEP-HPC), were inhibited. 5) The nociceptive reflex muscular discharge was inhibited. 6) The M- H wave and photo-evoked eyelid microvibration(MV) were inhibited. 7) Lesions in the nucleus ventralis anterior(VA) almost eliminated the inhibitory effect of RF, HPC, AEP-HPC and MV. 8) The administration of barbiturate or carbamazepine almost eliminated the inhibitory effect(1-6).

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FLUCTUATIONS IN EEG ALPHA WAVES RELATING TO CARDIAC BEAT-TO-BEAT OSCILLATIONS.

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Analyses of the fluctuations in EEG alpha waves relating to cardiac beat-to-beat oscillations were performed. Subjects were 10 healthy college students. They lay supine on the bed with their eyes closed. The ECG and EEG were recorded for 10 min, which were analyzed for 2 min after 4 min from the beginning. In the ECG, we first detected the peaks of R-waves and then calculated the R-R intervals. Continuously, the AR modeling spectral analyses of fluctuation curves in R-R intervals (RR) were done. In the EEG, spectral analyses were also done every 2 sec at 0.5-sec intervals. Fluctuation curves in the frequency of alpha waves (FQ) were analyzed like those of the RR. In the power spectral densities of RR and FQ, there were two major peaks at about 0.1 Hz (low frequency component: LFC) and 0.3 Hz (high frequency component: HFC). In both LFC and HFC, no significant frequency differences were found between RR and FQ, but, LFC:HFC ratio of FQ was greater than that of RR. The coherences between RR and FQ had also two peaks at around same frequencies. Their mean values were more than 0.5. In conclusion, it is suggested that the frequency of alpha waves fluctuates relating to cardiac beat-to-beat oscillations.

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FRONTAL MIDLINE THETA-LIKE ACTIVITY DURING "HIBIKI" SENSATION CAUSED BY ACUPUNCTURE STIMULATION. LIAO, T-J., SUZUKI, H., MAEDA, A. and TASAKI, K., Dept. of Physiol., Tohoku Univ. Sch. of Med., Sendai, 980

Successful acupuncture treatment causes specific sensation called "Hibiki", the strength of which is a measure of effectiveness of the treatment. To evaluate strength and duration of the sensation objectively, we recorded brain waves, fed them to the FFT analyzer, and compared results with those obtaind under the other sensations, such as pain, pressure and so on. Neither insertion of the acupuncture needle into an acupoint (CHU SAN LI) nor hand manipulation of the needle caused noticeable change in EEG before subjects claim the "Hibiki" sensation. When the sensation occurred, theta activity was recorded from the frontal midline (Fz) and not from any other recording sites. Time course of its power was in agreement with that of subjective sensation measured psychophysically (cross modality matching; Liao, 1987). As long as the sensation remained even after removal of the needle, theta component of the power spectra was evident. The other sensations did not induce thete activity at any recording sites. These results suggest that the frontal midline theta-like brain wave have close relation with the "Hibiki" sensation" and that there is no simple correlation between the "Hibiki" sensation and a specific cutaneous and/or deep sensation.

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EYE MOVEMENT-INDUCED INCREASE IN TONUS OF THE CERVICAL MUSCLE, WHICH IS INDEPENDENT OF THE EYE HEAD COORDINATION. WATANABE, K., LIAO, T-J., SUZUKI, H. and TASAKI, K., Dept. of Physiol., Tohoku Univ. Sch. of Med., Sendai 980

Voluntary eye movement without rotating a head results in increase in tonus of the tissue around a needle whichi is inserted into the anterior cervix of a patient suffering from neural disorder (Watanabe et al., 1987). To identify the origin of this phenomenon, we recorded force pulling the needle, time course of the head rotatin, spike discharges, and tonus of the cervical muscle. Eye movement-induced change in force abruptly increased when the tip of needle reached at aobut 35 mm from the surface of skin. An image of X-CT scan revealed that the tip was on the surface of the Longus colli at this depth. The force increased in 1-3 sec after the onset of the eye movement and lasted 30-60 sec after the offset. Eye head coordination-ralated change in tonus, which was detected through change in electric impedance of the muscle, ended in 600-800 msec after the onset of the eye movement and did not continue any more. These results suggest that the origin of change in tonus of the anterior cervix is the Longus colli, and that longlasting increase in tonus of the muscle can not be simply explained by the neural mechanism which is responsible the the eye-head coordination.

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RELATIONSHIP BETWEEN CEREBRAL AND CEREBELLAR FIELD POTENTIALS EVOKED BY MOLAR PULP STIMULATION OF RATS. Yoshino,H.,Kamata,Y.,Nishikawa,T. AND Shimizu,S. Dept.Pharmacol., Kagoshima Univ.Dent.Sch., Kagoshima 890.

Electrical stimulation of the first lower molar pulp of rats was previously shown to produce pain sensation in awake rats. Therefore we examined cerebral and cerebellar potentials evoked by such a stimulation procedure in anesthetized rats with urethane-chloralose. Under pulp stimulation, cerebral potential was recorded in MI and the anterior SI, and cerebellar potential was in the medial Sim and crus 1. When MI or SI was stimulated, cerebellar potential of the same wave form as that by pulp stimulation was recorded in the medial Sim and crus 1, after shorter latency. Under pulp stimulation and cerebellar recording, as a cerebral recording electrode of especially large diameter was inserted in MI or SI, cerebellar potential disappeared. These results indicate a possibile pulp-cerebrum-cerebellum pathway which might relate to tooth pain or behavior induced by pain.

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THE EFFECTS OF HYPOXIA ON AUDITORY BRAIN-STEM RESPONSE AND SOMATOSENSORY EVOKED POTENTIALS.

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We studied the effects of hypoxia on auditory brain-stem response (ABR) and somatosensory evoked potentials (SEP) in dogs. The dogs anesthetized with pentobarbital sodium (30 mg / kg body weight, i.v.) were intubated and ventilated with room air in the control period. After the control period, they were subjected to hypoxia (10 % O_2- 90 % N_2) for 5-minutes hypoxic period, then returned to room air. Click acoustic stimuli (90 dB, 0.25 msec) were used to elicit ABR. SEP was elicited by electrical stimulation (150 V, 0.2 msec) of the forepaw. ABR and SEP were repeatedly monitored and averaged for every 10 sec. The amplitude of ABR IV wave increased by about 48 % of control at 150 sec after starting hypoxia. There were no remarkable changes in amplitude or latency of the other ABR and SEP waves. At 270 sec after starting hypoxia, systemic blood pressure decreased by 35 mmHg from control, and all the ABR and SEP waves were depressed. When systemic arterial pressure is in or above the normal range, brain electrical activity increases with hypoxia.

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EFFECT OF AGE ON SCHEDULE-CONTROLLED REVERSE DISCRIMINATION LEARNING TASK IN FISCHER 344 RATS. NOMURA, M. Dept. of Physiol. School of Med. Fujita-Gakuen Health Univ., Toyoake, Aichi 470-11

To clarify the effect of age on spatial discrimination learning ability, 3- and 24-month-old Fischer rats were studied on a schedule-controlled left-right discrimination task using an operant type Skinner box. The learning task was tested by food reinforcement on a Multiple Variable Interval 15 Second Extinction schedule. The first task was composed of S+ with a light on the right going on, and S- with a light on the left going on and off. After learning for 30 days, the reverse task was tested for 30 consecutive sessions. Both responses to R+ and R- in the aged rats were less than in the young on the first and the reverse tasks. Therefore, the correct response ratio ((R+)/(R+)+(R-)) of the aged rats was less than that of young rats on the first 30-day task. Moreover, on the reverse task, the correct response ratio of the aged rats was much less than that of young rats. The low level of left-right discrimination learning in aged rats represented disturbances in space recognition and memory.

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EFFECTS OF TRANSPLANTATION OF CHOLINERGIC NEURONS TO THE HIPPOCAMPUS ON THE SPACIAL LEARNING OF THE AF64A-TREATED RATS. IKEGAMI, S., NIHONMATSU, I., HATANAKA, H., TAKEI, N. and KAWAMURA, H. Dept. of Neuroscience, Mitsubishi-Kasei Institute of Life Sciences, Minamiooya, Machida-shi, Tokyo 194.

Effects of grafting embryonic septal or striatal neurons to the damaged hippocampus in young adult rats treated with AF64A, a cholinergic neurotoxin, were studied in comparison with the hippocampal cholinergic activity and learning performance. About 3 months after the transplantation, these rats were trained in eight-arm radial maze over 8 weeks. Learning performance of rats bearing bilateral septal transplants was improved siginificantly compared with the AF64A-treated rats without transplants. However, the group with transplants did not recover to the normal level of the control group without AF64A. In the rats with transplants which showed good performance, surviving grafts and marked ingrowing of acetylcholine esterase(AChE)-positive fibers in the hippocampus were observed. On the other hand, transplantation of striatal neurons to the hippocampus of the AF64A-treated rats had hardly significant effects on the radial maze learning. Also, AChE staining showed poor ingrowths of the striatal grafts in the hippocampus. These results suggest that septal implants can produce a partial recovery of the cholinergic function of the chemically damaged hippocampus leading to an improvement of the spacial learning performance.

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EFFECTS OF ALUMINUM SULFATE ON LEARNING, CENTRAL TRANSMITTER SUBSTANCES AND THE TURNOVER RATE OF ACETYLCHOLINE IN THE DEVELOPING RAT. SUNAYASHIKI-KUSUZAKI, K., HARA, C.,[1] HIGASHIOKA, Y.,[2] MITANI, A., OGAWA, N.,[1] AND KATAOKA, K. Dept. of Physiol., Pharmac.[1] and Orthop.[2], Sch. Med., Ehime Univ., Ehime 791-02

Offspring of Wistar dams given orally with 10 mM Aluminum Potassium Sulfate aq. daily from gestation Days 10-20 were exposed to it till five weeks after birth. At 15 weeks after birth, animals were examined an aquisition of discrimination avoidance learning using a two-compartment shuttle box. A marked damage of the learning was observed in aluminum treated male rats. At 20 weeks after birth, methyl-[^{3}H]choline (100 μCi) was injected in an int.carotid artery. Animals were sacrificed by microwave irradiation (5 Kw, 1.2 sec), then submitted to cerebral tissue dissection for the analysis of transmitter substances and of acetylcholine (ACh) turnover using HPLC-ECD system. A striking reduction of ACh turnover rate (ATR) was observed in the medial septum of aluminum treated male rats. ACh content was increased in several cerebral regions including the medial septum, while significant decreases of serotonin as well as norepinephrine content were noted in these regions. Thus, we demonstrated that neurotoxicity of aluminum during the immature period induced impairment of learning with concomitant alteration of ATR and contents of transmitter substances, which suggest a possible mechanism of aluminum inducing a kind of neuronal death.

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FACTORS AFFECTING ACQUISITION OF CONDITIONED TASTE AVERSION IN RATS.
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The conditioned taste aversion (CTA) is acquired when ingestion of a taste stimulus (CS) is paired with gastrointestinal disorders produced by administration of a toxic substance (UCS). To reveal the background neural mechanisms for this learning process, factors that might affect acquisition of CTA were examined in Wistar male rats. 0.1M NaCl was used as CS. As for UCS, LiCl (0.15M, 2% body weight) was injected intraperitoneally after licking of the CS. Deafferentation of only the chorda tympani, by means of either surgical section or local anesthesia, disrupted the CTA to 0.1M NaCl, indicating that this nerve plays a crucial role. To cease the responses of the chorda tympani to licking of the CS, the rats were allowed to lick enough water during CS-UCS interval. Water licking interposed 1.5 - 6 min after the first lick to the CS disrupted or attenuated the CTA, whereas water licking after 6 min had no effects on acquisition of the CTA. Chronic intraventricular application of AP5 (aminophospho-valeric acid), which is an N-methyl-D-aspartate (NMDA) receptor antagonist, greatly attenuated the CTA. These results suggest that taste information lasting more than 6 min via the chorda tympani is stored in a memory system involving NMDA receptors when 0.1M NaCl is used as a CS.

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CHANGES IN MEMBRANE PROPERTIES OF NEURONS OF THE MOTOR CORTEX IN AWAKE CATS AFTER RAPID CONDITIONING OF EYEBLINK REFLEX.
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Excitability and input resistances were studied in neurons of the motor cortex before and after rapid acquisition of conditioned eyeblink resposnes using awake cats which were kept and used in accordance with the NIH Guide. Pairing of click-conditioned stimulus (CS), glabella tap-unconditioned stimulus (US), and electrical stimulation of the hypothalamus (HS) at an interstimulus interval of 570 and 10 ms between CS-US and US-HS, respectively, elicited short-latency eyeblink conditioning within 20-30 trials. Threshold levels of intracellularly injected current needed for spike elicitation were significantly lower after the conditioning than before conditioning. CS-responsive cells showed lower threshold level than CS-unresponsive cells. Mean input resistance was significantly increased after rapid conditioning mainly through eye muscle-projective cells. The present study indicates that the increases in excitablity and input resistance of the neurons may be fundamental to support the development of the conditioned responses.

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MODULATION OF THE SPINAL MOTONEURON EXCITABILITY IN MAN DURING THE FOREPERIOD ON THE REACTION TIME TASK.
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Changes in excitability of the spinal motoneuron pool during the foreperiod in simple and choice reaction time experiments were studied by combining the visually guided tracking method and the H-reflex testing on 13 subjects. Ankle dorsiflexion and plantar flexion movements were used for response. Significant changes in the excitability of the soleus motoneuron pool could occur particularly within a few hundred milliseconds prior to the response signal but the subjects were divided into three groups; 1) no change (6 cases), 2) facilitation (3), and 3) inhibition (4). Marked facilitation and inhibition were accompanied with very weak and unintended EMG activities in the soleus and pretibial muscles, respectively. The effects did not depend upon task modality or duration of the foreperiod. We suggest that the motoneuronal excitability changes are reciprocally organized and represent a preparatory postural adjustment for the response signal in individual subjects.

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NEURONAL ACTIVITY IN THE AMYGDALA AND THE BED NUCLEUS OF THE STRIA TERMINALIS DURING COPULATORY BEHAVIOR OF MALE RATS. SHIMURA, T. AND SHIMOKOCHI, M. Dept. Behav. Physiol., Faculty of Human Sciences, Osaka Univ., Suita 565

The corticomedial amygdala has been considered by lesion studies to be involved in the maintenance of male rat's copulation and the achievement of ejaculation. In the present experiment, we recorded neuronal activity in the amygdala, the bed nucleus of the stria terminalis (BNST) and the medial preoptic area (MPO) during copulatory behavior of male rats. Immediately after introduction of a receptive female, more than half of the amygdaloid neuronal activity increased (42.9%; 12/28) or decreased (10.7%; 3/28) for a few seconds in comparison with the baseline firing level. On the other hand, 29.4% (5/17) of BNST units and 23.8% (5/21) of MPO units increased in firing frequency in the same period. In the copulatory period, amygdaloid and BNST units did not show the apparent firing change correlated with pursuit-mounting behavior as MPO units did. The present data indicate an involvement of the amygdala-strial system in the initiation of copulation rather than in the performance of copulation.

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RESPONSE PROPERTIES OF AUDITORY NEURONS IN THE FOREBRAIN OF THE MYNAH BIRD TO THE BIRD'S OWN MIMIC VOICES. UNO,H. AND MIYAMOTO,K. Dept. Behav. Engineer., Fac. Human Sciences, Osaka Univ., Suita 565

We investigated responses of auditory neurons to the Mynah's own mimic voices in the telencephalic vocal control nucleus, the Hyperstriatum Ventrale, pars caudale (HVc) and the surrounding area, the Neostriatum Caudale (NC). These neurons could be separeted into three groups based on the responses to white noise. Several neurons having the inhibitory response as well as the excitatory one to white noise also exhibited 4 patterns of responses to the mimic voices: 1) The neuronal response disappeared in the case of playback in reverse (N=7). 2) The ON-phasic response suffered the temporal suppression from a preceding part (N=4). 3) The response was shown to sequences of two vocal segments but not to the segment in isolation (N=1). 4) The response selectivity was shown to particular stimulus or segment within the voice (N=9). These auditory responses may suggest that the HVc and the NC are also involved in the feature extraction from complex acoustic signals.

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FIRING PATTERNS IN MOTONEURONS PRODUCING JAW MOVEMENTS DURING THE FOOD-INDUCED RESPONSE IN SEMI-INTACT APLYSIA. NAGAHAMA, T. AND TAKATA, M. Dept. of Physiol., Sch. of Dent., Tokushima Univ., Kuramoto-cho, Tokushima 770

In semi-intact Aplysia the jaw-opening phase covered not only the radula-protraction phase (O-1 phase) but also the earlier time of the radula-retraction phase (O-2 phase) during a cycle of rhythmic buccal mass movements induced by application of seaweed extract. We identified one jaw-opening motoneuron (JO1) producing jaw movements during the O-2 phase and three jaw-closing motoneurons (JC1-3) in the buccal ganglion. During the initial latency of the rhythmic response, the membrane potential of jaw-opening and -closing motoneurons was firstly depolarized or hyperpolarized, respectively. During the rhythmic response, the membrane potential of jaw-opening and -closing motoneurons underwent synchronous depolarization. The JO1 always started firing before the JC1, while both terminated firing simultaneously. The slope of the rising phase of the membrane potential in the JO1 was steeper than that in the JC1, suggesting that the phase shift in their firing is caused by additional inputs from some premotor neurons.

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PERIORAL PROJECTION TO THE SUBESOPHAGEAL GANGLION RELATING FEEDING BEHAVIOR IN CRAYFISH. CHIBA, A. KOSAKA, M. HAMAGUCHI, M. AND CHICHIBU, S. Dept. Physiol., Kinki Univ. Sch. Med., Osaka-Sayama, Osaka 589

The neuronal connection between the afferent and secondary neurons on the feeding behavior on the crayfish (P. clarkii) was studied histologically and electrically. The sensory nerve fibers from the maxillipeds to the subesophageal ganglion were used. The nerve fiber bundles from the maxilliped nerve distributed four or five different areas in the ganglion. With Holmes-Blest silver impregnation, five soma clusters on the midline of the subesophageal ganglion were observed. Three central clusters extended from the ventral side to the dorsal through the ganglion. Using Lucifer Yellow CH-filled glass micropipetts, the central soma clusters contained spiking local interneurons. The neuronal response pattern was the oscillation of repeating bursts spikes ,and the burst duration was 4 -5 sec. These results show that a part of local interneurons in the subesophageal ganglion are the secondary neurons for feeding behavior.

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ROLE OF ADRENERGIC NEURONS IN FEEDING BEHAVIOR ELICITED BY CHEMO- AND ELECTRICAL STIMULATION IN RAT LATERAL HYPOTHALAMUS. Takemasa SHIRAISHI Dept. of Physiol., Tokai Univ. Sch. of Med., Bohseidai, Isehara 259-11 Japan

The lateral hypothalamus (LHA) is important in feeding behavior. Neurotransmitter and receptor mechanisms in the control of feeding behavior elicited by electrical and chemical stimulation to each side of the LHA were studied by electrodes and cannulae chronically implanted in sated rats. Studies were performed in the light period (0700-1900). Chemical stimulation (C.S.) by norepinephrine (NE), epinephrine (E) or dopamine (DA) dose-dependently (1-10 n mole) increased food intake (g/ 8 hrs). E and DA did not affect LHA-electrical stimulation induced feeding (ESIF), but lower doses (0.5-10 n mole) of NE significantly ($p<0.05$-0.01) enhanced ESIF. Pretreatment with higher doses (50-500 n mole) of NE significantly ($p<0.05$-0.01) inhibited ESIF. The results indicate that feeding-related catecholaminergic neurons in the LHA are noradrenergic. Pretreatment with phenoxybenzamine (10-150 n mole) or propranolol (5-80 n mole) dose-dependently inhibited ESIF. Propranolol was more potent than phenoxybenzamine. This indicates that the feeding-related adrenergic receptor in the LHA is a beta-receptor. Electrophysiological data strongly support these results. Take together, it suggests that LHA-ESIF might be caused by NE release from certain neurons.

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EFFECTS OF ANTISERUM TO NERVE GROWTH FACTOR ON THE DEVELOPMENT OF AMYGDALOID KINDLING FUNABASHI, T., HIRUMA, H. and KIMURA, F. Department of Physiology, Yokohama City University School of Medicine, 3-9 Fuku-ura, Kanazawa-ku, Yokohama 236

The present study investigated whether nerve growth factor (NGF) was implicated in the development of kindling in adult rats. Ovariectomized female rats were chronically implanted with a cannula in the third ventricle and an electrode in the basolateral amygdala. Kindling stimulation was performed daily at the parameter of 60Hz, 10ms duration and 100-450uA for 1sec, and the first three-day's stimulations were followed by an injection of 5ul rabbit anti-2.5S NGF serum into the third ventricle. The number of stimulations required to reach full kindling was increased significantly in rats injected with anti-NGF serum compared to that in rats injected with normal rabbit serum as the control. The results demonstrate that NGF may play some role in the long-lasting neuronal changes induced by daily electrical stimulation of the amygdala.

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AN ELECTROMYOGRAPHIC STUDY OF DAILY ACTIVITY OF MASSETER MUSCLE IN THE RAT. HIRAKAWA, T., HONDA, E. AND NAKAHARA, S. Dept. Physiol., Kyushu Dental College, Kokurakita-ku, Kitakyushu 803

Daily activities of both masseter muscles in rats were investigated in the whole day. Nine Wister white rats, weighing from 400 to 500 gm. of male sex, were used. Monopolar electrodes of silver wire with a diameter of 100 μ were placed subcutaneously on the left and right masseter muscles and led to a connector pedestal on the rat's head. The connector pedestal was attached to the skull by dental cement. Activities of both masseter muscles were recorded by data recorder for 24 hours. Rats could move freely around the cage during records. Solid food and water were freely available.

Jaw movements, chewing, drinking and grooming were active in the night and these behaviors had circadian rhythms. Period of jaw movement in a day was from 7 to 12 hours and different among individuals. Period of chewing in a day was about 2 hours. When rats ate, drinked and groomed, typical patterns of EMG were recognized. EMG bursts and single unit activities often generated even during sleep. Activities of both masseter muscles were similar in chewing and drinking, but often different in grooming. Activities in masseter muscles were rhythmical in chewing and drinking, but often rhythmless in grooming. Rhythms in chewing changed in one chewing series and different among individuals. Duration of activities in masseter muscles in chewing was shortened in the latter half of a series of feeding behavior. Series of feeding behavior in a short time were increased in the night.

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LONG-TERM OBSERVATIONS ON JAW BEHAVIOR OF THE FREELY MOVING RABBIT. YAMADA,Y., Dept. Physiol., Sch. Dent., Nagasaki Univ., Nagasaki 852

This study was carried out to understand possible relationships underlying occlusion and masticatory muscle activities. Because of the similar chewing pattern to that of the human's, the rabbit was selected as the experimental model. In this study, long-term jaw behavior was recorded to obtain control data. Jaw movements as well as bilateral masseter EMGs were recorded from freely moving rabbits. To record the two dimensional jaw movements two small magnetic sensors were implanted in the maxillary bone and a powerful magnet made of a rare earth metal implanted in the mandibular bone. Recording was carried out for five hours (6:00pm-11:00pm) in each session. Although there was no consistent behavior pattern, totally two hours rhythmical chewing behavior, two hours resting period, and one hour irregular jaw behavior were observed. The rhythmical chewing behavior was composed of food chewing, wood chip chewing and soft plastic chewing. Their chewing frequency was around 3-4 Hz and relatively constant. During the resting period the lower jaw rested at the jaw position of inter-incisal contact position. At this moment bruxism and clenching were frequently observed.

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OPTIMUM STIMULI PROMOTING THE DEVELOPMENT OF SYNAPSES, OONUKI, M., Dept. Physiol., Sch. Med., Kitasato Univ., Sagamihara-shi, Kanagawa 228.

A pattern of optimum stimulli which brings the maximum excitation to neurons are obtained theoretically. When synapses($k=1,2,\ldots$) of the target neurons($j=1,2,\ldots$) are activated by the output frequencies of $f(i)$s from preneurons($i=1,2,\ldots$) and each synapse generates a psp of $a(i,k)f(i)u(i,k)\exp -t/g(i,k)$ with the rate of connectivity $u(i,k)$(= the number of synapses specified by k of target neurons/ the number of all synapses of target neurons), the maximum excitation of target neurons are caused under the condition that $a(i,k)f(i)u(i,k) \propto b(i,k)(\equiv \exp -d/g(i,k)$; d,an absolute refractory period). This shows that for the maximum excitation, the axonal branches of a preneuron increase or the firing frequency of the neuron increases as the terminals of the branches develop close to the end of dendrites of target neurons, because $f(i)u(i,k)(\propto b(i,k)/a(i,k))$ increases as a synapse is located apart from a cell body on a dendrite. Thus, in development, the terminal connections are promoted and, when a neuron is mature, it is shown stimuli to those terminals bring also the maximum excitation; the firing frequency of target neurons is given by $\sum_j \sum_k a(i,k)u(i,k) \sum_i f(i)$.

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FUNCTIONAL SUBDIVISION OF AREA TE IN MONKEY INFEROTEMPORAL CORTEX.
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In monkeys, area TE in the inferotemporal cortex participates in visual recognition and memory. Recent anatomical study in our laboratory showed that the anterior part of area TE (TEa) has denser reciprocal fiber connection with each of the amygdala and the hippocampus than the posterior one (TEp). In addition, whereas connection with the amygdala is denser in the dorsal part (TEd) than in the ventral one (TEv), connection with the hippocampus is limited in area TEv. In this experiment, we tested whether those differences in corticolimbic connection are reflected in functional differences among subdivisions within area TE. On a concurrent object discrimination task, a test of visual recognition and memory, lesions of either area TEa or area TEv resulted in a impairment which was much severer than any impairment followed lesions of either area TEp, area TEO, or area TG, and was comparable with that followed total lesions of area TE. The results suggested the importance of area TEa and TEv in the corticolimbic pathway that mediates visual recognition and memory.

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SELECTIVE ATTENTION AND DETECTION OF THE VISUAL STIMULUS CHANGE.
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1) Selective attention to the stimulus dimension, such as shape, color and motion, was proved to exist by analysing th reaction time of monkey and human subject at the multi-dimensional visual discrimination task. In the grouped-block, where the subject could predict the dimension of the change, the reaction time was shorter ($p<0.01$) than in the mixed-block where the change dimension was scheduled in random order. 2) The selective attention has the effect to shorten both the stimulus detection process and memory write/read and comparing process. In motion detection task, the grouped-block schedule had almost no effect to shorten the time. But when the low velocity of motion, which delayed the reaction, was applied, the grouped schedule had a distinct effect. The motion-direction-change detection task, where the subject had to memorize the motion direction and compare to the new motion each time, the grouped schedule also had clear effect. 3) The selective attention causes the augmetation of the signal or lowering the threshold of judgement, as well as shortening the processing time. In the grouped block, the subject, responding more quickly, made greater number of ommission error (false alarm) than in the mixed block.

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ANALYSES OF THE RELATIONSHIP BETWEEN ONEIRIC BEHAVIOR AND RAPID EYE MOVEMENTS IN CATS.
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The analyses of the relationship between oneiric behavior and rapid eye movements(REMs) in paradoxical sleep were carried out on 2 cats. For the behavioral observation and analyses a monitoring system with VTR was used. Concerning "isolated" REMs, the percentage of direction-oriented coincidence of eye-head movements is about 80%. And there is a positive correlation between the amplitude of "isolated" REMs and its percentage. On the other hand, concerning "burst" of REMs, there is a negative correlation between the number of REMs within one REMs burst and the above-mentioned percentage. The "burst" of REMs have a tendency to be related to generalized body movements, such as jump, attack, etc.

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THE STRUCTURE OF POSSIBLE PHOTORECEPTIVE MEMBRANES IN AN EXTRAOCULAR PHOTORECEPTOR OF ONCHIDIUM. KUBOZONO, T.*, SAMESHIMA, M.*, NISHI, T., GOTOW, T. AND HASHIMURA, S. Dept. Physiol., *Anat. and *Ophthal., Kagoshima Univ. Sch. Med., Kagoshima 890

An extraocular photoreceptor, the photosensitive neuron (A-P-1) in the abdominal ganglion of the marine gastropod mollusc, Onchidium verruculatum responds to light with a depolarizing receptor potential which is due to the light suppression of membrane K+ conductance. In this kind of photoreceptors, Ca2+ release from the lipochondria activated by light is thought to be essential to evoke the generator potential. Injection of Ca2+ into A-P-1, however, inhibited the light-induced response. Thus the " lipochondria theory " was not available to A-P-1. On the other hand, in the study of the ultrastructure of A-P-1, the entire cell surface was enveloped in structures which were composed of complicated foldings of many glial processes and cell membranes of A-P-1. These processes were several times arrayed along the cell surface in case of the dark-adapted A-P-1, but the arrangement in cytoplasmic side of such structures was destroyed in case of the light-adapted A-P-1. Such destruction of photosensitive portion is common in the invertebrate photoreceptors.

Thus it is possible that the photosensitive part of A-P-1 is not the lipochondria, but the complicated structure on the cell surface.

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THE EFFECT OF RETINOL ESTER IN THE LIVER OF A FROG ON THE REGENERATION OF RHODOPSIN IN THE RETINA
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Rhodopsin is produced in the retina from opsin by combining with 11 cis-retinal, supplied from the retinol ester stored in the liver. Therefore, the greater the storage of retinol ester in a liver, the greater the regenerated rhodopsin in the retina. The regeneration curve of rhodopsin in the dark shows sigmoid form. When the storage of retinol ester in a liver is fairly high, the curve becomes almost horizontally after 80 min of dark adaptation. However, if the storage is low, regenerated rhodopsin not yet reaches at the maximum value in 80 min.

When the contents of glucose and fatty acid in the blood of the frog, show show low value, the velocity of the regeneration of rhodopsin may slow down.

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STUDIES ON EXCITATORY AMINO ACID RECEPTORS INDUCED BY RETINAL mRNA INJECTION. ANDO, H AND NAKAMURA,M Dept. of Physiol., Sch. Med., Kobe Univ., Kobe 650

The application of L-glutamate (Glu) to the *Xenopus* oocytes injected with retinal mRNA induces a smooth depolarization with conductance increase when the concentration is less than 0.1mM, contrasting to an oscillatory potential changes observed in the cerebellar-mRNA-injected oocytes. Higher dose of Glu induces a complex potential changes; initial rise of the potential followed by a depressed phase, then a rebound at the end of the application. Quisqualate has almost the same action as Glu but is 20 to 50 times more effective. Kainate induces just a smooth potential changes even at high concentrations. Aspartate and N-methyl-D-Aspartate have only a little effects. The reversal potential for both the kainate and glutamate responses are the same at around -10 mV consistent with the assumption of a cationic channel opening. The kainate-induced conductance are suppressed by the additional application of Glu in a dose-depended manner. Glu receptors of retinal horizontal cell are reported to have the same properties indicating the faithful expression of retina specific Glu receptor by the oocyte.

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IMMUNOHISTOCHEMICAL ANALYSIS OF PINEAL PHOTORECEPTORS BY ANTI-OPSIN AND ANTI-VISININ. TAMOTSU, S., KUO*, C.H., MIKI*, N. and MORITA, Y. 1. Dept. Physiol., Hamamatsu Univ. Sch. Med., Hamamatsu 431-31 and *Dept. Pharmacol. Cancer Res. Inst. Kanazawa Univ., Kanazawa 920

Visual cells in the lamprey retina are classified into two types, short and long photoreceptors, which react to the antisera raised against bovine opsin (rod specific) and chick visinin (cone specific), respectively. Photoreceptor cells of pineal complex in lamprey, *Lampetra japonica*, showed multiple reactivities to these antisera. Opsin immunoreactivity was found in outer segments of both pineal and parapineal organs. Anti-visinin positive cells were distributed also in both organs, but they localized mainly in the peripheral portion of the pineal organ. There was a difference in density of fluorescence in the anti-visinin positive cells. Immunoreactivity in single cells against both antisera was observed. These results suggest the multiple cell types of photoreceptor cells in the pineal complex.

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Na/Ca EXCHANGE, Na-K PUMP AND INTERNAL Ca STORES IN THE HORIZONTAL CELL ISOLATED FROM THE GOLDFISH RETINA. SYOZO YASUI National Institute for Basic Biology, Okazaki 444, Japan

The voltage-gated Ca conductance is known to be present in retinal horizontal cells of the cyprinid fish. Since the physiologic dynamic range of these non-spiking second-order visual neurons overlaps the region of Ca-channel activating membrane potentials, some mechanism to drive out Ca ions needs to exist. Voltage clamp experiments were made on solitary horizontal cells isolated enzymatically from the goldfish retina, showing that the Ca-extrusion is subserved by Na/Ca exchange. Another set of voltage clamp experiments including tests by caffeine application indicate the presence of internal Ca stores that seem to accomodate Ca ions up to as much as about 5 mM. Some regulatory system is required with respect to intracellular Na ions as well, to compensate for three types of Na influx; TTX-sensitive one, one associated with the Na/Ca exchanger and synaptic one mediated by an excitatory neurotransmitter from photoreceptor terminals. The Na-K ATPase operates to fulfill this homeostatic demand, evidence being provided by an ouabain experiment.

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CORRELATIONS BETWEEN RETINAL HORIZONTAL CELL MORPHOLOGY AND SPECTRAL RESPONSE TYPE IN A FISH (MOJARRA; EUGERRES PLUMIERI). NEGISHI, K. Dept. Neurophysiology, Neuroinformation Res. Inst., Sch. Med., Kanazawa Univ., Kanazawa 920

Six different types of spectral response were recorded from horizontal cells under mesopic state in superfused retinas, isolated from the dark-adapted mojarra. They were tentatively termed as photopic Lr-, Lg1-, Lg2-, Lb- and C-type, and scotopic L-type. The Lr-, Lg- and Lb-type responses showed a maximum peak at 605, 550 and 516 nm, respectively, while the C-type was R/G type. The scotopic L-type has a peak at 516 nm in the spectral response and a slow decay phase in response waveform. Following a brief period of diffuse white illumination, Lg1-type responses were altered to Lr-type, while both Lg2- and Lb-type responses changed to C-type. Intracellular marking with Procion or Lucifer yellow identified the cellular origins of different types; external (He) and medial horizontal (Hm) cells for the Lr-type, internal horizontal (Hi) cells for the C-type, and rod-horizontal (Hr) cells for the scotopic L-tyep. Only He cells were found to possess an axon, while dye coupling was seen between axon-less Hm, Hi or Hr cells. The morphology of these marked cells was the same as that of the respective cells observed in Golgi-stained materials. Externally applied dopamine interfered with the lateral spread of responses and dye diffusion normally taking place along a given layer of horizontal cells.

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DOSE DOPAMINE WORK SIMILAR TO LIGHT ADAPTATION ON HORIZONTAL CELL RESPONSE IN THE CARP RETINA ?

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A comparison between light adaptation and dopamine application on the receptive field properties of carp horizontal cells is presented. A slit of flash light was used to map the response of H1 horizontal cells at various points in its receptive field. It had been reported that dopamine(DA) made the central part of receptive field narrower and enhansed it. Light adaptation by steady background light also changed the spatial profile of the H1 horizontal cell responses. All response amplitudes to silt flash light under adapting light became smaller than those in darkness, because the adapting light decreased the sensitivity of the photoreceptor cells. The degree of decrease between the central responses was smaller than that between the peripheral ones, and the central response area became narrower. The spatial profile under light adaptation in the soma had clear dual components and, as a result, the central component was emphsized. The result suggest that light adaptation and dopamine both act to gap junction of the soma syncytium while having little effect on axon terminal coupling.

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A ROLE OF ROD PARTICIPATION IN C-TYPE HORIZONTAL CELLS IN THE DACE.

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The established theory of color vision is based upon three cone systems, but recently many experiments are now being reported the interaction between the rod and cone systems. Histological investigation in the dace was testified by C-type HCs contact with many rods. The dark adapted spectral responses of C-type HCs at low intensity show the monophasic curve peaked at blue to green spectral region. This would be the direct physiological evidence of the rod contribution to C-type HCs. Trezona's color matching data and Walls's model indicate that rods and blue cones existing as separate receptors but sharing a neural pathway and rods elicit a blue sensation in human under photopic conditions. If this idea is applicable to dace retina, C-type HCs would be a neural pathway of signal sharing. Indeed, dace C-type HCs are very sensitive to blue or violet lights than those of carp. Especially, Tri- and Tetraphasic HCs make contact with many rods while they are connected with only 3-4 cones and with 1 cone, respectively. This suggests that rods participate in the blue (or the violet) mechanism in C-type HCs.

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EFFECTS OF N-METHYL-D-ASPARTATE AND ITS ANTAGONIST ON HORIZONTAL CELLS IN THE TURTLE RETINA.

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L-glutamate or L-aspartate is a leading candidate for the transmitter released from the vertebrate photoreceptors. In the carp and mudpuppy retina, the transmitter is generally believed to act on the receptor subtypes of kainate and quisqualate rather than that of N-methyl-D-aspartate (NMDA).

In the present study, effects of the excitatory amino acids and the NMDA antagonist (2-amino-5-phosphonovalerate, APV) were examined on horizontal cells in isolated retinae of the turtle, Geoclemys reevesii. In addition to L-glutamate, L-aspartate, kainate and quisqualate, bath application of NMDA (250 μM - 5 mM) also caused a depolarization and accompanying suppression of light-evoked responses. Superfusion with APV (250 μM) hyperpolarized horizontal cells. These results suggest that non-NMDA receptors coexist with NMDA receptors on turtle horizontal cells.

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REVERSAL POTENTIALS OF LIGHT RESPONSES OF ON-OFF AMACRINE CELL IN THE CARP RETINA
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For accurate measurement of a reversal potential of a postsynaptic potential, uniform polarization in a postsynaptic neuron is essential. So far as the conventional intracellular current injection is employed, uniform polarization cannot be achieved in such neurons as retinal amacrine cells which have extensive dendritic arborizations, and a reversal potential value is inevitably overestimated. In the present experiment, we employed a new technique; carp amacrine cells were polarized by a Ca action potential produced in the cells themselves. To evoke the action potential, the retina was superfused with a Ringer solution containing TEA, and amacrine cells were depolarized either by intracellular or by extracellular electrical stimulation. The action potential appeared in a regenerative manner, and showed a refractoriness. In addition, Co application suppressed the action potential, indicating its Ca-dependent nature. The Ca action potential was more readily evoked or occurred even spontaneously in a solution containing high-Ca, Ba and some K-channel blockers. It showed an overshoot and its duration was several sec. During the overshoot, the transient light responses appeared in reversed, hyperpolarizing polarity, and their reversal potential were measured at -10 mV.

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EXAMINATION OF THE BIPOLAR INPUTS TO THE AMACRINE CELLS OF THE CARP RETINA USING KYNURENIC ACID.
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We examined the bipolar-amacrine transmission using kynurenic acid (Kyn) which has been reported to block off-pathways selectively. Kyn rather increased the light response of the on-center bipolar cell and suppressed almost completely the response of the off-center cell. The light response of the on amacrine cell increased and off amacrine cell disappeared. The off-transient of the on-off amacrine cell was not abolished completely, whereas the sustained potential level between on- and off-transients moved toward depolarizing direction. This made the response shape of the on-off amacrine cell resemble that of the on amacrine cell. These changes were not affected by the depolarizing current applied through the recording electrode. Kyn also exerted the same effect on the responses evoked by repetitive transretinal current. These results add a new piece of evidence to the hypothesis that on and off amacrine cells receive the inputs from on- and off-center bipolar cells respectively, while on-off amacrine cells receive both inputs.

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THE DENDRITIC COVERAGE FACTOR OF DOPAMINE CELLS DURING GROWTH OF CARP RETINA.
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The dendritic morphology of dopamine (DA) cells in the inner plexiform layer of the retina of different-sized carp was investigated by identifying their fluorescent cell bodies in isolated, aldehyde-fixed flatmounts and injecting them iontophoretically with Lucifer yellow CH under microscopic control. In this study, DA cells located in an intermediate region were dealt with, and the spatial parameters (soma diameter, cell density, distribution regularity, dendritic field size and dendritic coverage factor) were measured. The form of the dendritic branching pattern of DA cell processes was similar regardless of fish body lengths. However, as fish increased in size (for instance, from 8.6 to 33.6 cm), the average density decreased by 0.26-fold, the dendritic field size increased by 2.6-fold, and the dendritic coverage factor reduced by 0.65-fold. The difference in the coverage factor was statistically significant. Provided that the injected dye diffuses to the far periphery of dendrites, the data suggest that the expansion of dendritic field for individual DA cells is not only due to passive towing but also to self-determining during retinal growth.

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MEMBRANE CURRENTS OF RETINAL BIPOLAR CELLS FROM THE MOUSE (C57BL/6crSlc).

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Solitary bipolar cells were obtained by enzymatic (papain) dissociation of the adult mouse retina. We measured membrane currents under the whole-cell clamp condition (120 mM K-gluconate pipette solution). Hyperpolarizing voltage-clamp steps from the holding voltage (V_h) of -40 mV evoked a slowly-activated, Cs-sensitive, inward current (h-current), and depolarizing steps evoked an outward current that could be blocked by Cs and TEA in the bathing solution, together with Cs substituted for K in the patch pipette. The latter current was probably a combination of $I_{K(V)}$ and $I_{K(Ca)}$. Depolarization from more negative V_h (*e.g.*, -80 mV) evoked a transient inward current (activation threshold, -55 mV) that had maximal amplitude at -30 to -20 mV. This current was identified as a Ca-current: it was blocked by 4 mM Co^{2+}, but not by Cd (50 μM) or TTX (5 μM), and its amplitude varied directly with $[Ca^{+2}]_o$. This Ca current lasted only about 25 ms, in contrast to the sustained Ca current in goldfish bipolar cells. Since the Ca current in the mouse is activated by depolarizing the membrane to near the presumed resting value, this current may participate in synaptic transmission. The transient character of the current may also help to shape transient responses of ganglion cells.

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EFFECT OF DOPAMINE ON BIPOLAR CELLS IN THE CARP RETINA:

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Bipolar cells in the carp retina are electrically coupled, which makes the receptive field size of these cells much larger than their dendritic field (Kujiraoka and Saito,1986). we used a long narrow slit of light of various positions to characterize the receptive field size of ON bipolar cells. Stimulation at the receptive field center produced a large depolarizing response and a small hyperpolarizing response which is mediated by horizontal cells. The peak amplitude of the depolarizing response was plotted against the slit displacement from the center in semilogarithmic ordinates. The decay of the response could be fitted by a straight line whose slope allowed the measurement of the length constant. the length constant value varied from 52-95 um. Dopamine (50 um) hyperpolarized the membrane potential, enhanced the depolarizing response and reduced the hyperpolarizing response. Dopamine also produced a narrowing of the receptive field surround, while had little effect on the size of the central receptive field in the present experimental condition.

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SIGNAL CONVERSION AT THE SYNAPSES BETWEEN SECOND- AND THIRD-ORDER NEURONS OF INSECT OCELLI.

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Signal transmission between second- and third-order neurons of the ocellus of the cockroach, Periplaneta americana, was studied using current and light stimuli. The synapse between second- and third-order neurons was sine non-inverting (excitatory) and had sigmoidal transfer characteristics with an exponentially-growing part near the transmission threshold. The normal membrane potentials of second-order neurons were just above the transmission threshold, and there was a sustained transmission at normal membrane potentials. The response of second-order neurons linearly related to modulation stimulus, whereas that of third-order neurons was non-linear. The time-course of the response of third-order neurons was more transient than that of second-order neurons. Analysis using sinusoidally-modulated light and step incremental/decremental light showed that these differences in the responses of second- and third-order neurons were due to static (time-independent) and exponential transfer characteristics of the synapse between these neurons.

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TRANSFER FUNCTIONS BETWEEN AMACRINE AND GANGLION CELLS.

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Intracellular recordings were made simultaneously from two retinal neurons in the eye-cup preparation of channel catfish, *Ictalurus punctatus*. Step, sinusoidal or white-noise modulated current was injected through one of the two electrodes and resulting responses were recorded from the other electrode. In the case of white-noise modulated test signal, the kernels are filters that interface two neurons.

We found that 1) ganglion cells were extensively involved in the signal processing in the retina, 2) signal transmissions were often bi-directional, 3) strong connections were found between neurons of the same response polarity, and 4) slow and complex signals were transmitted between cells of the opposite response polarity. These results indicate that retinal circuitry is a highly interconnected network and that a neural response may be generated through the differences in the polarity and weight of numerous inputs impinging upon it and, consequently, the neuron network in the catfish inner retina may be represented as a "loosely-coupled" parallel processor.

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MORPHOLOGY OF ALPHA GANGLION CELLS IN THE ALBINO RAT RETINA. FUKUDA, Y., TAUCHI, M.[1], MORIGIWA, K.* and SAWAI, H.*, Dept. Neurophysiol. Biomed. Res. Center, Osaka Univ. Med. Sch., Osaka 530. [1]Dept. Sensory Impairments, Res. Inst., Nat. Rehab. Center for the Disabled, Tokorozawa 359.

Under chloral hydrate anesthesia 5% granular blue (GB) in DMSO was stereotaxically injected into the lateral geniculate nucleus or superior colliculus. After 48 to 72 hrs survival the animals were deeply anesthetized and the left or right eye removed. A whole mount preparation was made in a petri dish soaked with warm Ames' solution, placed in a chamber, and the GB-labeled cells viewed under a fluorescence microscope through a BV filter (excitation wavelength 400-450 nm). The alpha cells with soma of over 20 um in diameter and 3-7 thick primary dendrites were then penetrated with glass micropipettes filled with 3% Lucifer Yellow (LY) and 2-5 nA currents passed through their tips. Of the 185 LY-injected alpha cells from 42 whole mount retinas, 159 cells with fully labeled dendrites were subclassified into ON- and OFF-types: ON-cells extended their dendrites in sublamina b of the IPL, OFF-cells in sublamina a. Their denditic field diameter increased towards the peripheral retina, but ON-cells had larger dendritic field diameters (mean 607 um) than OFF-cells (mean 499 um) at all eccentricities. The soma diameter was also larger in ON-cells (mean 32.0 um) than in OFF-cells (mean 27.1 um). The number of primary dendrites were 4 to 7 (mean 5.6) in ON-cells and 3 to 6 (mean 4.3) in OFF-cells.

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FRACTAL ANALYSIS OF ALPHA CELL DENDRITIC MORPHOLOGY IN THE ALBINO RAT RETINA. MORIGIWA, K.*, FUKUDA, Y. and TAUCHI, M.[1] Dept. Neurophysiol. Biomed. Res. Center, Osaka Univ. Med. Sch., Osaka 530. [1]Dept. Sensory Impairments, Res. Inst., Nat. Rehab. Center for the Disabled, Tokorozawa 359.

As a sequel to the above study, using the same labeling method, we quantitatively studied the branching pattern of 8 pairs of ON and OFF LY-labeled alpha cells at 8 different eccentricities from the optic disk by means of fractal analysis. Fractal dimensions were measured using the box-counting method: the drawing of a labeled alpha cell is covered by grids of different scales made from a large equilateral square dissected into smaller and smaller equilateral squares (the minimum grid, 10 X 10 um); the number of boxes entered by the dendritic branches for each scale grid is then plotted as a function of the number of boxes on one side of the grid on the logarithmic scale. Least square estimates yielded fractal dimensions of 1.2 to 1.6 (mean 1.38) for the ON-types, decreasing with eccentricity; those for OFF-types were relatively constant between 1.43 to 1.58 (mean 1.53). The results indicate that the branching pattern of ON-types are less complex than that of OFF-types, especially in the peripheral retina. Further quantitative study of intersections of dendritic branches and concentric circles of different diameter in 9 ON-cells and 8 OFF-cells revealed that irrespective of eccentricity OFF-types had more profuse proximal dendrites than ON-types.

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RECIPROCAL CONNECTION BETWEEN CAT THALAMIC RETICULAR CELLS AND THALAMIC LATERAL POSTERIOR-PULVINAR COMPLEX. HADA, J., MORITA,F.*, SASAKI, H., AND HAYASHI, Y. Dept. Physiol. and Physical Education*, Hyogo Coll. Med., Nishinomiya, Hyogo, 663

While cat perigeniculate cells respond well to visual and optic chiasm stimulation, most of thalamic reticular(TR) cells located dorsolateral to the dorsal lateral geniculate nucleus(dLGN) do not. The great majority of TR cells discharged with a burst of spikes in response to stimulation of thalamic lateral posterior-pulvinar complex(LP-Pul). Thirty-seven out of 60 TR cells were driven synaptically and 20 cells antidromically. Antidromic response latencies ranged from 0.4 to 2.1 ms(mean, 1.1 ms), while synaptic ones from 1.1 to 6.5 ms(mean, 2.8 ms). Antidromic responses were always followed by transsynaptic discharges. Of 56 TR cells activated by LP-Pul stimulation, 37 cells also responded to optic chiasm and/or optic radiation stimulation. After injections of horseradish peroxidase into LP-Pul, many TR cells were labeled retrogradely. These results suggest strongly that TR cells located dorsolateral to dLGN have a reciprocal connection with LP-Pul cells. TR cells may act as inhibitory interneurons for LP-Pul cells.

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CORTICAL AND THALAMIC AFFERENT CONNECTIONS OF CAT'S AREA 21a

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Area 21a of the cat was identified based on the neuronal responsiveness to photic stimulation and the mode of efferent projection to area 17 which were characteristically different from those for the neighboring cortical areas (area 19 and PMLS) (Mizobe et al., 1988), and a small amount (0.1-0.2 μl) of WGA-HRP was injected into area 21a. In 4 of the 5 cats in which injection was successfully localized in area 21a, afferent neural connections were determined as the total number of efferent cells (every 200 μ) retrogradely labelled by HRP in both ipsi- and contralateral cortices and ipsilateral thalamic nuclei. Area 21a received the strongest projection (about 400 cells) from the ipsilateral areas 18 and 19, modest projection (50) from the ipsilateral areas 17 and 20a, and slight projection (2-3) from the ipsilateral area 20b and PMLS and the contralateral area 21a. Thalamic afferent projections were strongest from LPl (about 200), modest (about 50) from Pul and LIc, and slight from MIN and LPm (2-3). Therefore, area 21a receive major visual inputs from areas 18 and 19, and also from area 17 probably through LPl.

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STUDIES ON GLUTAMATE RECEPTOR-MEDIATED RESPONSES FROM RAT'S VISUAL CORTICAL NEURONS. TAKAHASHI, Y., TAKIMORI, T. AND OGAWA, T. Dept. of physiol., Akita Univ. Sch. of Med., Akita 010

In the present study, we used slice preparations of rat's visual cortex. In 1.0 mM Mg^{2+} containing normal medium, electrical stimulation of the white matter produced conventional fast EPSPs(<30 msec in duration) occasinally followed by long lasting EPSPs(>50 msec in duration). The long lasting EPSPs were identified as N-methyl-D-aspartate (NMDA) receptor-mediated responses by the fact that their amplitude was significantly reduced by administration of a specific NMDA receptor antagonist(2-amino-5-phosphonovaleric acid, APV). The amplitude of the NMDA receptor-mediate EPSPs was found to be voltage dependent and enhanced in Mg^{2+} free medium as already have been demonstrated in somatosensory cortex of the rat. We also investigated dose response relationship of the neurons with glutamate and NMDA, and found that the effective minimum dose of L-glutamate was about 100 micro M, while that of NMDA was 3.0 micro M.

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EFFECTS OF EXCITATORY AMINO ACID ANTAGONISTS ON SYNAPTIC POTENTIALS IN THE CAT'S VISUAL CORTEX. SHIROKAWA, T., NISHIGORI, A., KIMURA, F* and TSUMOTO, T. Dept. Neurophysiol. Biomedical Research Center, Osaka Univ. Med. Sch. Kitaku, Osaka, 530

Excitatory amino acids such as glutamate and aspartate are probably the transmitters at excitatory synapses in the cat striate cortex. Their receptors were classified into three subtypes according to their affinities for agonists. They are N-methyl-D-aspartate (NMDA), quisqualate and kainate receptors. In the present study, we asked which type of receptors mediated excitatory postsynaptic potentials (EPSPs) evoked by electrical stimulation of white matter. The antagonists used were 2-amino-5-phosphono-valerate (APV), a selective antagonist for the NMDA receptors and kynurenate (KYNA), a non-selective one. We found two types of EPSPs of layer II/III striate cells in slice preparations of adult cats. One was an EPSP followed by a long-lasting hyperpolarization (EH-type); the other, without the hyperpolarization (EWH-type). The bath application of KYNA (200 μM) suppressed the EPSP slope in both types. By contrast, APV (50 μM) suppressed the EPSP slope of the EWH-type while it failed to suppress the EPSP slope of the EH-type. However, when bicucullin (5 μM) was added to the medium, not only did it abolish the hyperpolarization in the EH-type, but it also appeared to induce the APV suppressive effect on the EPSP. These results suggest that there is a correlation between NMDA receptor function and inhibitory mechanisms in the striate cortex of cat.

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NEURONAL ACTIVITY IN THE DORSO-MEDIAL PART OF THE PRELUNATE GYRUS (DP). TANAKA, M. Dept. Aerospace Physiol., Res. Inst. Environm. Med., Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-01

We have recorded from 86 single neurons in the area DP, i.e. the dorso-medial portion of the prelunate gyrus, of an awake monkey (Macaca mulatta). In the same monkey, neurons were previously recorded in the lateral part of the prelunate gyrus and showed typical visual responses. Neurons in the dorso-medial prelunate gyrus, on the other hand, respond only little if at all to stationary or moving light stimuli, and circumscribed receptive fields could not be determined. However, about 25% of the units became active at a certain gaze position. The majority had an ipsilateral, a minority a contralateral gaze position field, some were active during upwards, others during upwards looking. About 70% of neurons responded vigorously when the monkey looked attentively at an object, such as a living face, a glove, a hand or simply towards opening door. These responses have an attentive as well as an emotional component. Photographed faces flashed on a screen produced only little if any response. Our observations, therefore, suggest that the dorso-medial and the ventro-lateral part of the prelunate gyrus may be related to different aspects of vision.

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VISUAL RESPONSES OF LENS-RELATED UNITS IN THE EXTRASTRIATE CORTEX IN CATS. BANDO,T., TODA,H., AWAJI,T. Dept.Physiol., Niigata Univ. Sch. Med., Asahi-mati 1, Niigata 951

Visual responses of lens accommodation-related units were studied in the lateral suprasylvian area (LSA) in cat occipital cortex. Lens-related units were defined by the same criteria as in the previous study (J.Neurophysiol. 52:879,1984). Cats were anesthetized by a mixture of N_2O and O_2, immobilized by gallamin triethiodide, and artificially respired. Dioptric power of the eye was monitored by an infrared optometer. Visual responses of 55 LSA units were studied: 32 responded to fronto-parallel movement of the target (FP); 3, to approaching movement (APR); 1, to recessive movement, and 19 both to fronto-parallel and approaching/recessive movement (NS). Five of them were lens-related, and were activated 300-700 ms before the onsets of spontaneously-occurring fluctuations of dioptric power of the eye. One of them were an APR unit, and 4, NS units. All of lens-related units responded vigorously to the approaching visual target, and much less so to recessive movement under binocular condition. They showed reduced but still considerable activities under monocular stimulation. Based on these results, it is concluded that lens-related units in LSA belonged to a class of visual neurons which responded to approaching movement of the target, and were driven by both binocular disparity and other features of visual stimulation such as the changes of the size of the target.

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STIMULUS SELECTIVE NEURONAL ACTIVITIES IN THE SUPERIOR TEMPORAL SULCUS OF MACAQUE MONKEYS.

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Stimulus selective neuronal activities have been investigated in the middle portion of the superior temporal sulcus (STS) of 2 macaque monkeys during performance of a sequential discrimination task (A.Mikami, J. Physiol. Soc. Japan 49, 457, 1987). In the task, the monkey kept pressing the lever when the picture was same as the first sample picture, and released the lever when the picture was different. Pictures used in the task were 32 human faces (including side and back views), 24 monkey faces and 24 non-face objects (food, bottle, hand etc.). In 66 neurons which responded to human and/or monkey faces, 37 also showed response to non-face objects, and 29 showed no clear response to non-face objects. Other 8 showed respond only to non-face objects. In most cases (66/74), a STS neuron has more than 2 preferred pictures. This may suggest the possibility that the group of neurons which are preferred several different features are involved to select a unique feature.

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RODS ALSO PARTICIPATE IN HUMAN COLOR VISION.

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In the retinal periphery, rod and cone thresholds to the same green light were measured. After the rod-cone break in the course of dark adaptation, cone sensitivity decreases gradually as rod sensitivity progressively increases. Cone sensitivity, however, increases when rod sensitivity is decreased by blue light. The emergence of the facilitatory effect of rod activation requires at least a few hundred msec after rod stimulation. It is concluded that rod activation plays a major role in sensitivity regulation of the cone system, i.e., in human color vision.

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EFFECT OF HYDROLYSIS-RESISTANT GTP ANALOG ON THE ROD LIGHT RESPONSE MIMICS LIGHT ADAPTATION.

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We compared inner segment, suction current responses to light of larval salamander retinal rods before and after introduction of the hydrolysis-resistant GTP analog 5'-guanylylimidodiphosphate(GppNHp) into outer segments using the whole-cell patch technique. GppNHp is taken up by transducin and prolongs cyclic GMP hydrolysis by transducin-mediated phosphodiesterase(PDE) activation. We found however that the light response does recover in the presence of the analog, which requires acceleration of guanylate cyclase rather than inhibition of PDE. Furthermore, after introduction of the analog the dim flash responses are not only smaller in amplitude but also faster in recovery, which mimics light adaptation. These results suggest that acceleration of PDE and of PDE-guanylate cyclase cycle mediates both response recovery and the light adapted response.

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EXACT PARALLELS BETWEEN PSYCHOPHYSICALLY AND ELECTROPHYSIOLOGICALLY (ERG) DETERMINED DUPLICITY IN THE HUMAN RETINA. ITABASHI, R., SUGITA, Y., TAKAHASHI, A. and TASAKI, K., Dept. of Ophthalmol. and Dept. of Physiol., Tohoku Univ. Sch. of Med., Sendai 980

Few objective experiment on functional separation between human rod and cone systems have been done. To develop simple, reliable and objective method to identify both systems, we developed an LED mounted contact lens electrode, recorded electroretinogram (ERG), and compared results with those of simultaneously performed psychophysical experiment. Intensity-amplitude relations consist of two components (high- and low-sensitivity) when green flashes were given to the fully dark adapted eye and one component to the red stimuli. Dark-adaptation curve consisted of two sections when the eye was illuminated with green flashes (criterion to determine sensitivity at any moment was 1/6 of the maximum amplitude of rod component in the first experiment) and one section to red stimuli. Time to rod-cone break under present light adaptation was about 8 min, which is exactly the same as that obtained from psychophysical experiment. Difference between intensities to determine psychophysical threshold and those to elicit criterion response was about 3 log units throughout the time course of dark adaptation. These results suggest that newly developed method is useful to avoid subjective factors to prove duplex system in the human retina.

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CHARACTERISTICS OF A POSITIVE WAVE IN PARIETAL ZONE, EVOKED BY A RANDOM-DOT VISUAL STIMULUS WITHOUT DEPTH PERCEPTION. NIKARA, T., FUJII, H.* and OSANAI, T.*, Lab. of Physiol., Sch. of Allied Med. Sci., Hirosaki Univ., Hirosaki 036

We reported that the positive large wave(peak time: 240-300 msec) recorded in CZ was observed in transition from a static random-dot stereogram to an uncorrelogram on a TV screen. We provided four screens of visual stimulus: a yellow random-dot screen without no retinal disparity, two uncorrelograms without depth perception, a stereogram with depth perception. Two screens of them were presented alternately to normal subjects, wearing a red-green goggles, at 500 msec of interval. Recording electrodes were placed on OZ, PZ, CZ, FZ, C3, C4, T3, and T4 in their scalp. 1. The wave diffused from PZ to FZ in anteroposteriol and from C3 to C4 in lateral, and its greater amplitude was often recorded in CZ in change of TV screens; from the uncorrelogram to the other, from the uncorrelogram to the yellow screen and from the stereogram to the uncorrrelogram. 2. The wave was also observed in OZ when a pair of yellow screen and the uncorrelogram or a pair of the uncorrelograms was monocularly presented. 3. The appearing of the wave varied among individuals: 6 of 24 have no the the wave in the disparity screen. 11 of 24 have the wave in both screens of disparity and nondisparity. 8 of 24 have no the wave in both screens. Conclusively, even though the wave appears slightly in monocular condition, it tends to be bigger in amplitude when an amount of disparity in the screen was reduced.

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INFLUENCE OF GRAVITY ON OPTIC CELLS AS THE CAUSE OF DISTORTED APPARENT SIZE. TSUKEDA, K., Dept. Physiol., Facul. Med., Univ. Tokyo, Tokyo, Hongo 113.

The sun and moon look larger when they are near the horizon than the zenith. However, the same object should look the same wherever the objective and subjective conditions were constant. For elucidation of this problem, we prepared a round visual mark of a visual angle of 1° with a constant brightness at a constant distance (e.g. 2m). Attempts were made to measure the visual angle of the mark when the light proceeded perpendicularly, anti-perpendicularly, from the direction of the magnetic pole (deviation angle: 6° ; inclination angle: 49°), and horizontally. A small cylinder (e.g. 30cm) was placed in front of one eye. Small perforated holes of various sizes were attached , one by one, at the end of the cylinder. The hole which was identical with the round visual mark was selected for calculation of the visual angle. The results: the visual angle was smallest when one saw a perpendicularly proceeding light (visual angle s) and largest when one saw a light coming from the direction of the magnetic pole of the earth (visual angle m). The ratio s : m=1 : 1.28. Intermediate values were obtained under the conditions other than the above. In other words, one may say that the visual angle was smallest when the optic cells receive the action of gravity most strongly and largest when it was cooperative with the earth's magnetism. One of the reasons why the sun and moon look large near the horizon seems to be the effect of the sensitivity to long wave lights of the cones, besides the action of the sun's magnetism.

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RETINALS IN THE EGG OF XENOPUS LAEVIS. AZUMA, M., SEKI, T., FUJISHITA, S.
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Xenopus eggs included almost equal amounts of all-trans retinal and 3-dehydroretinal (total; about 50 pmol/egg). During development, the amounts of these retinals decreased and all-trans retinyl ester and 3-dehydroretinyl ester appeared. All-trans retinals disappeared from the eyes at stage 41/42 and from the internal organs at stage 46.

An existing state of egg retinals was examined as follows. Egg homogenate was suspended in ammonium sulfate solution. The fraction containing retinals was precipitated by 65% saturation. After the addition of sodium borohydride to the fraction, the retinols or N-retinyl-products were not extracted by organic solvent. The precipitate including retinals was soluble in 200 mM NaCl-10 mM Tris/HCl buffer-5% SDS and emitted fluorescence due to N-retinyl-product after the addition of sodium borohydride. These results suggest that egg retinals are binding with a protein to form the Schiff base. The properties of the binding protein, i.e. the solubility in NaCl solution and the precipitation in 65% saturated ammonium sulfate, are similar to those of lipovitellin, a lipoprotein contained in yolk platelets.

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MEMBRANE RESISTANCE OF CRAYFISH PHOTORECEPTORS RE-INCREASES GRADUALLY DURING LIGHT ADAPTATION UNDER "VOLTAGE CLAMP BY LIGHT"
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Retinula cells of the crayfish eye were studied on the basis of the voltage clamp idea that utilizes the natural stimulus, namely light. The system we developed is characterized by fast clamp action and by a built-in bridge-balance circuit which allows measurement of the membrane resistance, R_m, under the "voltage clamp by light". As soon as a stepwise depolarization was induced by controlled light, R_m decreased by several MΩ from its control value measured in the dark. This was expected as being a general property of invertebrate photoreceptor cells. As time passed, however, R_m was found to re-increase slowly with a single time constant of 5-15 sec, even though the same constant depolarization was maintained through servomechanical control automatically adjusting the intensity of light. The constant-voltage R_m re-increase was still observed when external Na was replaced by Li, but R_m did not re-increase when 10 mM Ni was added to the superfusate. Perhaps, therefore, inactivation of the depolarization-triggered Ca gate underlies this phenomenon which seems to bear intimate relevance to the mechanism of light adaptation.

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ROLES OF TRANSDUCIN IN THE PHOTOTRANSDUCTION OF THE TOAD ROD. SHIMODA, Y.
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Biochemical studies have shown that transducin activates phosphodiesterase(PDE) which hydrolyze cyclic-GMP(c-GMP) into 5'GMP. The role of transducin was investigated physilogically in the toad, Bufo bufo rod. Choleratoxin(CTX) inhibits GTPase activity in the transducin molecule, resulting that activity of transducin would be maintained. CTX was injected into rod outer segment through a microelectrode by pressure.

An injection of CTX in the dark causes slight hyperpolarization in the rod membrane. When the illumination was applied just after an injection, rod membrane has been kept hyperpolarized for over 2 minutes, that is, recovery from hyperpolarizing photoresponse was remarkably elongated. Long lasting hyperpolarization represents that c-GMP has been still hydrolyzed by activated PDE which was, in turn, activated by transducin. Consequently, it is approved physiologically that transducin mediates light isomelization of rhodopsin to activation of PDE.

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THE HORIZONTAL CELL INNERVATION ON THE PHOTORECEPTORS IN THE CARP RETINA: EM STUDY OF LUCIFER YELLOW-HRP DOUBLE STAINING

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The overlapping of the synaptic connections of three types of horizontal cells -luminosity (LHC), biphasic chromaticity (BHC) and triphasic chromaticity (THC)- on the cone terminals were studied with double staining technique. After the electrophysiological identification of the subtypes, HRP and lucifer yellow were intracellularly injected into THC (or BHC) and LHC, consequently. Lucifer yellow was electron microscopically visualized with photo-oxidation using DAB as the chromogen. The HRP products in the dendrites of the THC (or BHC) and photo-oxidation products in LHC dendrites were clearly distinguishable by their density and texture.

LHC connected with most cones located in its dendritic field, and its dendrites ended as the lateral elements of the ribbon synapses in most cases. BHC innervated into about 1/2 of the cones. In half of those cones, the dendrites of the BHC ended as the central elements. In the remainder, BHC dendrites ended as the lateral elements. In both cases, the dendrites of the LHC were co-localized as the lateral elements. THC innervated about 1/5 of the cone terminals as central and/or lateral elements. LHC dendrites were co-localized in the half of those cones, but not correlated with the ending positions at ribbon synapse.

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GLIO- AND NEUROTOXIC EFFECTS OF ALPHA-AMINOADIPIC ACID ISOMERS IN THE CARP RETINA.

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We previously reported that α-AAA isomers affect neurons as well as glial cells in the carp retina. To further analyse the actions of isomers, we followed up histological and physiological changes of the retina after intravitreal injections of α-AAA isomers (L-,D-) and their mixture (DL-). L-α-AAA was most effective among them: a dose of 3 μmole L-isomer was sufficient to induce edema in glial Müller cells, and a dose of 8-16 μmole produced severe histological damages in both INL and IPL. The effect of 16 μmole DL-α-AAA was comparable to that of 8 μmole L-isomer. The damages caused by injections of 8 μmole L-,16 μmole DL-, and 16 μmole L-α-AAA recovered completely in 2, 2, and 4 weeks, respectively. The b-wave of ERG disappeared after injection of any isomers, but returned incompletely in 1-2 months. All the isomers of α-AAA suppressed light-induced discharges of ganglion cells, which recovered completly in 4 weeks when D- or DL-α-AAA (16 μmole) was used but did not return when L-α-AAA (>4 μmole) was used. The results indicate that the D- and DL-α-AAA act as a relatively specific gliotoxin, while the L-isomer as a cytotoxin for glial and neuronal cells in the carp retina, and that the neurotoxic action of L-isomer appears to be antagonized by D-α-AAA.

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RESPONSE RANGE AND NEURONAL CONNECTION OF PHOTOSENSORY PINEAL ORGAN.

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In order to investigate the neuronal connection between pineal photoreceptors (PRs) and ganglion cells (GCs), response ranges and membrane properties were studied intra- and extracellularly in the PRs of 525nm and in achromatic GCs of lamprey, *Lampetra japonica*. The intensity-response curves of receptor potentials and slow potentials of GCs fitted well to the Naka-Rushton's hyperbolic function. The value of n was 0.71±0.11(sd) in PRs and 0.46±0.10 in GCs, hence the active range of the latter group was broader. The duration of slow potentials changed in the same range of intensity in both groups. The spectral sensitivity curve of achromatic GCs measured by the inhibition of spike discharges peaked at 525nm and was in the same pattern as obtained from the PRs. The input membrane resistance of GCs increased during the hyperpolarization by photic stimulation. These observations indicate that the achromatic GCs receive their inputs mainly from PRs of 525nm with different sensitivities through the disfacilitating synaptic connections.

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THE AUDITORY SENSITIVITY CURVE AND SIGNAL RECOGNITION OF THE JAPANESE MONKEY. KAMADA, T., KAMEDA, K., AND KOJIMA, S.**, Dept. Oral Physiol., Hokkaido Univ. Sch. Dent., Sapporo 060 and Primate Research Inst. Kyoto Univ., Inuyama 484**

Auditory sensitivity of Japanese monkeys measured by behavioral reaction time showed W-shaped threshold curve with two sensitive negative peaks for frequency. This was also true for chimpanzees. Behavioral audiograms were compared to ones obtained by auditory brain stem response (ABR) of 3 Japanese monkeys. ABRs were recorded by averaging 2048 times the potentials between vertex and ear lobe. Stimuli were 20 ms tone burst with 5 ms rise-fall time. Amplitudes, latencies and thresholds of peak V were measured. As the result, audiogram of Japanese monkey was less sensitive in 6 kHz, which corresponds to behavioral audiogram. Preliminary measurement of AP from external canal in Japanese monkey showed less response in 6 and 8 kHz than in other frequencies, in spite of low threshold of ABR to 8kHz. ABRs were also recorded in a chimpanzee. Behavioral response was more sensitive in 8 kHz than in 2 or 4kHz, while ABR audiogram of chimpanzee showed decrease in sensitivity with frequency up to 8 kHz.

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MECHANISM ELICITING RESPONSE IN BAND OF NOISE RECEIVERS. MARUYAMA, N., KUDOH, M., FURUKAWARA, M. AND SHINZAWA, H. Dept. Neurophysiol., Brain Res. Inst., Niigata Univ., Niigata 951

In the auditory cortex (AI) of cats, about half of the units responded best to the band of noise (BN). In most cases of these units, which are called BN receivers, the effective range of center frequency (CF) of BN was extended over a wide frequency range. But the effective range was restricted in some units, which are called consonant detectors. We found a few units in which the effective range of CF was more restricted than in the consonant detector. The effective range was a single frequency band for amplitude-modulation (AM)-BN, but the effective range for frequency-modulation-BN consisted of two separate patches at both sides of the effective range for AM-BN. The response of such a unit may be caused by fluctuation of the stimulus across the boundary between excitatory and inhibitory area of a lower neuron which sends an input to the unit.

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TWO DIFFERENT SORTS OF HAIR CELLS IN THE GOLDFISH SACCULUS. SUGIHARA, I. and FURUKAWA, T. Dept. of Physiol., Tokyo Med. & Dent. Univ. Sch. of Med., Yushima, Bunkyo-ku, Tokyo 113.

Hair cells in the rostral part of the goldfish saccular macula are short in length (spherical or barrel-like in shape, and 13 20 um long), while those in the caudal part are much longer (slender or rod-like in shape, and 25 50 um long). Upon studying on enzymatically isolated hair cells with a patch clamp method, we found that these two morphologicall different groups of hair cells differed in their electrophysiological properties too. Short hair cells in the rostral macula had a lower resting potenital of -70 -80 mV and responded to a depolarizing current with oscillatory potenital changes (frequency: e.g. 200 Hz), while long hair cells in the caudal macula had a higher resting potential of -90 -100 mV, and responded with all-or-none spike potentials (amplitude: 50 mV or smaller than that). Voltage clamp studies disclosed that ionic channels activated by voltage steps differred substantially between the two grups.

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Ca-ACTIVATED K CHANNELS IN SPIKE-GENERATING GOLDFISH HAIR CELLS. SUGIHARA, I. and FURUKAWA, T., Department of physiology, Tokyo Medical and Dental University School of medicine, Yushima-1, Bunkyo-ku, Tokyo, Japan, 113.

Ca-activated K channels were found in basolateral membrane of isolated slender hair cells of caudal part of the goldfish saccular macula which generate action potentials. Characteristics of these channels were examined with inside-out patch clamp method. They had large conductance (150 - 320 pS in symmetrical 125 mM KCl) and showed similar trends in permeability ratios as observed in skeletal or smooth muscle membrane: $K(1.0)>Rb(0.8)>NH_4(0.14)>>Na,Cs(<0.05)$. Open state probability was found to increase with an increase in the membrane potential and internal Ca concentration, a feature very characteristic to Ca-activated K channels of every tissue. However, sensitivity to internal Ca concentration was lower in these channels, for as much as 20 μM Ca was required to obtain an open state probability of 0.5 at 0 mV membrane potential. This might explain the small outward K conductance of the hair cells under depolarization examined with whole-cell clamp mode. Response to the step change of membrane potential was examined by averaging the single channel current records. Time courses of rising and decay phases were fast (in the order of ms). The rising phase became faster and the decay phase became slower with increase of internal Ca concentration.

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THE POSTSYNAPTIC POTENTIALS OF THE VESTIBULAR HAIR CELLS TO THE STIMULATION OF THE EFFERENT FIBERS. SUGAI, T., OOYAMA, H., YANO, J. AND SUGITANI, M. Dept. Physiol., Kanazawa Med. Univ., Ishikawa 920-02

Intracellular potentials were recorded from hair cells in the frog saccular and utricular epithelia isolated with the eighth nerve, to study the properties of the efferent synapses. In sacculus, electrical stimulation of the eighth nerve produced slow hyperpolarizing postsynaptic potentials of 20-30 mV in amplitude, lasting 200-400 ms. During the hyperpolarization, there was a reduction in the amplitude of the spontaneous oscillatory potentials and of the receptor potentials for vibratory stimuli. The postsynaptic hyperpolarization could be reversed by hyperpolarizing current injection. The reversal potential was -77±4 mV, in six hair cells with a resting potential of -50±3 mV. In most cells, however, another faster hyperpolarization with the reversal potential of -56±3 mV, 6 mV negative to the resting potential, appeared. Thus, in sacculus, most efferent synaptic potentials consisted of two components, a fast and a slow hyperpolarizations with different reversal potentials. In utriculus, some hair cells showed slow hyperpolarization, and some showed slow depolarization in response to efferent stimulation. These results coincide with the observations that efferent stimulation elicits inhibitory or facilitatory effect on spontaneous activity of utricular afferents, but only inhibitory effect on the saccular afferent activity.

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GENERATION OF INTERMODULATION DISTORTION PRODUCTS IN OTO-ACOUSTIC EMISSION. MORIYAMA, T., HOSOKAWA, Y., MINAMI, S., & MURATA. K. Dept. of Neurophysiol.,Med. Res. Inst., Tokyo Med. & Dent. Univ., Kandasurugadai, Tokyo, 101.

Acoustic emissions to the ear canal were elicited by alternating current (AC) injection through a Pt electrode into the scala media of guinea pigs anesthetized with urethane (120mg/kg i.p.). The ACs through the cochlea and the emitted sounds were FFT-analyzed to obtain their frequency spectrograms. Distortion products in the current through saline or the cochlea were far larger than those in the original current sources, suggesting that the metal electrodes in saline must have a nonlinearity. Content of the distortion products in the emitted sounds was 20dB as large as the value expected from their contents in the cochlear currents. Therefore, there may be one more nonlinearity in the cochlea to generate these larger distortion products. Electrically induced sideband emissions were suppressed reversibly by intense sound exposure or COCB stimulation without change in the fundamental emissions; i.e., electromechanical transduction may not changed, but a nonlinearity(ies) in the cochlea may decreased reversibly. Changes in emissions of sidebands and of combination tone (F2-F1) by temporary anoxia indicated fast monophasic suppression of the transduction and slow increase in the nonlinearity(ies).

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INTRACELLULAR RECORDING FROM THE RAT INFERIOR COLLICULUS NEURONS USING BRAIN SLICES. HOSOKAWA, Y., MURATA, K. & KATAYAMA Y. Dept. of Neurophysiol., Med. Res. Inst., Tokyo Med. & Dent. Univ., Kanda-surugadai, Tokyo 101.

Intracellular recordings were made from neurons in the inferior colliculus (IC) of the rat in vitro. Male or female Wistar-strain rats (150-300g) were deeply anesthetized with ethylether and decapitated. Frontal-cut slices (300um thick) containing the IC were prepared with a vibratome in cooled (4 C) modified Krebs solution. The IC slices were placed in a recording chamber and superfused with warmed saline (36 C). The resting membrane potential and resistance of IC neurons were between -52 and -89 mV and between 25 and 200 M ohm, respectively. The IC neurons responded to a depolarizing current pulse (up to 100 ms duration) with one or repetitive spikes. A train of action potentials in some cells were followed by a long lasting after-hyperpolarization. The slow after-hyperpolarization reversed polarity at -76 mV. Focal stimulations caused either depolarizations or hyperpolarizations in many cells. Since these were reversibly abolished in low Ca / high Mg solution, they might be EPSPs and IPSPs. EPSPs reversed its polarity at about -5 mV and IPSPs at about -80 mV. Superfusion of L-glutamate (1 mM) caused membrane depolarizations accompanied by discharges.

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TARGETS OF THE RE-ESTABLISHED AXONS OF THE COMMISSURE OF THE INFERIOR COLLICULUS AFTER ITS TRANSECTION. TANIGUCHI, I. and TANAKA, H.* Med. Res. Inst., *Dept. of Otolaryngology, Tokyo Med. & Dent. Univ. Bunkyo-ku, Tokyo 113

Axonal regeneration in the commissure of the inferior colliculus (CIC) of mice following its transection was previously reported (Taniguchi and Saito, 1982). In this study we examined whether the regenerated CIC axons could re-establish synapses with the proper targets in the inferior colliculus (IC) or not. We electrophysiologically identified the best frequency (BF) of the IC neurons in which the CIC fibers newly established the synapses. The mean BF for the operated animals was slightly lower than that for the unoperated controls. This result suggests that the neurons identified in the operated animals are distributed more superficially than in the unoperated controls. The regenerating CIC axons will most likely cease to grow if they encounter the appropriate targets at a closer location.

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EFFECTS OF CALCIUM CHANNEL BLOCKER AND OF CALCIUM CHELATING AGENTS ON THE ENDOCOCHLEAR DC POTENTIAL IN GUINEA PIG. SATO, Y. Dept. Physiol. Kawasaki Med. Sch. Kurashiki, Okayama 701-01

The endocochlear DC potential (EP) in guinea pig was investigated under influence of nifedipine and calcium chelating agents. The artificial perilymph solution with or without nifedipine or calcium chelating agent was perfused from scala tympani to scala vestibuli through a small hole made in basal turn. EP decreased gradually after the start of perfusion of nifedipine solution, but did not decrease less than 100 ng/ml. At the concentration 200 ng/ml, EP decreased from +70 mV to +14 mV. At 1 μg/ml, EP decreased from +70 mV to +54 mV and stayed at the steady level during perfusion. It turned back towards the initial level if the control solution was perfused again. Cochlear microphonics (CM) was also decreased by 200 ng/ml nifedipine, not so much as the decrease in EP. Removal of Ca ions from the perfusing solution (10 mM EGTA) decreased EP from +80 mV to 67 mV. The change was not maintained even if perfusion of EGTA solution was continued, but recovered spontaneously to the cotrol level. 4 mM EDTA did not change EP significantly, probably because Ca ions were mobilized from the surrounding tissue. The results suggest that Ca ions play a role in maintaining EP in the way that Ca modulates Na-K pump activity of the marginal cells in stria vascularis.

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GLUTAMATE RECEPTOR CHANNELS IN THE CULTURED CHICK COCHLEAR GANGLION NEURON.

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Properties of the glutamate (Glu) receptor channels were investigated in the cultured chick cochlear ganglion (CG) neuron. CG neuron was enzymatically dissociated and cultured for 3 to 14 days. Glu (30 μM)-activated currents were recorded under the whole-cell voltage-clamp condition. Glu-activated current was blocked by Mg^{2+}(1mM) in a voltage-dependent manner. 2APV (100 μM) blocked this current. Therefore, the major subtype of the Glu-receptor in this cultured CG neuron would be the NMDA type. Permeabilities to particular ions were estimated from the reversal potentials. P_{Na}/P_{Cs} was 0.96 and P_{Li}/P_{Cs} was 0.95. Current reversal was not observed in TMA- and TEA-solutions. Large permeabilities to divalent cations were demonstrated; P_{Ca}/P_{Cs}=3.7, P_{Ba}/P_{Cs}=3.5 and P_{Sr}/P_{Cs}=2.4 on the concentration basis. These ionic selectivities were consistent with those of the NMDA-receptor channel reported in the cultured mammalian central neuron.

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OPTICAL IMAGING OF NEURONAL ACTIVITY OF AUDITORY CORTEX.

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With the aid of a voltage sensitive dye optical recording of neuronal activity was tried on the auditory cortex of a guinea pig in response to sound stimulation under light pentobarbital anesthesia. Infrared reflection from the cortical surface stained with a potentiometric dye, merocyanine-rhodanine (NK2761) was monitored with a Newvicon TV camera. The video signal was fed into an image processor and the video images could be accumulated in the frame memories under different conditions of auditory stimulation. The optical image synchronizing with stimulus presentation was sampled through a time window and integrated sequentially along the time lapse from the stimulus initiation. The functional organization of the auditory cortex was investigated with the analysis of the recorded sequence of optical images associated with fast neuronal signals of cortical activity in response to a sinusoidal click and a natural call of the animal.

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RESPONSES OF RAT AUDITORY CORTICAL NEURONS TO SYNTHESIZED NOISES AND SPECIES SPECIFIC CALLS.

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Responses of single auditory cortical neurons to synthesized noises and species specific calls were studied in Wistar-strain rats anesthetized with Nembutal (40 mg/kg), using tungsten microelectrodes. Band noises having uniform or random phases in spectral components were synthesized with an inverse Fast Fourier Transformation method. Rat's 22-kHz calls, which contained an initial descending and a final ascending FM components, were A/D sampled and stored in disk files. Those wave data were output to an ultrasonic earphone inserted into the ear canal contralateral to the recording side. Most neurons responded more vigorously to pure tones than to band noises, but some (6/19) responded more to the noises. Tuning curve analysis showed that those noise-preferring neurons had wide response area, and that pure-tone-preferring neurons had narrow response area or strong inhibitory side bands. Effect of randomizing phases in the spectral components of the noises on the neural responses was little, suggesting that the rat auditory cortical neurons mainly process frequency information rather than phase information. Responses to rat calls were seen only at the initial and final portion, when the neurons had response areas containing the frequencies of the calls.

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EFFECTS OF EXTERNAL IONIC ENVIRONMENT CHANGE ON THE ODORANT-ACTIVATED CONDUCTANCE IN THE SOLITARY OLFACTORY RECEPTOR CELLS OF NEWT.

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A current through the conductance activated by an odorant (N-amyl acetate) was recorded under a whole-cell voltage-clamp condition. A polarity reversal of the current was observed at +6 mV in the normal Ringer's solution. The reversal potential shifted proportionally to logarithm of external Na^+ concentration ($\log[Na^+]o$) when Na^+ was replaced with choline . The shifted value was about -13 mV by half decreasing of $[Na^+]o$. However, when the external Na was substituted for the other alkali metal ions (Li, K, Rb and Cs), such large shift was not observed. It seems likely that each of alkali metal ion has a capacity to carry the current. On the other hand, the anion replacement had little effect on the conductance (Cl^- was replaced with glutamate$^-$). These results suggest that the odor response in the olfactory receptor cells is caused by the increase of membrane cation permeability.

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EFFECTS OF SODIUM PENTOBARBITAL ON UNIT ACTIVITY IN THE CAT OLFACTORY BULB.

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Effects of anesthetic level on single unit activity in the olfactory bulb were examined. Twenty-two cats were anesthetized with sodium pentobarbital. The anesthetic level was determined by means of field potentials in the olfactory bulb evoked by stimulation of the lateral olfactory truct. A total of 272 units were recorded on two different anesthetic levels,that is, low (less than 15 mg/kg) and high dose (more than 25 mg/kg). The animals respired spontaneously through the nose or a trachectomy tube. Under nasal respiration, respiratory moduration of unit activity and burst pattern of discharge were reduced in the high dose. In addition, mean discharge rates were less in the high dose (3.5 spikes/sec) than in the low dose (10.1 spikes/sec). Under tracheal respiration, mean discharge rates were also less in the high dose (3.6 spikes/sec) than in the low dose (10.0 spikes/sec). However, spontaneous discharge pattern was unaffected by anesthetic level. Respiratory moduration of discharge was not detected under tracheal respiration. The sensitivity of the olfactory units to pure air or amyl acetate was examined under tracheal respiration. There was no marked difference in mechano- and odor-sensitivity between both anesthetic levels.

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EFFECT OF OLFACTORY BULB STIMULATION ON THE TASTE RESPONSES OF THE CORTICAL NEURONS IN RATS.

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Thirty neurons were recorded in 23 rats during application of four basic tastants. The olfactory bulb (OB) was stimulated bipolarly with 50 Hz pulses at an intensity of 8 - 10 mA constant for 30 s, and induced an effective change in 24 neurons. In some neurons any effect was observed in all the four taste qualities, while in others the effect differed considerably depending upon the taste quality. The response to HCl had a trend to be diminished after OB stimulation. The effect of stimulation tended to be stronger in the responses facilitated by the stimulation and to be weaker in those inhibited, as typically found in the response to sucrose. The difference between the response intensity to the best taste and that to the 2nd taste (contrast) was often modified by the stimulation. The modification of contrast between the 2nd and 3rd tastes was usually stornger than that between the best and 2nd, suggesting that the stimulation acts to decrease the ability of discriminating the best taste from the 2nd. The mode of change in the taste responses of different neurons recorded with the stimulation electrode remaining at the same place was not identical, but showed a marked individual difference, indicating that the wide variety of responses of the cortical neurons recorded in the present experiment was not mainly due to the difference in the electrode position in the OB.

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THE INTRAVITAM STAINING OF THE BULLFROG TONGUE LINGUAL PAPILLAE.

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The fungiform papillae of bullfrog tongue are the best materials to research the stimulus and response by the electric potential on receptor of the ciliated cell and the taste cell by many taste substances using the method of suction electrode and glass tube microelectrode.

About 700-800 fungiform papillae can count on all dorsal area of tongue surface.

At the observation after the intravitam staining by immersing method using 2% metylenblue physiological salt solution, the peripheral parts of fungiform papillae are surrounded with the ciliated cell and the outer layer are composed of the supporting cell, as well as the inner layer of the taste cell on the central parts of fungiform papillae.

And then these fungiform papillae are observed "like sunflower" on the plane surface and "like saeanemone" on the three dimensinal surface.

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TETRODOTOXIN-SENSITIVE RECEPTOR MECHANISMS FOR "ELECTRIC TASTE".

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Receptor mechanisms for "electric taste" were studied by examining responses of rat single chorda tympani fibers to ionic chemical and electrical (anodal) tongue stimulations with NaCl, LiCl, KCl, $CaCl_2$ and HCl. In 10 out of 32 single fibers sampled, the lingual application of 100 μM amiloride for 2 min significantly reduced responses to both chemical and electrical stimulations with NaCl and LiCl (t-test, $p < 0.05$), while in other 10 fibers that of 1 μM TTX for 10 min suppressed responses to anodal currents with dilute NaCl and LiCl without affecting responses to chemical stimuli. Responses of 2 fibers to chemical and electrical stimulations with NaCl were suppressed by either amiloride or TTX. The remaining 10 fibers were insensitive to both drugs. These results suggest that there are at least three different receptor mechanisms for "electric taste" in the rat taste system, such as amiloride-, TTX-sensitive and amiloride - TTX-resistant. Among them, the TTX-sensitive receptor mechanism is highly specific for "electric taste" and its selective sensitivity to ion in the bathing medium indicates that the TTX-sensitive mechanism possibly exists on the apical side of the taste cell membrane.

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AN ANALYSIS OF MEMBRANE CURRENTS OF ISOLATED BULLFROG TASTE CELLS.

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To examine the membrane properties of bullfrog taste cells in detail, we isolated them enzymatically from the fungiform papillae and the whole cell clamp technique was applied to them. Isolated taste cells were identified by its characteristic morphology. They had a resting potential of -75 ± 1 (SE) mV (26 cells), a membrane capacitance of 15 ± 1 pF and an input resistance of 0.2 to 20 GΩ when the bathing solution was normal saline and the pipette filling solution contained 111 mM KCl. Most of isolated taste cells were electrically excitable, and under the voltage clamp condition they generated a fast transient inward Na current followed by a slowly activated outward K current by voltage steps of -65 to -20 mV or more positive. No Ca current was found in this experiment. When K^+ concentration in the bath was raised, isolated taste cells depolarised with a pronounced decrease of input resistance even in the absence of Na^+ in the bath. This suggests the presence of K current depending on the external K^+ concentration.

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ELECTRICAL RESPONSES OF ORAL EPITHELIAL CELLS TO TASTE STIMULI IN BULLFROGS. SATA, O. AND SATO, T.
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Electrical responses of epithelial cells in the fungiform papilla (FUP), the filiform papilla (FIP), the ventral surface of the tongue (VST) and the palate to the four basic taste stimuli and water were examined with an intracellular recording technique. The mean resting potentials of the cells in the four regions ranged from -12 to -20 mV, which were smaller than that of taste cells in FUP. In all the epithelial cells, depolarizing responses like in taste cells were elicited by 0.5 M NaCl and 10 mM quinine-HCl. Depolarizing responses of epithelial cells in FUP and FIP to 0.5 mM acetic acid were the same as those of taste cells, whereas those in VST and the palate were smaller. Depolarizing responses of epithelial cells in FIP and VST to 1 M sucrose were smaller than those of taste cells, whereas the cells in FUP and the palate responded to 1 M sucrose with hyperpolarization. Hhyperpolarizing responses were elicited in all epithelial cells by water. The water responses in FIP were larger than that of the taste cell. It is obvious that oral epithelial cells respond to taste stimuli.

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INHIBITION OF THE FROG TASTE RECEPTION BY TRIAMINOPYRIMIDINE SOEDA, H., SAKUDO, F., KAJIYA, H. AND NODA, K. Dept. Physiol., Fukuoka Dent. Coll., Sawara-ku, Fukuoka 814-01

Stimulation of the frog tongue with NaCl produces a transepithelial response across the dorsal epithelium, and this may be related to taste reception. In the gallbladder and small intestine of rats and frogs, 2,4,6-triaminopyrimidine (TAP) is a specific inhibitor of paracellular sodium movement across the tissue. We examined the effects of TAP on the frog neural response to taste chemicals in vivo. When 1 mM TAP was applied to the tongue surface, responses to NaCl and water were markedly inhibited, while those to acetic acid, quinine and sucrose were not. TAP also inhibited the response produced by salts similar to NaCl, and its rate was greater in the responses to NaCl, KCl, LiCl and $NaNO_3$ than in those to choline Cl and tetramethylammonium Cl. The inhibition of these responses with TAP was stronger than that with amiloride. The results indicate that NaCl stimulation of frog tongue causes paracellular sodium movement across the dorsal epithelium responsible for the transepithelial response, and this affects the process of generating neural response.

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CHARACTERISTICS OF THE CHORDA TYMPANI RESPONSES TO VARIOUS SUGARS IN INFANT RATS. MAEDA, S., HARADA, S., and KASAHARA, Y., Department of Oral Physiology, Kagoshima University Dental School, 1208-1 Usuki-cho, Kagoshima 890

Integrated responses from the rat chorda tympani nerve to six sugars (sucrose, fructose, lactose, maltose, glucose and galactose) were recorded in 1- to 4-weeks-old infant and 8-weeks-old adult rats. Relative response magnitudes against 0.1 M NaCl for each sugars in infant rats were larger than those in adult rats. Although clear phasic and succeeded tonic responses to sucrose were observed in every infant rats, phasic portion was not observed in about half of adult rats. Although there was a negative correlation between on- and off-response (sugar and water response) in adult rats (r=-0.715), no correlation was observed in infant rats (r=-0.033). Lactose had strong stimulatory effects next to sucrose through 1 to 4 weeks among six sugars, while fructose got stronger than lactose at 8 weeks of age. Cross-adaptation experiment revealed that the specificity for each sugars were more evident in adult rats. These results suggest that the sugar receptive mechanisms in the rat taste system may developmentally change in infant.

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TASTE RESPONSES OF THE CHORDA TYMPANI NERVE UNDER ANESTHETIC AND AWAKE CONDITIONS IN RATS. MATSUO, R. and YAMAMOTO, T., Dept. of Oral Physiol., Faculty of Dentistry, Osaka Univ., 1-8 Yamadaoka, Suita, Osaka 565

Electrical activity of the chorda tympani nerve was chronically recorded in rats. Taste responses during the licking of taste solutions under awake condition were compared with those obtained by pouring the solutions on the tongue surface under anesthesia. The following results were obtained: 1) The rats licked sucrose and NaCl solutions continuously; large responses were obtained. Responses to HCl and quinine hydrochloride were small and irregular, partly because of a small number of licks and frequent face washing or gaping which occurred after licking. 2) Threshold intensities shown during the licking of sucrose and NaCl were similar to those obtained under anesthesia. 3) Magnitude of responses to sucrose under awake condition were about four times larger than those obtained under anesthesia, while NaCl showed slightly smaller responses under awake condition than anesthetic condition. 4) Larger responses under awake condition were observed in other sweet substances. Sugars (mono- and di-saccharides) and amino acids (Ala, Ser, Gly) showed about four and three times larger responses during licking, respectively. Sodium saccharin and sodium cyclamate, however, showed slightly larger responses during licking.

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SALT TASTE RESPONSES IN THE FROG GLOSSOPHARYNGEAL NERVE : ENHANCEMENT BY Ni AND Co. KITADA, Y., Dept. of Oral Physiol., Okayama Univ. Dent. Sch., Okayama 700

The frog glossopharyngeal nerve responds to $CaCl_2$, $MgCl_2$ and NaCl. The responses to these salt stimuli were enhanced by addition of $NiCl_2$ or $CoCl_2$ to solutions which contain Ca, Mg or Na. The dependence of enhancement of the salt response upon concentration of $NiCl_2$ was the same in responses to Ca, Mg and Na. The enhancing effect of Ni appeared in 0.01-0.1 mM and reached a saturation level around 1 mM. It has been demonstrated that Ca, Mg and Na have different receptor sites. The affinity of the receptor sites for Na was increased by Ni, but the affinities for Ca and for Mg were not affected. Ni increased the maximum response in dose-response curves for Ca, Mg and Na. In contrast to its enhancing effect, Ni competitively inhibits the Ca response. Therefore, the enhancing effects of Ni on the salt responses are not due to binding of Ni to the receptor sites responsible for the salt responses. It appears, then, that the receptor sites for salt responses interact secondarily with a component of the receptor membrane affected by Ni and thereby Ni induces the enhanced response.

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PHYSIOLOGICAL STUDIES ON AFTER-TASTE IN MAN. HORIO, T. AND KAWAMURA, Y. Faculty of Nutrition, Koshien University, 10-1 Momijigaoka Takarazuka 665

The after-taste of eating materials is one of important factors in man for food preference and selection. This experiment was performed to evaluate the relations between taste quality and continuations of after-taste in 1M sucrose, 0.1M NaCl, 0.03M HCl, 0.0005M quinine-HCl, 0.1M momosodium L-glutamate(MSG), 0.1M inosine 5'-monophosphate(IMP) and 0.1M guanosine 5'-monophosphate(GMP).

All subjects felt sucrose sweet and quinine-HCl bitter in both immediate taste and after-taste respectively. However, in case of NaCl and HCl, most subjects tasted salty and sour respectively, although some subjects tasted different in the after-taste. Regarding MSG, IMP and GMP, subjects felt different taste, but in the after-taste most subjects answered umami. The continuations of after-taste of MSG, IMP, GMP and quinine-HCl were longer than the other taste solutions of NaCl, sucrose and HCl. These results suggest that the characters of after-taste of MSG, IMP and GMP are well contributive to make the good taste of food.

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DISTRIBUTION OF AFFERENT NERVE TERMINALS IN THE CRAYFISH NEUROPILES.
CHICHIBU, S., CHIBA, A., KOSAKA, M., HAMAGUCHI, M. AND SHIMADA, Y.*
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Neuropile structures in the cerebral ganglion of American crayfish, Procambarus clarkii, were differentiated into three classes according to observations on the Holmes-Blest. Neuropiles which receive the afferents from the mechanoreceptors of the first antenn are located in two different loci in the ganglion. (medial and lateral ant. I. nps.) The glomerular structures in the latter have cores with calcium salt deposition. In the med. ant. I. neuropile, the afferents relating to the phasic inforemation terminated rostrally and the tonic afferents ended caudally. In the lateral ant. I. neuropile, in the latero-dorsal part of the ganglion, a thick bundle of the input fiber formed small glomeruli clustering around the bundle. The center of clusters was not dense as that in the medial ant. I. The calcium salt cores were arranged mostly in scattered fashion.

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EFFECTS OF APAMIN ON THE AFFERENT RESPONSES OF ISOLATED TONIC MUSCLE SPINDLES IN THE SNAKE.
ICHIKI, M. Dept. of Physiol., Sch. Med., Mie Univ., Mie, Tsu 514

Changes of the afferent responses of the isolated tonic muscle spindles in the snake to ramp-and-hold stretches were examined in the bathing solution containing 10 nM order of concentration of apamin. And the results were compared with those of frog's muscle spindles', in which sensory terminals Ca^{2+}-dependent K^+ channels(K(Ca)) have been reported to exist. Apamin is known as a specific blocker of some type of K(Ca). Application of 12.5 nM of apamin to the tonoc spindles increased the inter-spike intervals of the afferents to static(hold) periods of stretches to 10-30 % longer than the normal responses'. The remarkable changes with larger standard deviation were observed at the initial period of static stretches continued just after dynamic(ramp) ones whereas the minimum changes occured in the dynmic responses. Latency to the first spikes after stretches and the rate of spontaneous discharges showed little changes. Frog's spindles immersed in the same concentration of apamin reduced the intervals to about 1/2 of the control responses and increased greatly the regularity during the whole period of static responses while no changes occured in the dynamic period of responses. These results indicate some different mechanism of adaptation may exist in the sensory terminals of muscle spindles of two species.

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IMMUNOHISTOCHEMICAL CLASSIFICATION OF THE INTRAFUSAL MUSCLE FIBERS IN THE FROG MUSCLE SPINDLE.
YOSHIMURA,A., FUJITSUKA,N., ITO,H. and ITO,F.
Dept. Physiol., Nagoya Univ. Sch. Med., Nagoya 466

The intrafusal muscle fibers of muscle spindle in the semitendinosus muscle were classified by immunohistochemical staining and compared with the fiber types on the basis of myosin ATPase reactions after alkaline and acid preincubations in transection of quick-frozen specimens. The antibody to myosin was obtained from rabbit serum which was immunized with myosin purified from rat extensor digitorium longus (EDL) muscle by ion-exchange chromatography (Mono-Q) and by a gradient of KCl concentrations. FICT (labeled rabbit-goat) was used as a secondary antibody and normal rabbit serum was used as the primary antibody for control. Some extra- and intrafusal muscle fibers in the frog reacted with the antibody to rat EDL myosin. Those fibers were correspnded to types 1, 4, 5 and 7 fibers in ATPase activities, which were recognized as fast fibers. It is concluded that some of the frog intrafusal muscle fibers compare to chain fibers in mammalian muscle spindle.

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INTRAMEMBRANE PRTICLE DENSITY OF NON-MYELINATED SENSORY NERVE TERMINALA IN SIMPLE AND COMPLEX FROG MUSCLE SPINDLES. FUJITSUKA,N., FUJITSUKA,C., YOSHIMURA,A. and ITO,F., Dept. Physiol., Nagoya Univ. Sch. Med. Nagoya 466

The density of intramembrane particles (IMPs) in protoplasmic face along the non-myelinated sensory nerve terminals of both complex and simple types of bullfrog muscle spindle was studied. The complex and simple spindles were isolated from semitendinosus and sartorius muscles, respectively. Their afferent responses to ramp-and-hold stretch were recorded and freeze-fracture replicas were made. The complex spindles were composed of sensory terminals with both high (4000 μm^{-2}) and low IMP densities (1700 μm^{-2}), which were found separately on the slow and fast types of intrafusal muscle fiber, respectivley. The simple spindles possessed terminals with low density IMPs. The stretch responses of complex spindle consist of dynamic and static components, whereas the simple type showed mainly the dynamic component. These results suggest that the difference in afferent discharge pattern might be due to the difference in particle density.

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SPINDLE POTENTIAL IS AN IONIC MECHANISM TO PROHIBIT MISFIRING OF THE SENSORY TERMINAL IN FROG MUSCLE SPINDLE. ITO, F., FUJITSUKA, N., YOSHIMURA, A., and SOKABE, M. Dept. Physiol., Nagoya univ. Sch. Med. Nagoya 466

During stretching of muscle spindles isolated from semitendinosus muscles of the frog, Rana catesbeiana, the terminal responses were recorded from an axon placed in an air-gap. When a spindle receptor is stretched in an isotonic sucrose solution containing 1 mM L-arginine, a small depolarizing potential at the end of the dynamic stretch is followed by a larger hyperpolarization, which is abolished by K^+-channel blockers. The experiments of imposed polarizing currents and application of K^+-channel blockers suggest that K^+-channels in an axonal region around the first node act with both orthodromic and antidromic depolarizing currents in normal Ringer's solution. The K^+-channel activation may contribute to the slow adaptation of the spindle potential elicited by orthodrommic depolarization, and may also protect misfiring by decreasing the impedance to antidromic depolarizing currents, as in large muscle action currents.

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HOW ARE VISCERAL POLYMODAL RECEPTORS SENSITIZED BY NOXIOUS THERMAL STIMULATION ? Mizumura, K., Sato, J. and Kumazawa, T. Dept. Nervous & Sensory Functions, Research Inst. Environ. Med., Nagoya University, Nagoya.

It is well known that after thermal injury even warm water is perceived as painful (hyperalgesia), but its mechanism is not yet understood at the sensory receptor level. The polymodal receptor is characterized by responses to noxious thermal stimuli and heat sensitization, and is a candidate transmitting the hyperalgesic state. To know the sensitizing mechanisms of polymodal receptors, effects of heat on bradykinin (BK) responses and effects of prostaglandins (PG) and acetylsalicylic acid (ASA) on heat responses were studied in vitro using testis-superior spermatic nerve preparations excised from dogs deeply anesthetized with pentobarbital (30 mg/kg, i.v.). Heat stimulation and chemical solutions were applied by replacing the Krebs solution bathing the receptive field with pre-warmed Krebs or test solutions. After heat stimulation at 55 °C-30 sec, responses to heat stimulation near the threshold (45 and 48 °C) and to BK 9×10^{-8} M were strongly augmented. PG-E_2 up to 1.4×10^{-6} M (for 2-3 min), had only a weak augmenting effect on the responses to heat near the threshold temperature. Under ASA 550 μM as well clear heat sensitization of the heat response and response to BK was observed, though all the responses to thermal stimuli were smaller than those of the control group without ASA. These results suggest that PG-E_2 might not be a sole agent of heat sensitization.

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NOXIOUS INPUT FROM MASTICATORY MUSCLE TO THE CAUDAL PART OF THE SPINAL TRIGEMINAL NUCLEUS IN RAT. YAMAKAMI, Y., KOJIMA, Y., *TSURUOKA, M. and*MATSUI, Y., The 1st dept. of Prosth. and *Dept. of Physiol. Showa Univ. Sch. of Dent., Tokyo 142

The present experiment was carried out to study the afferent input from the masseter muscle to the caudal part of the spinal trigeminal nucleus in anesthetized rat. By electrical stimulation of the masseter muscle, the evoked potentials having a short latency of 1.4ms(SR) and a long latency of 5.9ms(LR) were recorded. When the masseter muscle was stimulated by various intensities, the range of stimulus intensities in SR which followed the power function was wider than the range in LR, although the exponents of the power function were almost the same. When electrical stimulation of various frequencies was applied to the masseter muscle, the amplitude of SR and LR decreased to 25% and to 1% of the control at 100Hz, respectively. From this result, even if the synaptic delay and the number of synapses were considered, it seems that the difference of latencies between SR and LR depended partly on the conduction velocity of the primary afferent fibers. The amplitude of both SR and LR decreased by morphine (8mg/kg, i.v.) and recovered by naloxone(1mg/kg, i.v.) immediately. This result indicates that both SR and LR contain noxious information from the masseter muscle. The recording area of SR was located at the caudal part of the n. caudalis and the reticular formation, that of LR was located at the rostral part of the n. caudalis.

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Effects of the lesion and stimulation of the rat arcuate nucleus on pain control and electroacupuncture analgesia. HAMBA, M., Dept. Physiol., Sch. Dent., Showa Univ., Shinagawa-ku, Tokyo 142.

To evaluate the possible role of the arcuate nucleus of the hypothalamus (ARH) in the antinociceptive system, two experiments were carried out, using Wistar male rats. 1) The effects of the electrolytic lesion of the ARH on pain control and on the electroacupuncture (EA) analgesia were tested. The mean value of pain intensity rating of the ARH-lesioned rats (n = 6) in the formalin test was significantly higher than that of the sham-operated animals (n = 6), indicating that the lesion produced hyperalgesia to nociceptive stimuli. An analgesia estimated by the suppression degree of the magnitude of m. digastric EMG was induced by EA (3 Hz, 300-600 μA, 15 min) in the control rats, but scarcely observed in the lesioned rats. 2) The effects of the ARH stimulation on the neuronal activity of the lateral hypothalamic area (LHA) were tested. Both the responses of the LHA neurons and the jaw opening reflex induced by tooth pulp stimuli were suppressed by the ARH stimulation (10-45 μA, 1-3 Hz,30 s). The ARH region thus appears to be one of the important parts in the central pain control system.

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INHIBITION OF DORSAL HORN NEURONAL DISCHARGES TO NOXIOUS HEATING BY Aβ AND Aδ AFFERENT NERVE IMPULSES. TSURUOKA, M., LI, Q.J*, MATSUI, A and MATSUI, Y., Dept. of Physiol. Showa Univ. Sch. of Dent., Tokyo 142

Inhibition of noxious thermal input from rat tail by Aβ and Aδ afferent nerve impulses was investigated. Eighty-four convergent dorsal horn neurons were recorded at the sacral and the coccygeal levels in anesthetized intact rats. When an Aβ fiber was stimulated at the hind limb for 15 min, the activity of 17/21 of neurons was inhibited to about 30% of the control. The activity of 14/21 of other neurons we tested was inhibited to about 40% of the control by Aδ fiber stimulation applied to the hind limb for 15 min. Simultaneous stimulation of both Aβ and Aδ fibers resulted in the inhibition of the activity of all 10 neurons. These inhibitory effects produced by Aβ or Aδ fiber stimulation were not reversed by naloxone (1mg/kg, i.v.). When Aβ or Aδ fiber stimulation was applied during noxious heating, nociceptive discharges were not inhibited in all neurons we tested (14 of 14 neurons in Aβ fiber stimulation, 12 of 12 neurons in Aδ fiber stimulation). When Aβ and Aδ fiber stimulation was applied to the same neuron alternately, the following three types of convergent dorsal horn neurons could be distinguished: Type I, neurons inhibited by only Aβ afferent nerve impulses; Type II, neurons inhibited by only Aδ afferent nerve impulses; Type III, neurons inhibited by both Aβ and Aδ afferent nerve impulses.

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IS THE TOOTH PULP INNERVATED BY MESENCEPHALIC TRIGEMINAL NUCLEUS CELLS? AMANO, N., YOSHINO, K., ANDOH S. AND KAWAGISHI, S. Dept. Oral Neurosci., Kyushu Dental College, Kitakyushu, 803

The purpose of this study is to examine possible dual innervation of tooth pulp from the mesencephalic trigeminal nucleus (MTN) as well as trigeminal ganglion (TG) in the cat using retrograde transport of horseradish peroxidase (HRP). Great care was taken to avoid a leakage of HRP through the apical foramen into periodontal tissue and to minimize inhibition of axonal transport of HRP due to acute pulpitis in the tooth applied with HRP. Pulp chamber of the left lower canine in 8 adult cats was opened with a dental air turbine under water cooling. Following partia pulpotomy, 1—2μl of 30% HRP saline solution soaked into gelfoam was placed in each pulp chamber. The openings were sealed with dental glass-ionomer cement. Immediately after the surgery and throughout the subsequent 3-day survival period, 6 cats were subjected to systemic administration of anti-inflammatory drug, prednisolone, whereas the remaining 2 control cats were not. Histological sections were processed according to TMB technique by Mesulam. As shown below, only in 6 prednisolone-treated cats many HRP-labeled neurons were observed in both MTN and TG on the side ipsilateral to the HRP application.

Cat No.	1	2	3	4	5	6	7	8	
Teeth applied with HRP	C	C	C	C	C	C	"C	C+M	C: canine
Prednisolone treatment	×	×	○	○	○	○	○	○	M: molars
No. of labeled TG cells	24	25	77	81	82	149	60	933	"C: incom-
No. of labeled MTN cells	0	0	23	26	33	45	40	92	plete root
Ratio of TG/MTN cells	—	—	3.3	3.1	2.5	3.3	1.5	10.1	formation

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RESPONSE PROPERTIES OF PERIODONTAL MECHANOSENSITIVE THALAMIC NEURONS IN THE CAT.

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Periodontal mechanosensitive (PM) units were investigated to clarify the information processing mechanism of somesthetic sensation in the thalamus of cats anesthetized with chloralose (40mg/kg, i.v.). Three hundred and fifty-five PM units responsive to mechanical stimulation of the teeth were recorded from the medioventral aspect of the VPM nucleus. Of all the units, 155 (43.7%) were observed to be slowly adapting. The directional selectivity of these slowly adapting units was duller than that of the primary afferent neurons, most of which were also slowly adapting. Of all the units, 45 (12.5%) had receptive fields on a single tooth. This finding was appreciably different from that in the primary afferents, 98.4% of which were single tooth units. Eigthy-eight units (24.9%) responded only to ipsilateral mechanical stimulation. The response properties of these ipsilateral units were relatively similar to those of primary afferent neurons. The ipsilateral units had sharper directional selectivity, a lower stimulus threshold and less polymodality than contralateral units. These results suggest that ipsilateral thalamic PM neurons might receive less convergent fibers than contralateral neurons.

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NEURONAL ACTIVITY IN THE VPM OF THE THALAMUS IN RESPONSE TO MECHANICAL TOOTH STIMULATION.

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We have examined the response properties of the periodontal mechanosensitive neurons and their distribution in the posteromedial ventral nucleus (VPMpc) of the cat's thalamus. Experimentals were carried out under ketamine anesthetic (initial dose 35mg/kg, i.p., maintenance dose 2mg/kg i.p.). The periodontal mechanosensitive (PMS) in the thalamus were influenced in the direction of the mechanical tooth stimulation. These neuronal discharges were mainly of the rapidly adapting type (86%). PNS neurons were located mainly in the lateral parvocellular part of the VPM (VPMpcl). A small number of neurons were located in the medial parvocellular part of the VPM (VPMpcm) and the monocellular part of the VPM (VPMmc). Many neurons responded to the mechanical tooth stimulation of canine teeth and whole teeth. Thresholds of the PMS units of the slowly adapting type were lower than those of the rapidly adapting type. PMS neurons received input from tongue, gum, lip, facial skin, whisker, mucosal zone of the palatum and mucosal zone of the bucca.

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ANALGESIA AND PLASMA β-ENDORPHIN-LIKE IMMUNOACTIVITY IN COMPOUND 48/80-INDUCED HYPOVOLEMIA OF THE RATS. IZUMI, H., Dept. Physiol., Tohoku University School of Dentistry, Seiryo-Machi 4-1, Sendai 980,

The effects of subcutaneous (s.c.) administration of compound 48/80 (a well known histamine liberator) on latency to thermoalgesic stimulus, hematocrit (Hct) and plasma levels of beta-endorphin-like immunoreactivity (β-END-LI) were investigated in male rats. The s.c. administration of compound 48/80 in doses ranging from 0.5 to 5.0 mg/kg into the rats produced significant analgesia in the hot plate test and increased Hct in a dose-dependent manner. Concomitant variation was observed between the analgesia and the increase of Hct. This analgesic effect, but not the increase of Hct, was diminished by pretreatment with the opiate receptor antagonist, naloxone (5 mg/kg, s.c.). A significant increase of plasma β-END-LI was observed by s.c. injection of compound 48/80. Together with a previous finding that compound 48/80 induced-hypovolemia increases the renin release from kidney and then causes water intake in the rats, it is suggested that s.c. administration of compound 48/80 induced analgesia mediated through stimulation of an opioid system, may be closely related to stimulation of the renin-angiotensin system.

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ORAL REPRESENTATION BY MECHANORECEPTIVE NEURONS AT RAT CEREBRAL CORTEX. MURAYAMA, N., MIKI, K., ITO, S. AND OGAWA, H. Dept. of Physiol., Kumamoto Univ. Med. Sch., Honjo 2-2-1, Kumamoto 860

While applying mechanical stimulation to the entire oral cavity, we recorded mechanoreceptive neurons at the cerebral cortex of SD rats. Of the 284 neurons recorded, 29, 178 and 77 were found in the primary somatosensory area (PC area), the granular insular area (GI) and agranular insular area (AI), respectively, and their receptive fields (RFs) were examined. Surveyed regions of PC, GI and AI areas were divided into several blocks, two dimensions and averaged scheme of the receptive properties were studied in each block. A majority of the neurons at the rostro-dorsal part of the lower PC had an RF contraterally on a single tissue, the lip in particular, but most of the neurons in the ventro-caudal part had RFs bilaterally on two or three tissues of the lip and oral cavity. Although a majority of neurons had RFs on the anterior tongue instead of the lip, such a trend of variations of RF characteristics along the dorso-ventral and rostro-caudal axes were noticed in both GI and AI areas, except for a rostro-ventral part of AI area. In the latter region, some neurons had RFs contralaterally on the lip. No significant chang of the receptive properties of neurons was evident across the cortical layers of PC, GI and AI areas.

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ANATOMICAL AND FUNCTIONAL ORGANIZATION OF THE CORTICAL GUSTATORY AREA IN HAMSTERS. KITAMURA, R.**, KIYOMITSU, Y.*, MATSUO, R. AND YAMAMOTO, T., Depts. Oral Physiol., *Dental Anesthe. and **Oral Surg., Osaka Univ. Fac. Dent., 1-8 Yamadaoka, Suita 565.

Mapping of evoked potentials following electrical stimulation of the chorda tympani and glossopharyngeal nerve showed that the cortical gustatory area (CGA) existed in the agranular insular cortex just dorsal to the rhinal sulcus near the middle cerebral artery. Bilateral lesions of the CGA attenuated or disrupted the conditioned taste aversion that had been acquired preoperatively, indicating an important role of this area in some cognitive processes of taste. Experiments using anterograde and retrograde transport of WGA-HRP showed that neurons in layer VI sent axons to the thalamic and pontine taste relays, while layer V, to the thalamic, pontine, and bulbar taste relays, amygdala, and contralateral CGA. The responses of 57 CGA neurons to the four basic taste stimuli were recorded in urethane-anesthetized hamsters. Neurons responding best to sucrose tended to be located rostrally, and those best to NaCl, caudally. Judging from the breadth of responses to the four tastes, and across-neuron correlation coefficients, responsiveness of neurons in layer V is more narrowly tuned than that in layers II-IV and VI.

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Somatotopic organization of the facial lobe in the channel catfish, Ictalurus punctatus. Hayama T. and Caprio J.* Dept. of Zool. & Physiol., Louisiana State Univ., Baton Rouge, 70803 USA

We histologically studied lobule structure of the facial lobe (FL) of the channel catfish and examined tactile input into lobules and the intermediate nucleus of the facial lobe (nIF). The FL is composed of 6 lobules, receiving segregated excitatory input from the medial and lateral mandibular barbels, maxillary barbel, nasal barbel, face-flank and pectral fin, respectively. The caudalmost portion of the FL having no obvious lobule structure received input from the lips and the oral cavity. The antero-posterior axis of the face-flank and the proxima-distal axis of the barbels were represented postero-anteriorly in the FL. In the rostro-dorsal portion of the nIF, neurons responded to tactile stimulation or deflection of the barbels. Neurons having a large inhibitory receptive field were also found. In the caudo-ventral portion, neurons receiving input from the lips, teeth and the oral cavity were arranged in the dorso-ventral direction. The present findings indicate that the FL of the channel catfish is highly organized to locate tactile stimuli on the external body surface.

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EFFECTS OF ELECTRIC CURRENT STIMULATION ON THE PERIODONTAL MECHANORECEPTOR OF THE MAXILLARY CANINE TOOTH OF THE CAT. TABATA,T. AND KARITA,K. Dept. Physiol. Tohoku Univ. Sch. Dent. 4-1 Seiryo-machi, Sendai 980

Periodontal mechanoreceptors fired when an electric pulse was administered through a pair of stimulus electrodes; one electrode was inserted in the dental pulp cavity, the other on the lateral mucosa of the canine tooth root. Six out of ten units tested were excited by an electric current when stimulus electrodes were arranged as pulp-negative and mucosa-positive. Others were fired by reversal current. The polarity of the electric current for exciting the receptor did not change when the mucosal electrode was moved around the canine tooth. In 11 cats, the alveolar bone, covering the lateral aspect of the canine tooth root, was pared away until it became a thin and transparent layer of bone. The mucosal stimulus electrode was applied to the thin layer of bone just above the receptor site or the surrounding area. The current direction for exciting the receptor was frequently reversed when the stimulus electrode was moved more than 2 mm away from the receptor site. These findings suggest that the stimulus direction of electric current results from the orientation of the receptor in the periodontal membrane.

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THE EFFECTS OF MUCOSAL STIMULATION ON THE PERCEPTION OF MANDIBULAR POSITION IN DENTURE WEARING SUBJECTS.

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The effect of mechanical stimulation of the denture-supporting mucosa on the perception of mandibular position (MP) was studied with five edentulous subjects. In order to provide mucosal stimulation of different intensities, six types of punctate plates with various number of raised points were prepared. And each of these stimulus plates was fixed to the mucosal surface of the anterior part of the upper denture base. The MP was altered by adjustable hydraulic jacks attached to the lower denture base. The MP which began to perceive as high (HMP) was measured by using these devices. When the incisal palatal mucosa was subjected to increased mechanical stimulation, the HMP was shifted toward the jaw-closed position in all subjects. Furthermore, the increase in the shift of the HMP was correlated with the increase in the stimulus intensities plotted on a logarithmic scale. On the other hand, the reproducibility of the HMP was increased according to increases in stimulus intensity. From these findings, it was suggested that the mechanoreceptors in the denture-supporting mucosa may be involved in the perception of the MP by providing the information as to both the distribution and the intensity of the bite pressure.

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CENTRIFUGAL INFLUENCE FROM THE CORTICAL GUSTATORY AREA ON NEURONAL ACTIVITIES OF THE PARABRACHIAL NUCLEUS IN RATS. KIYOMITSU, Y.*, YAMAMOTO, T., MATSUO, R. AND KITAMURA, R.**, Depts. Oral Physiol., *Dental Anesthe. and **Oral Surg., Osaka Univ. Fac. Dent., 1-8 Yamadaoka, Suita, Osaka 565.

Mode of interconnections between the cortical gustatory area (CGA) and the parabrachial nucleus (PBN) was studied neuroanatomically, and then effects of electrical stimulation of the CGA on activities of PBN neurons were examined electrophysiologically in Wistar male rats anesthetized with urethane. Tracing of anterograde and retrograde transport of WGA-HRP, which was injected into the CGA in animals with lesions of either the dorsal tegmental area (DTA) or pyramidal tract (PT), revealed that majority of PBN-CGA and CGA-PBN fibers passed through the DTA, while only a small portion of CGA neurons reached the PBN via the PT. Of 26 PBN neurons which responded to either one or more of the five taste solutions (sucrose, NaCl, HCl, quinine hydrochloride, and monosodium L-glutamate), 5 showed facilitatory (F) responses, 2, inhibitory (I), 5, F-I, and 1, I-F responses to electrical stimulation of the ipsilateral CGA. Some of these PBN neurons might mediate cortically induced salivary secretion, since micro-injection of glutamate into the PBN induced salivary secretion, and increased the secretion which was elicited by electrical stimulation of the CGA. Lesion experiment suggests that axons of CGA neurons responsible for the salivation pass through the PT.

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PARTIAL DEFFICIENCY OF THE ABILITY TO PERCEIVE "SWEETNESS" DETERMINED BY THE dpa GENE IN MICE. SAKO, N., NINOMIYA, Y., AND FUNAKOSHI, M. Sch. Dent., Asahi Univ., Gifu 501-02

Lack of the ability to perceive "sweetness" of D-phe discovered in mice was inherited as a unit autosomal recessive. Linkage tests indicated that the gene(designated as dpa) located on the chromosome 4(Ninomiya et al., 1986). The present study examined whether or not the dpa gene would also affect taste sensitivity to the other D-amino acids. Behavioral responses to 7 D-amino acids measuring generalization patterns from a conditioned aversion of one of 7 D-amino acids to various taste substances were not significantly different between C57BL (showing "sweet response" to D-phe; genotype Dpa/Dpa) and BALB mice (no "sweet response" to D-phe; genotype dpa/dpa). In both strains, aversion conditioned to D-try, -leu, -met, -val or -his typically generalized to sucrose. Correspondingly, in both strains, neural responses of the chorda tympani to D-try, -leu, -met, -val or -his were typically suppressed by the lingual treatment of Pronase which is known as a proteolytic specifically inhibits the sweet taste response. These results indicate that the lack of "sweet response" determined by the dpa gene is probably selective to D-phe.

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EARLY OCCURRENCE OF SUPPRESSION OF CHORDA TYMPANI RESPONSE TO NaCl, CAUSED BY AMILORIDE IN DEVELOPING RAT EXPOSED TO SUCROSE. YAMADA, T., HUKUSHIMA, Y. AND KIMOTO, M. Physiol. Lab., Japan Women's Univ., Bunkyo-ku, Tokyo 112

In rats applied to their tongues a filter paper soaked either with 40% sucrose (Suc. group) or with distilled water (D.W. group) from the 2nd postnatal day and normal rats (C. group), the integrated responses of the chorda tympani nerve to 0.3M NaCl, NH_4Cl, KCl, 0.3M, 0.5M sucrose, $3x10^{-3}$M HCl, quinine hydrochloride and also responses to NaCl after lingual application of 250uM, 500uM amiloride were recorded on the 14th, 17th, 19th-21st, 23rd and 26th postnatal day.

The magnitude of responses in the ratios of NaCl, LiCl and sucrose to HCl was larger in Suc. group than in the other groups on the 19th postnatal day. The responses to NaCl after amiloride were unaffected in all rats aged 14 days; however they were suppressed by 75-65% during the period of 17-23 days in Suc. group, 19-26 days in D.W. group and 23-26 days in C. group. The response ratio $NaCl/NH_4Cl$ concomitant with development correlated closely with the percent of NaCl suppressed by amiloride. These results indicate the increase of chorda tympani nerve response to NaCl in developing rat exposed to sucrose results from the development of postnatal process of the peripheral taste system.

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ROLE OF THE RECEPTOR AND BASOLATERAL MEMBRANES OF TASTE CELL IN WATER RESPONSE.

OKADA, Y., MIYAMOTO, T. AND SATO, T.
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Ionic mechanism of generation of the receptor potential in a bullfrog taste cell elicited by deionized water was examined with an intracellular recording technique. The taste cells in the proximal portion of the tongue generated a depolarizing receptor potential in response to water. The magnitude of the receptor potential decreased as the concentration of Cl^- added to water was increased. The reversal potential for the receptor potential was almost equal to the eqilibrium potential of Cl^- across the receptor membrane of taste cell. When interstitial Na^+ or Cl^- was removed, the water-induced depolarization disappeared. Interstitial 1 mM furosemide decreased the receptor potential to 20% of the control. These results suggest that an electroneutral Na^+/Cl^- cotransport in the basolateral membrane of taste cell accumulates Cl^- inside the cell, and that the receptor potential elicited by deionized water may be related to a secretion of Cl^- across the taste receptor membrane.

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POTASSIUM CHANNEL CURRENTS IN THE SMOOTH MUSCLE CELLS OF GUINEA-PIG TAENIA COLI. YAMAMOTO, Y., HU, S. L.,* and KAO, C. Y.* Dept. Physiol., Nagoya City Univ. Med. Sch., Nagoya 467, Japan, and *Dept. Pharmacol., SUNY Downstate Med. Ctr., Brooklyn, N.Y. 11235, U.S.A.

Using patch-clamp method, macroscopic and single K channel currents were studied in the smooth muscle cells dispersed from the guinea-pig taenia coli. Macroscopic K current had both a Ca^{2+}-activated component and a voltage-dependent component which was resistant to external Co^{2+}. The reversal potential was -84 mV. When studied in the presence of external Co^{2+}, the activation followed n^2 kinetics, with a voltage-dependent time constants of 10.6 ms at 0 mV and of 1.7 ms at +70 mV. During a long depolarization, K channel current inactivated with 2 exponential components leaving some non-inactivating residue. In the single channel recording, 3 types of K channels were observed, among which the channel with the largest conductance (150 pS in physiological K^+ concentrations) and $[Ca^{2+}]_i$-sensitivity contributed to the most outward current observed in the whole-cell clamp experiments. Supported by NIH grant HD00378.

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MULTIPLE TYPES OF CA CHANNEL CURRENTS IN SMOOTH MUSCLE CELLS ISOLATED FROM GUINEA PIG TAENIA COLI. YOSHINO, M., SOMEYA, T. AND YABU, H. Dep. Physiol., Sapporo Med. Coll., Sapporo, 060

Unitary Ca channel currents were studied from enzymatically isolated smooth muscle cells of guinea-pig taenia coli by applying the cell-attached patch clamp techniques with 50 or 100 mM Ba as the charge carrier. Three types of Ba currents were identified. Two of them exhibited properties similar to those type L and T Ca channels which had been characterized in neuronal and cardiac cells. L type channel activated at 0 mV and peaked at potentials near 30 mV. T type channel activated at -30 mV. The third type of Ba current whose conductance was intermediate between L and T types of Ca channels activated at -10 mV and had slow inactivating kinetics. Effects of DHP Ca antagonist and agonist on L type channel were investigated. Nifedipine (0.2 μM) increased the rate of mode 2 sweeps and resulted an increase of averaged Ba currents. While, nifedipine (2 μM) increased the rate of mode 0 sweeps and resulted a decrease of averaged Ba currents. Bay K 8644 acted as a Ca channel antagonist and agonist depending on the holding potentials.

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ACTIONS OF DBCAMP ON BARIUM IONIC CURRENT OF GUINEA-PIG VAS DEFERENS SMOOTH MUSCLE. INOMATA, H. Dept. Applied Physiol., Sch. Med. Tohoku Univ., Sendai 980

Effects of dibutyryl cyclic AMP (DBcAMP) on Ba ionic currents were investigated in voltage clamped preparation of the guinea-pig vas deferens in Na-free tetraethylammonium (TEA) medium containing 2.5- 5 mM Ba ions. Inward Ba ionic current through Ca channels was consisted of a fast transient component followed by a slow long-lasting component. DBcAMP showed a differential effects on the two components; it caused an increase in the amplitude of the former component current at lower voltage, but a reduction at higher voltage, while failing to change the latter one. It is suggested that the long lasting current may be independent of cAMP memtabolism. On the transient Ba ionic current (I_{Ba}) during exposure to DBcAMP, the reversal potential was shifted to less positive voltage. The slope conductance was increased appreciably in voltage up to the maximum I_{Ba}, wheares the maximum conductance was not affected. Time constants for inactivation as well as for activation were significantly greater over whole voltage range.

These observation on Ba ionic machinery in response to DBcAMP are found to be contradictory to the fact that an augumentation of inward Ca ionic current by DBcAMP was observed, as previously reported eleswhere.

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Actions of the Ca antagonist on single Ba currents in smooth muscle cells of longitudinal muscle of the rabbit ileum. Kitamura, K., Inoue, Y.* and Kuriyama, H. Department of Pharmacology, Faculty of Medicine, Kyushu University, Fukuoka 812, Japan.

The single channel Ba current was recorded from enzymatically dispersed single smooth muscle cells, using the cell-attached patch clamp technique. Various concentrations of $BaCl_2$ (<100mM) were filled in the pipette and high-K solution (0.1mM EGTA) was superfused in the bath. Values of the single channel conductance depended on the concentration of Ba and values observed in the presence of 100mM $BaCl_2$ were about 25pS (Km=18mM; Vmax=42pS). Open state probabilities in individual traces (150ms in duration and depolarisation to 0mV from the holding potential of -60mV) varied and could be classified into three different states depending on the open state probability ($p < 0.2$; $p \fallingdotseq 0.4$; $p \risingdotseq 0.8$). Nifedipine (0.3μM) reduced the mean open time of the single Ba current and increased the number of traces with no channel opening ("blank"). Latency of the first incidence of the channel opening was not significantly affected by nifedipine, however, the period between the times at the last incidence of channel closing and the end of the depolarisation pulse was markedly increased. These results suggest that nifedipine inhibits Ca channels in an open state as well as those in an inactivated state. Our data also show no evidence for another type of the Ca channels with a small single channel conductance in the smooth muscle cells of the rabbit ileum.

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EFFECTS OF ADENOSINE ON PHOSPHORUS COMPOUNDS IN THE TAENIA OF GUINEA-PIG CAECUM. NAKAYAMA, S., TOMITA, T. AND WATARI, H. Dept. Physiol., Sch. Med., Nagoya Univ., Nagoya 466 and Natl. Inst. Physiol. Sci., Okazaki 444

In the isolated preparations of guinea-pig taenia caeci, intracellular phosphorus compounds were measured with 31P-NMR. Addition of adenosine (1 mM) to normal solution increased phosphocreatine (PCr), probably resulting from relaxation due to purinergic stimulation, but during a prolonged exposure for more than 60 min, ATP was slowly increased by about 10%, accompanied by a concomitant decrease in PCr to a similar degree. After severe depletion of high energy phosphate copmpounds by causing K contracture under hypoxic condition or in the absence of glucose, ATP recovered only to 75% in normal, or in Ca-free, solution, although a complete recovery of PCr was observed. Application of adenosine (1 mM) produced a nearly perfect recovery of ATP in 60 min. The facilitating effect of adenosine on the recovery process was also observed in K-contracture. The results suggest that ATP was hydrolysed and deaminated to inosine monophosphate or hypoxanthine, causing a decrease in adenylate pool after excessive energy consumption.

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EFFECTS ON CARBACHOL-INDUCED CONTRACTIONS IN THE CIRCULAR MUSCLE OF GUINEA-PIG STOMACH. SYED, M., NAKAYAMA, S., UNO, Y. AND TOMITA, T. Dept. Physiol., Sch. Med., Nagoya Univ., Nagoya 466

When carbachol (CCh, 30 μM) was applied for 4 min at 20 min intervals in Mg-free medium containing 2.4 mM Ca, the response was slowly reduced to 60-70% in 100 min. On the other hand, Mg removal markedly increased the samll contraction produced by 1 μM CCh in the presence of a low concentration of Ca (24 μM), probably by increasing Ca permeability. The small tonic contraction could be repeatedly produced by 30 μM CCh in the absence of Ca for several hrs without any reduction. When Mg was also omitted, this response slowly disappeared in about 100 min. Intracellular free Mg concentration, estimated from P-31 NMR, remained constant in Mg-free solution containing 2.4 mM Ca, whereas it decreased from 0.3 to 0.01 mM during 100 min exposure to Mg- and Ca-free solution. Readmission of Mg (more than 0.3 mM), still in the absence of Ca, recovered the CCh-response. CCh-responses also reappeared on readmission of Ca only, but for the recovery of spontaneous activity, application of both Ca and Mg was necessary. Mg ions are playing important roles both in the plasma membrane and inside the cell.

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EFFECTS OF INTRACELLULAR pH ON Ca-ACTIVATED K CHANNEL IN RABBIT TRACHEAL SMOOTH MUSCLE. KUME, H., TOKUNO, H. AND TOMITA, T. The 2nd Dept. Int. Med., and Dept. Physiol., Sch. Med., Nagoya Univ., Nagoya 466

In the inside-out patch of smooth muscle cells freshly disparsed from the rabbit trachea, the sensitivity of Ca-activated K channel to Ca^{2+} was strongly affected by intracellular pH. When the open probability of the channel was plotted against intracellular Ca concentrations ($[Ca]_i$), alkalinization shifted the curve to the left and make it steeper, whereas acidification had opposite effects. The $[Ca]_i$ for a half activation was 0.02, 0.3 and 5 μM at pH 8.0, 7.4 and 6.8 respectively, i.e. the change in hydrogen concentration ($[H^+]_i$) was equvalent to $\sqrt{[Ca^{2+}]_i}$. The kinetic analysis indicated that the main effect of acidification was to decrease the duration of open state. The intracellular pH also modified the relationship between open probability and membrane potential. Acidification shifted the relationship in a depolarizing direction, and this effect became stronger with decreasing $[Ca]_i$. The effects of pH can be partly explained by competition between H^+ and Ca^{2+}, but in addition to this, H^+ seems to affect the gating mechanism of the channel, probably by changing the affinity to Ca^{2+}.

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EFFECTS OF CALMODULIN ANTAGONISTS ON Ca-ACTIVATED K CHANNEL IN SMOOTH MUSCLE. TOKUNO, H., KUME, H. AND TOMITA, T. Dept. Physiol., and The 2nd Dept. Int. Med., Sch. Med., Nagoya Univ., Nagoya 466

Ca-activated K channels in smooth muscle are highly sensitive to intracellular Ca. In the guinea-pig taenia caeci, a possibility of calmodulin involvement in the activation of this channel was examined with the inside-out patch clamp. When the channel had been fully activated by more than 1 μM Ca, a calmodulin antagonist , W-7 (1-30 μM) reduced the open probability dose-dependently, the decrease being by 50% at 30 μM. This was mainly due to shortening of the open time. The kinetics of the closing process was not significantly affected. The single channel conductance was only slightly reduced, and this probably results from a high frequency activity (flicker) of the channel caused by W-7. On the other hand, when the open probability was very low at a low Ca concentration, W-7 increased the open probability. Another calmodulin antagonist, trifluoperazine had essentially the same effect as W-7. Calmodulin (1 μM), applied intracellularly was ineffective. It is likely that calmodulin antagonists are not blocking the channel activation caused by Ca, but directly modifying the channel kinetics.

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MEASUREMENT OF REDUCING ACTIVITY IN SMOOTH MUSCLE. KATAYAMA,N., NAKAYAMA, S. AND TOMITA, T. Dept. Physiol., Sch. Med., Nagoya Univ. Nagoya 466

Reduction of ferricyanide caused by the guinea-pig taenia caeci was measured using a luminescence spectroscopy (Union Giken, MCPD-100). Ferricyanide concentration was measured as changes in optical density of the solution at 420 nm taking 700 nm as a reference wave length. Ferricyanide (0.5 mM) was slowly reduced by itself at a rate of 1.6 ± 0.1 nmoles/min/ml, but in the presence of the preparation, the rate was markedly increased to 143 ± 14 nmoles/min/g tissue (n = 15). This was comparable with the values reported for the liver (216) and for the heart (77.8 nmoles/min/g). Reduction of ferricyanide without preparation was not affected by EDTA (0.4 mM), whereas the increase in reduction caused by the preparation was significantly (about 50%) decreased by EDTA. On the other hand, NaCN (1-4 mM) had no detectable effect. It was concluded that the smooth muscle has a reducing activity and that this is not related to respiration, but to some process in the plasma membrane in which metal ions are involved.

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TWO ISOPRENALINE SENSITIVE MECHANISMS REGULATING CYTOPLASMIC CA IONS IN THE SMOOTH MUSCLE OF THE GUINEA-PIG VAS DEFERENS. FUKUSHI, Y. & WAKUI, M.* Dept. of Applied Physiol. and Dept. of Physiol.*, Sch. Med., Tohoku Univ., Sendai 980

In order to obtain some information about the mechanism by which intracellular Ca^{2+} of smooth muscle cells can be diminished in quantity after the muscle excitation, the time course of contractions evoked by currents was examined under various conditions. The magnitude of evoked contraction was different in different intensity of stimulus current, but the time to peak and the time constant of decay of contraction were nearly constant. Isoprenaline (ISO) reduced the resting tension and magnitude of current-induced contraction, and shortened the time to peak and the time constant of decay. On the other hand, the effects of low temperature on the tension were reverse of ISO. In this cold condition, ISO brought back the resting tension and the magnitude of the evoked contraction to the normal or rather below the normal, but only slightly affected the time to peak or time constant of decay. It is concluded that in this tissue, the mechanisms regulating the cytoplasmic Ca concentration at the resting state and active state are different; ISO can accelarate mainly the former one. A possibility that a part of Ca ions entering into cytoplasm during excitation of the membrane is soon lost by ISO-sensitive mechanism before reaching the contractile machinery was also presented.

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INFLUENCE OF EXTERNAL MAGNESIUM ION ON THE BETA-ACTION IN RAT MYOMETRIUM. MARUTA,K. AND OSA,T. Dept.of Physiol.,Yamaguchi Univ.Sch.of Med.,Ube 755

The uterine longitudinal muscle of estrogen-treated rat showed phasic contraction in Locke solution when electric stimulation was applied. Isoprenaline (10^{-11}-10^{-8}M) and dibutyryl cyclic AMP (DBcAMP,0.1-0.8mM) suppressed the phasic contraction, and the inhibition was potentiated in the presence of 0.6mM Mg. Membrane potential was -61mV, and action potential was composed of spike and plateau. Isoprenaline hyperpolarized the membrane potential accompanied with decrease in membrane resistance, and inhibited the action potential. These effects were augmented by external Mg ion. DBcAMP had the same effects on membrane property as isoprenaline, and external Mg ion enhanced the inhibition of action potential. Relaxation by isoprenaline of K-contracture was enhanced by external Mg, while that by DBcAMP was not affected. Forskolin (0.1-3μM) behaved as DBcAMP except that hyperpolarization and membrane resistance decrease were more augmented by Mg. It was assumed that external Mg ion could affect receptor-agonist interaction and cAMP-mediated inhibition of membrane in β-action.

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INCREASED Ca^{2+} SENSITIVITY UNDER STIMULATION OF α_1-ADRENOCEPTOR IN CONCENTRATIONS OF ISOLATED PORTAL VEINS FROM CHRONIC PORTAL HYPERTENSIVE RATS. YOSHIMURA, T. AND ARITA, M. Dept. of Physiol. Medical College of Oita, Oita 879-56

We studied contractile properties of portal veins isolated from chronic portal hypertensive rats (PHR), a model for liver cirrhosis made by repeated subcutaneous injections of CCl_4 (2mg/kg) twice weekly for over 45 weeks. Portal venous pressure in vivo was significantly higher in PHR than control (NWR). A pair of portal veins from PHR and NWR were mounted longitudinally in an organ bath and perfused with high K^+ (86.4mM) Tyrode's solution with various norepinephrine (NE, 0.1-100μM) and $[Ca^{2+}]_o$ (0-5.4mM) concentrations. The isometric tension was measured by a strain-gauge. In the presence of NE (10μM), the Ca^{2+} sensitivity of the tonic contraction increased both in PHR and NWR preparations. However, the increase was more pronounced in PHR and was completely reversed in the presence of α_1-adrenoceptor blocker, prazosin (0.1μM). The sensitivity to NE per se was not increased in PHR preparations. The rate of release and uptake of intracellular Ca^{2+} seemed identical in both preparations. Results suggest that the PHR preparations have a higher affinity to external Ca^{2+} in the presence of NE which may be additional factor contributing to elevation of portal blood pressure in rats with chronic liver cirrhosis.

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MITOCHONDRIAL CREATINE KINASE (MtCK) ACTIVITIES IN SMOOTH MUCLES. ISHIDA, Y., HONDA, H., HIGUCHI, T.*[1], Mitsubishi-Kasei Institute of Life Sciences, Machida, Tokyo 194 and [1]Fac. of Pharm. Sci., University of Tokushima, Tokushima 770

We previously reported that phosphocreatine (PCr) production of the guinea pig taenia caeci is highly dependent on oxidative metabolism (Ishida & Paul, 1986, 1987). To further investigate the link of PCr production to oxidative metabolism, MtCK activities of the taenia were determined in comparison with those of rabbit thoracic aorta, rat heart and rat liver. Mitochondria were isolated by the modified method of Tyler & Gonze (1967) using a centrifugator. Mitochondria were incubated in a solution containing PCr, ADP, AMP, $MgCl_2$ and Tris at 30 °C, pH 7.4 and yielded amounts of ATP were determined by using luciferase. Isolated mitochondria did not possess Na,K-ATPase activities. MtCK activities were approximately 900 nmol/min/mg Mt protein for the taenia and 300 for the aorta. MtCK activities for rat heart and liver were 2000 and 20 nmol/min/mg Mt protein which were in a reported range (Jacobs & Lehninger, 1973). These results suggest that PCr of the taenia is produced through the mitochondrial "PCr shuttle" under aerobic conditions. Relatively greater MtCK activity of the taenia presumably represents the fact that PCr and ATP in the taenia do not distribute in a simple Lohmann reaction equilibrium.

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Ca-ACTIVATED NON-SPECIFIC CATION CHANNEL IN VASCULAR SMOOTH MUSCLE CELL. Kokubun, S., Saigusa, A*., Dept. Physiol. Dept. Internal Medicine* The Jikei Univ. Sch. of Med. 3-25-8 Nishi-shinbashi Minato-ku, Tokyo 105

Although it is well known that the tension development due to noradrenaline is followed by the graded depolarization of the membrane, the mechanisms underlying the membrane depolarization remains obscure. In this study we investigated Ca-activated non-specific cation channels in cultured vascular smooth muscle cell which may contribute the membrane depolarization when the intracellular Ca concentration increases. By incubation of cells in the Tyrode solution with 50-100uM noradrenarine, we observed the channel activity. The current was inward at resting membrane potential. The channel activity remains in inside-out patch in Tyrode solution with Ca. However, perfusion of Tyrode with 1mM EGTA inactivated the channel. Apparent Kd for Ca was about 0.1mM. The channel showed inward-rectification in symmetrical 150mM NaCl. The conductance of the channel in such a condition was 34 pS and 25 pS in negative and positive potentials, respectively. Potassium ions are equally permeable as Na ions, though Ca is not detectably permeable.

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POSSIBLE CONTRIBUTION OF ARACHIDONIC PRODUCTS TO THE ADRENALINE RESPONSE IN THE CIRCULAR MUSCLE OF GUINEA-PIG STOMACH. TSUGENO, M., KABEYA, R., NAKAYAMA, S. AND TOMITA, T. Dept. Physiol., Sch. Med., Nagoya Univ., Nagoya 466

In the circular muscle of guinea-pig stomach, adrenaline, in the presence of propranolol, usually produced a triphasic response; an early relaxation, a contraction, and a late slow relaxation. The last phase became clear with increasing concentrations. Inhibitors of phospholipase A_2 (meclofenamate or quinacrine) or cyclooxygenase (indomethacin or acetylsalicylate) increased the contractile response and prolonged the response by blocking the slow relaxation, and this was often accompaniecd by a decrease in muscle tone. The contractile response was markedly inhibited by prazosin, not by yohimbine, suggesting involvement of the α_1-adrenoceptors. Prostaglandin (PG) $F_{2\alpha}$ and E_2 produced a sustained contraction. In the presence of $PGF_{2\alpha}$, adrenaline still produced a contractile response, whereas pretreatment with PGE_2 reversed the adrenaline response to relaxation. It is likely that under the normal condition the muscle tone is maintained, and the adrenaline response is modified, by arachidonic products, mainly PGE_2.

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ECONOMIC FORCE MAINTENANCE IN A NON-CATCH SMOOTH MUSCLE OF *MYTILUS*. IWAMOTO, H., SUGAYA, R., TAKEI, T. AND SUGI, H. Dept. Physiol., Sch. Med., Teikyo Univ., Tokyo 173

The changes in the ability of active shortening were measured during the course of contraction in the pedal retractor muscle (PRM) of *Mytilus*, which shows only phasic contractions in contrast to the catch muscles (e.g., anterior byssal retractor muscle). The PRM was electrically stimulated for 1 s in artificial sea water at 10°C. The contractile force had its peak at 2 s after the onset of stimulus and decayed with a half relaxation time of 8.3 s. The maximal velocity of shortening, determined by the isotonic release method, was the largest at the rising phase of force, and decreased monotonically. At 2 s after the onset of stimulus, the velocity was 70% of the value at 1 s. At 6 s, the velocity decreased to 30% of the initial value while 70% of peak force was retained. The parameter of Hill's characteristic equation, a/P_o, was initially larger and decreased as the contraction proceeded, suggesting some alterations in the crossbridge kinetics towards economic force maintenance. This is a marked contrast to what occurs in the vertebrate skeletal muscle, in which crossbridge kinetics is invariant during the course of a twitch contraction. The ability of force redevelopment after a quick release also decreased with a time course similar to that of velocity decay. The results suggest that the mechanism of force maintenance with reduced energy expenditure also exists in this phasic muscle.

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EFFECTS OF E TYPE-PROSTAGLANDINS ON THE CIRCULAR MUSCLE OF GUINEA-PIG COLON. ISHIZAWA, M., School of Allied Health Professions, Sapporo Medical College, Sapporo 060

In general, prostaglandins (PGs) of the E type contract longitudinal muscle and relax circular muscle in the gastrointestinal tract.
In the circular muscle strip of guinea-pig proximal colon, PGE_2, at doses over 10^{-7}M, produced an initial contraction, followed by a relaxation. While 16R methyl PGE_2 and 16,16 dimethyl PGE_2 (10^{-9}-10^{-6}M) produced a sustained contraction.
The contractile effects by PGE_2 derivertives were not influenced by atropine and tetrodotoxin. But these contractions were partly inhibited by verapamil (10^{-5}M).

These results indicate that 16 methyl PGE_2 derivertives may have a contractile effect on the circular muscle, and may contract by an increase in Ca^{++}influx through the membrace, and by a release of $Ca^{++}$from the Ca sequestered sites of the circular muscle.

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FUNCTIONS OF THE VOLTAGE-DEPENDENT CALCIUM CHANNELS IN DOG CEREBRAL ARTERIES. ASANO, M. and MASUZAWA, K.* Dept. Pharmacol., Nagoya City Univ. Med. Sch., Nagoya 467

Vasoconstrictor effects of Bay k 8644, a dihydropyridine calcium channel agonist and vasorelaxant effects of nifedipine were investigated in helical strips of dog cerebral (basilar, posterior cerebral and middle cerebral) and peripheral (coronary and mesenteric) arteries. Bay k 8644 produced a dose-dependent contraction in the basilar artery with a pD_2 value of 8.53. Similar sensitivity to Bay k 8644 was observed in the posterior cerebral, middle cerebral and coronary arteries. Bay k 8644 was less effective in producing a contraction in the mesenteric artery. An elevation of the concentration of extracellular K^+ eliminated the difference between the responses to Bay k 8644 in the basilar and mesenteric artery. Increased sensitivity to K^+ was also observed in cerebral and coronary arteries when compared with the mesenteric artery. The addition of nifedipine to an unstimulated strip produced a dose-dependent relaxation in cerebral and coronary arteries, but not in the mesenteric artery. When the cerebral and peripheral arteries were contracted with K^+ to the same magnitude, nifedipine produced similar relaxations among these arteries. These results suggest that the voltage-dependent calcium channels in the cerebral and coronary arteries are in different states of activation from those in the mesenteric artery. The state of activation might be related to the degree of membrane depolarization.

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NEURONAL AND HORMONAL CONTROL OF RAT GASTROINTESTINAL MOTILITY. SAKAI, Y., INAZU, M. AND AIHARA, K.* Second Dept. of Physiology, Showa Univ. Sch. of Med., Tokyo 142, and *Third Dept. of Internal Medicine, Jikei Univ. of Med., Tokyo 105 , Japan

To study gastric emptying in diabetes, we examined gastrointestinal motility in vivo, and isometric tension of antrum smooth muscle, from diabetic and control rats, in vitro. Oral administration of soup containing protein, lipids, carbohydrate and salt, in milk, accelerated gastric emptying. Field stimulation (F.S.,10 Hz,0.5 msec, 10 V), before feeding soup, contracted the gastric body, relaxed the antrum and did not affect the duodenum. Stimulation of the cervical vagus (V.S.,10 Hz,2 msec,10 V) before feeding soup contracted the gastric body and the duodenum but relaxed the antrum. After feeding soup, gastric body motility was depressed by F.S. and V.S., but V.S. contracted the antrum. In diabetic rats, before feeding soup, V.S. induced body and antrum relaxation and off-contraction, and F.S. relaxed the body and contracted the antrum. Inhibitory response was greater in the body, but excitatory response was greater in antrum in diabetics. V.S. releases bombesin. Bombesin (0.1 nmol) contracted the body, antrum and duodenum in controls, but induced little change in diabetics in vivo; 0.1- 100 nM contracted smooth muscle isolated from diabetics and controls, and 1.5 to 2 times more potently in diabetics in vitro. In vivo and in vitro difference may depend on neuropathy and myopathy in diabetic.

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POLYMIXIN B-ACTIVATED Cl CHANNEL IN VASCULAR SMOOTH MUSCLE CELLS. A.Saigusa* S.Kokubun Dept. Physiol., Dept. Internal medicine* The Jikei Univ. Sch. of Med. 3-25-8 Nishi-shinbashi, Minato-ku, Tokyo 105

Pharmacological characteristics of voltage-dependent chloride(Cl) channel were investigated in cultured vascular smooth muscle cells. Cl channel was activated in cell-attached mode by application of Polymixin B at the concentration of higher than 50 uM. The activation of the channel was observed in 48 out of 176 successful patches. In the patch in which no channel activity was observed, we could not onserve the channel activity even after making excised patch, suggesting that the drug always activated the channel in cell-attached mode as long as it is in the patch. The effect of Polymixin B might be rather specific to the channel, since the wash out of the drug effect by perfusing control Tyrode solution was possible. The channel was completely blocked by application of about 500uM DIDS. In the presence of low concentration of DIDS, multi-conductance nature of the channel was more obvious. This suggests that voltage-dependent Cl channel in vascular smooth muscle cells consists of several passages for permeable anions and that DIDS bounds each of unit components to block its activity

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EFFECTS OF BIOLOGICAL ACTIVE AGENTS ON THE CROSS-SECTIONAL AREA OF PUPILS IN ISOLATED MONKEY IRIDES. FUKUNAGA, H.*, OHHASHI, T.**, SAKAGUCHI, M.*** AND SEGAWA, K.* Dept. *Ophthalmol. and ***Physiol., Shinshu Univ. Sch. Med., Matsumoto 390 and ***Dept. Elect. Eng. Nagano Tech. Coll. Nagano 380

Effects of biological active substances on the cross-sectional area of pupils were investigated in isolated monkey irides by means of a domestic-made area measuring gauge utilizing an area image sensor. Adrenaline (AD), noradrenaline (NA), dopamine caused dose-dependent increases of the cross-sectional area of pupils (mydriasis). The decreasing order of the responses was as follows : EP≧NE>dopamine. On the other hand, prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), 5-hydroxytryptamine (5-HT), acetylcholine (ACh), adenosine, ATP, ADP, AMP and histamine produced dose-dependent decreases in the cross-sectional area of pupils (miosis). The decreasing order of the responses was as follows : $PGF_{2\alpha}$ ≧ 5-HT>ACh≫adenosine≧ATP≧ADP≧histamine≧AMP. We also studied the effect of similar active substances on the cross-sectional area of isolated monkey punched preparations in which pupillary sphincter muscles were dissected by ophthalmic trepan. 5-HT and ACh caused dose-dependent mydriasis in punched pupils, the threshold concentrations being about 100 and 1000 times higher than those for miosis in normal pupil preparations. The results suggest that 5-HT and muscarinic receptors are located on the sphincter and dilator muscles.

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BIPHASIC RELEASE OF ENDOTHELIUM-DERIVED RELAXING FACTOR(S) BY A23187 FROM HOG CORONARY ARTERY.

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We previously found that A23187 elicited a biphasic, endothelium-dependent relaxation in hog coronary artery selectively resistant to hypoxia. In this study, A23187-induced relaxation was compared with the known endothelium-dependent effects of substance P (SP) and thrombine (TB) in the artery. SP (10 nM) and TB (0.5 U/ml) elicited an endothelium-dependent relaxation which was rapid but transient ($t_{\frac{1}{2}} \simeq 20$ s). Hypoxic conditions abolished the A23187 rapid phase ($t_{\frac{1}{2}} \simeq 20$ s) and the transient relaxation to SP or TB, but not the A23187 slow phase ($t_{\frac{1}{2}} \simeq 9$ m). Pretreatment with cyanide (5 mM), ouabain (10 μM), propranolol (10 μM), or indomethacine (10 μM) had no effect on the relaxation to A23187, SP or TB. In the presence of nordihydroguaiaretic acid (50 μM) the rapid phase of the A23187, SP and TB relaxations was abolished, but not the slow sustained relaxation to A23187. Our results suggest that the rapid relaxations to A23187, SP and TB might be related to the lipoxygenase pathway. The sustained relaxation induced by A23187 is characterized by properties quite distinct from those of the rapid phase, yet is endothelium-dependent, suggesting that A23187 releases by two distinct mechanisms and/or two kinds of endothelium-derived relaxing factor in the artery.

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THE ROLE OF CALCIUM IONS IN THE ACTIVATION OF CONTRACTURES IN INSECT SKELETAL MUSCLE YAMAGUCHI, T., *WASHIO, H. Dept. Biol. Intern. Christ. Univ., Mitaka 181, *Lab. Neurophysiol., Mitsubishi-Kasei Inst. Life Science, Machida, 194

To clarify the activating mechanism of K-induced contractures in insect skeletal muscle, 100mM K solution was applied to the retractor unguis muscles of the cockroach. The contracture was composed of phasic and tonic components. If the muscle was exposed to 0 Ca saline containing 2 mM EGTA, both types of contracture were eliminated, whereas the tonic was induced as soon as Ca^{2+} was added to this muscle. Elevation of external Ca^{2+} induced a large tonic contracture while the phasic was not modified. 10mM manganese, 1 μM Nifedipine and procaine reduced phasic contracture markedly. Caffeine induced rapid phasic contracture which was also reduced in 0 Ca saline containing EGTA. If caffeine was applied to the K-depolarized muscle, an increased contracture was induced followed by a large tonic one. The results suggest that the phasic type of K contracture is mainly induced by external Ca^{2+} flowing in through Ca channels and then releasing it from SR, while the tonic type is directly induced by external Ca^{2+} entering another path.

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FUNCTIONAL STRUCTURE OF IN-PUT SITE FOR EXCITATION-CONTRACTION (E-C) COUPLING IN SKELETAL MUSCLE FIBER OF FROG, R. JAPONICA. M. FUJINO, T. ARIMA, K. HARANO, M. GOTO, M. SENO-O, N. SHIMADA. 1. Dep. of Physiol., Natl. Def. Med. Coll., Tokorozawa.

1. Concanavalin A (Con A) of several ten μM inhibits E-C coupling (shift of tension-K concentration-relation curve, increase of peak time). Con A-ferritin does also similarly, though somewhat weak. 2. Electron-microscope studies revealed: In fibers immersed in Ringer containing Con A-ferritin particles, the particles are recognized in contact with luminal surface of T-membrane and in opposite to feet; the ferritin-site with respect to width of feet moves upon K-depolarization; and in presence of phenylglyoxal, which inhibits E-C coupling completely, the site remains the resting state under condition of membrane depolarization. Conclusion: Probably, feet form a path-way of signals for E-C coupling; thus, T-tubular sites in opposite to feet are of a differentiated structure for E-C coupling, and a moving of the structure due to depolarization forms the first-step for the coupling.

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ROLE OF TRIADIC JUNCTION IN EXCITATION-CONTRACTION (E-C) COUPLING OF SKELETAL MUSCLE FIBERS OF FROG, R. JAPONICA. M. FUJINO, T. ARIMA, M. GOTO, M. SENO-O, K. HARANO, N. SHIMADA. 1. Dep. of Physiol., Natl. Def. Med. Coll., Tokorozawa.

1. Muscle fibers immersed in Ringer of pH 9.0 containing 5 mM of NH_4Cl show a considerable inhibition of E-C coupling, accompanied by remarkable morphological changes in triadic junction such as a detachment of feet from T-tubular membranes. 2. In muscle fibers immersed in similar Ringer, which contains somewhat lower concentration of NH_4Cl, a contracture without membrane potential-change is produced by streching and glycerol-removal. 3. Similar contracture without potential changes occurs due to removal of high concentrations of glycerol (pH 7), urea (pH 7), and glycylglycylglycine (pH 9). 4. Morphological studies on glycylglycylglycine-removal contracture shows that the contracture is accompanied by a remarkable increase in frequency of occurrence of detachment-type of triadic junction. Conclusion: Detachment of feet from T-tubular membrane evokes activation of contractile machinery without mediation of electrical processes in membrane, suggesting that the transmission of signals from T-membrane to lateral sac is mechanical.

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DIFFERENT MECHANISMS OF POTASSIUM CONTRACTURES IN SINGLE TWITCH MUSCLE FIBERS OF THE FROG. TSUTSU-URA, M. and TAKAUJI, M. Dept. Physiol., Sapporo Med. College, Sapporo 060

We previously reported that in frog single twitch fibers a monophasic potassium contracture (K contracture) can be produced under such conditions that only Ca^{++} is the carrier of current and that this contracture consists of a DAN-sensitive phase and a DAN-resistant phase. From the results obtained by using the organic and inorganic Ca^{++} channel blockers and Bay K 8644, it was suggested that the DAN-resistant phase is closely correlated with Ca^{++} currents flowing through dihydropyridine-sensitive and voltage-dependent Ca^{++} channels (Takauji and Tsutsu-ura, J. Musc. Res. Cell Motility, 8: 282, 1987).

In the present report, the characteristics of the DAN-sensitive phase were examined. We observed the effects of DAN, lowering external Ca^{++} and various Ca^{++} channel blockers on the above mentioned K contractures. The results indicate that the properties of DAN-sensitive phase itself resemble those of the secondary component of the biphasic K contracture which can be observed at constant Cl^- concentration (Takauji et al., Jpn. J. Physiol., 1980, 1985; Tsutsu-ura et al., Jpn. J. Physiol., 1984). Therefore, it may be considered that a monophasic K contracture above mentioned is caused by two different mechanisms of contraction; one is correspondent to that of the secondary component, and the other is closely related with Ca^{++} currents.

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MECHANICAL INACTIVATION PROCESS OF SILVER ION-INDUCED CONTRACTURE AND ELECTRICAL TRANSPOTENTIAL IN SHORT MUSCLE FIBERS OF FROG. OBA, T., LIU, G. AND HOTTA, K. Dept. Physiol., Nagoya City Univ. Med. Sch., Mizuho-ku, Nagoya 467.

Based on detubulation experiments and electrical recordings of transmembrane potential, we have proposed a hypothesis that transient contraction-developing effects of silver ion are on the transverse-tubular membrane of frog toe muscle fibers. Membrane depolarization from the resting potential to less negative potential (less than -50 mV) led to a decrease in the peak tension induced by silver ion. Decrease in duration of the contracture, as well as the peak tension, was observed after pretreating fibers with 0.2 mM tetracaine for 3 min. These results indicate the occurrence of inactivation process in the silver ion-induced contracture. When dithiothreitol, a SH-group protector, was added at an approprite time during development of the tension, the fiber was kept contracting for a long time with no inactivation, thereby indicating that chemical sites for mechanical inactivation exist independently from activating sites. The possibility was examined by applying silver ions to short (about 1 mm) single fibers under voltage clamp control with the help of two flexible microelectrodes.

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EFFECTS OF SODIUM REMOVAL ON THE CAFFEINE CONTRACTURE IN FROG SKELETAL MUSCLE. KAWATA, H. and FUJISHIRO, N. Department of Physiology, School of Medicine, Fukuoka University, Jonan-ku, Fukuoka 814-01

Effects of sodium removal on the caffeine-induced contracture were investigated on both intact and skinned fibers of the semitendinosus and iliofibularis muscle of Rana japonica. At 20°C the removal of external sodium ions, replaced with choline, resulted in a marked potentiation of twitch as well as electrically induced contracture in TTX-containing solution. The contracture induced by 5 mM caffeine was first inhibited and then restored during sodium-free perfusion while a shift of the mechanical threshold to more negative membrane potential occurred under the same condition. At lower temperature, more marked potentiation of caffeine contracture was observed in sodium-free solution (10°C) whereas, in mechanically skinned fiber, the amount of calcium in the sarcoplasmic reticulum examined by applying 25 mM caffeine was paradoxically inhibited by depletion of sodium ions from the relaxing solution at 5°C.

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EFFECT OF FURA 2 AND AM FOR Ca INFLUX IN THE FRAGMENTED SARCOPLASMIC RETICULUM(FSR). NISHIJIMA,H.,KUCHIBA,K., Dept. Physiol., The Jikei Univ. School of Medicine. 3-25-8 Nishishinbashi, Minato ku, Tokyo,

The fluorescent Ca indicator fura 2 caused an increase in fluorescence intensity and a shift of the peak of its excitation spectrum from 362 to 338nm depend on the intracellular Ca concentration. And fura 2-AM is the pentamethyl ester of fura 2 have the peak to the excitation spectrum of 375 nm was readily diffuses into a cell where it is converted to fura 2 by acethylesterases.

In this study, when the FSR was incubated in the reaction solution including fura 2-AM, its were found that the Ca-uptake on FSR was inhibited and the bound Ca without ATPase activity markedly increased by fura 2-AM , and the besal ATPase activity inhibited by fura 2-AM. Otherhand, the exact conversion from fura 2-AM to fura 2 on the FSR was indicated in the early stages. But in the latter stage at over 30 min, the exact conversion from fura 2-AM to fura 2 could not clearly determined. The FSR in this stage not uptaked Ca by ATP. These results were indicated that fura 2 or fura 2-AM caused the structural chenge in the membrane of FSR.

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FRACTIONATION OF HEAVY SARCOPLASMIC RETICULUM BY DIFFERENT RESPONSES TO CAFFEINE. KOSHITA,M., OBA,T. AND HOTTA,K. Dept. Physiol., Nagoya City Univ. Med. Sch., Nagoya 467

Caffeine, thymol, quercetin, and p-chloromercuriphenylsulfonic acid (pCMPS) did induce release of Ca^{2+} from heavy fraction of frog sarcoplasmic reticulum (SR) vesicles, but Ca^{2+} release by these drugs was inhibited by treatment of Ca-loaded SR with caffeine, i.e., SR became insensitive or less sensitive to these drugs after caffeine-induced transient release of Ca^{2+}. This phenomenon may be explained by Ca^{2+} release from drug-sensitive SR and Ca^{2+} reuptake by drug-insensitive or less sensitive SR, or by a change in sensitivity of SR to the drugs. When SR was centrifuged through a sucrose density gradient, heavy SR banded at 40-42.5%(W/V) irrespective of Ca-loading. When the SR released Ca^{2+} in response to caffeine and took up the released Ca^{2+}, it banded at 40-42.5% and 42.5-45%. These results indicate that heavy SR consists of two subfractions which show different responses to caffeine.

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THE THICK FILAMENT MOVEMENT AND CALCIUM CONTENT OF THE TERMINAL CISTERNAE DURING CAFFEINE CONTRACTURE IN FROG SKELETAL MUSCLE. YOSHIOKA,T., TAMAKI,T., TAKEKURA,H., NAGAMI,K. and NAKANO,S. Dept. of Physiol., Tokai Univ. Sch. Med., Kanagawa 259-11

High voltage electron microscope (HVEM) and electron probe microanalysis (EPMP) were used to study the positional stability of thick filament and the calcium content of the terminal cisternae (TC) of sarcoplasmic reticulum (SR) during 5mM caffeine contracture for 3 min in frog skeletal muscles. Thick filament movement in the sarcomere was obtained from the drift of M-band position in the myofibril surrounded by the successive transverse tubule revealed by infiltration with osmium and silver (Golgi method). Normalized M-line movements (%) were 3.0±2.31 (mean±S.D.,n=77) and 5.6±3.74 (111) at rest and during caffeine contracture, respectively. The values are significant ($P<0.01$). Caffeine caused a large and highly significant ($P<0.001$) reduction in the Ca content of the TC from a resting value of 65 m mol kg^{-1} dry TC weight to 25 after 3 min contracture. Resting value of the calcium content was much lower than the result reported by Somlyo et al (1981). The Ca contents of the paired-TC in one myofibril are not always similar during contracture, suggesting a different rate of Ca release induced by caffeine from the SR. The movement of thick filament may produce a typical tension development during caffeine contracture depending on the rate of Ca release.

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LINKAGE BETWEEN SUPERFICIAL EXCITATION AND Ca^{2+} RELEASE FROM THE SARCOPLASMIC RETICULUM IN FROG SKELETAL MUSCLE. FUJINO, M. AND SATO, Y. First Dept. Physiol., Natl. Def. Med. Coll., Tokorozawa 359.

Ca^{2+} flux (ΔF_{Ca}) at the sarcoplasmic reticulum (SR) during a twitch in a single fiber was measured based on Baylor's kinetic model, and as novel approach, the Ca^{2+} transient was kinetically calculated directly from an observed arsenazo III response. It was found in the same fiber that the ΔF_{Ca} value was not appreciably influenced even when several parameters such as rate constants and temperature coefficients were varied in fairly large ranges, suggesting that ΔF_{Ca} is ensured by a relatively stable physiological mechanism at the SR. It was also found that the time-course of ΔF_{Ca} consisted of a spike-like rapid positive phase and a subsequent slow negative phase. The former is considered to correspond to Ca^{2+} release from the SR, and its time-course was similar to that of the action potential generated by the transverse tubular system. The present results suggested the possibility that the excitation-Ca^{2+} release linkage may be physicochemical sequence composed of a few elementary steps.

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CALCIUM AND MAGNESIUM BINDING TO TROPONIN C FROM BULLFROG SKELETAL MUSCLE. IMAIZUMI, M., TANOKURA, M. AND YAMADA, K., Dept. of Physiol., Medical College of Oita, Oita 879-56

Microcalorimetric titrations at pH 7.0, and potentiometric titrations at pH 5.0-7.5, were carried out on troponin C (TnC) from bullfrog skeletal muscle at 25°C, with Ca^{2+} (or Mg^{2+}) in the absence and the presence of Mg^{2+} (or Ca^{2+}). The enthalpy titration profiles with Ca^{2+} were divided into three stages both in the absence and the presence of Mg^{2+}. The first and the third stages were characterized as exothermic processes, but the second as an endothermic one. The enthalpy titration profile with Mg^{2+} in the absence of Ca^{2+} were divided into two stages. The first stage was characterized as an exothermic process, but the second as an endothermic one. With Mg^{2+} in the presence of 1 mM Ca^{2+}, only the endothermic process was observed. Analysis of these titration profiles has indicated that bullfrog TnC has two high affinity Ca^{2+}-Mg^{2+} sites, two low affinity Ca^{2+}-specific sites, and two Mg^{2+}-specific sites. In pH potentiometric titrations, Ca^{2+} (or Mg^{2+}) binding to the high affinity sites makes the molecule of TnC to absorb protons in the absence of Mg^{2+} (or Ca^{2+}). The number of protons as a function of pH indicates that Ca^{2+} (or Mg^{2+}) binding to the high affinity sites causes an increase in the pK_a of an ionizing group, which may be located at a certain distance from the high affinity sites.

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RELATIONSHIP BETWEEN THE PROTEOLYTIC ACTION OF Tn-I AND THE TENSION DEVELOPMENT OF GLYCERINATED MUSCLE FIBER. AOKI, H., NAKAYAMA, Y. WATANABE, K* AND YAMAGUCHI, M** Dept. of Physiol. & Anat. Kyoritsu Coll. of Pharm., Tokyo 105, *Dept. of Biol., Nihon Univ., Chiba 274 and **Dept. of Biochem. and Nutri. Juntendo Univ., Chiba 275.

It was previously reported that the proteolytic action of Tn-I was proved by SDS-PAGE of peptides cleaved from HMM, having 26 K and 28 K daltons. In this paper, the effect of trypsin or Tn-I was examined with tension development of glycerinated fiber by incubation in each solution for 15 min at 22°C. The initial tension was depressed soon by addition of trypsin or Tn-I, respectively. By washing, trypsin-treated fiber developed no tension at all, but Tn-I-treated one recovered the magnitude until half of original tension, although the latency and the rate of rise were kept declining. It was suggested that the proteolytic action of Tn-I differed from the trypsin digestion.

On the other hand, tension was also depressed without Tn-I in the solution by low NaCl or high KCl concentration of salt. Therefore, tension depressed with Tn-I includes the simultaneous effects of Tn-I itself, concentrations and kinds of salts, because Tn-I is soluble in 0.4 M NaCl or KCl solution. However, tension depressed with NaCl did not recover to original lebel by washing, in contrast to the fiber depressed with KCl. So, it was assumed that the relative inhibition of Tn-I was the difference of both tension developed with or without Tn-I which dissolved in 0.4 M KCl solution.

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^{31}P-NMR SCANNING SPECTROSCOPIC STUDY ON INTRACELLULAR pH ALONG MUSCLE FIBERS. YOSHIZAKI, K., NISHIKAWA, H. Dept. Physiol., Kyoto Pref. Univ. Med., Kamigyo-ku, Kyoto 602

^{31}P-NMR one dimensional chemical shift imaging technique was successfully applied on isolated frog muscle. The gradient pulse was applied along the muscle fibers placed in a solenoid coil and a set of ^{31}P-NMR absolute spectra as a function of position along the fibers was obtained by two-dimensional Fourier transformation of the phase-encoded spin-echoes. The spatial resolution was about 0.5 mm determined by the number and values of the gradients and the static field homogeneity. The scanned spectra showed the concentration distribution of creatine phosphate and inorganic phosphate, and the intracellular pH along the muscle fibers could be quantitated from the difference in the chemical shifts. The decrease in creatine phosphate and the corresponding increase in inorganic phosphate were observed along muscle fibers accompanied with intracellular acidification under anaerobic conditions, and the heterogeneity of muscular pH was kept within 0.2 pH unit in resting muscle along the fibers.

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EFFECTS OF CO_2 ACIDOSIS ON THE Ca-TRANSIENTS IN XENOPUS SKELETAL MUSCLE FIBER MEASURED BY ARSENAZO III. MATSUMURA,M. and OCHI,K. Dept. Physiol., Kawasaki Med. Sch., Kurashiki, Okayama 701-01

Arsenazo III (AZ) was iontophoretically injected into a xenopus skeletal muscle fiber to investigate the changes in myoplasmic Ca ion concentrations following electrical stimulation. The absorbance change of AZ was detected at the wavelength of a pair of 658-721 nm. In the separate experiments for contraction measurements, the relaxation process was found to be slowed in the CO_2-Ringer solution after the repetitive stimulations at the rate of 0.5 - 2/sec. The decay phase of the AZ signal was exponential and it was dependent on the sarcomere length; 25 msec at 4.0 μm and below 20 msec at 3.2 μm (23°C). When the standard Ringer was replaced with CO_2 Ringer, the peak amplitude of the AZ signal was decreased to 70 % in 5 min, more than expected by the diffusion of AZ and by the pH dependence of AZ. During the repetitive stimulations at the rate of 1/sec, the peak of the AZ signal was decreased to 50 % after 100 stimulations, while that in the standard Ringer was about 80 %. The decay phase in the CO_2 Ringer was markedly prolonged after 200 stimulations. The slowing of the signal is explained as the decrease of the rate of Ca-uptake into sarcoplasmic reticulum rather than the change in the reaction rate of AZ with Ca ions.

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EFFECTS OF L-CARNOSINE ON SKINNED FIBRES OF MAMMALIAN SKELETAL MUSCLE. WATANABE M. AND UMAZUME Y. Dept. of Physiol., Jikei Univ. Sch. of Med. Minatoku, Tokyo, 105

It has been known that L-carnosine(β-alanyl-L-histidine) is normally contained in sarcoplasm, 1-10mM in frog and 10-30mM in mammalian muscle. Although some studies presumed that since it is imidazole-containing substance, the effects are similar to caffeine, the exact role is still unclear. The effects of carnosine were examined in properties of both contractile system and sarcoplasmic reticulum (SR) by using "skinned" fibres from extensor digitorum longus muscle of guinea pig. Carnosine raised the Ca sensitivity of contractile system and slightly increased the maximum tension. These results confirm the report of Harrison et al. (J. Physiol. 371 197P 1986). Carnosine facilitated the speed of Ca uptake by SR and enhanced the rate of "Ca induced Ca release from SR" (CICR). These effects of carnosine were compared with PIPES of which pH buffering capacity is similar to carnosine. When PIPES was added to the solution containing carnosine of 0 or 20mM, the maximum tension and the speed of Ca uptake by SR were enhanced. On the other hand, Ca sensitivity was reduced and rate of CICR was not affected. These findings suggest that carnosine has not only pH buffering action but has other actions such as to maintain the functions of contractile protein and SR.

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AN X-RAY DIFFRACTION STUDY ON THE INHIBITORY EFFECTS OF 2,3-BUTANEDIONE MONOXIME ON THE CONTRACTIONS OF FROG SKELETAL MUSCLES.

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We studied the inhibitory effects of BDM (2,3-butanedione monoxime) on the tetanic contractions of frog skeletal muscles using X-ray diffraction technique. In over-stretched bullfrog semitendinosus muscles, 3mM BDM did not reduce the increase in the intensity of the 2nd layer-line of the actin-helix during activation. In frog sartorius muscles at 2.4μm, 3mM BDM reduced the tetanic tension by 60% and changed the equatorial intensity ratio ($I_{1,0}/I_{1,1}$) during contraction from 0.50 to 0.76. These results indicate that the inhibitory effects of BDM is due not to inhibition of calcium release from sarcoplasmic reticulum or reduced binding of calcium to troponin, but to inhibition of the actomyosin ATPase cycle.

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^{31}P-NMR STUDY OF THE INTRACELLULAR PH CHANGES IN NACN-POISONED FROG SKELETAL MUSCLE.

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Based on the pH-dependent chemical shift of P_i in ^{31}P-NMR spectra, we studied the intracellular pH changes in unaerobic frog skeletal muscle following contractile activities. Frog Sartorius muscles were mounted in a chamber installed in an NMR magnet (JEOL GX400), and superfused with Ringer solution containing 2 mM NaCN at 10 °C. Consecutive 2-s tetani were applied to the muscles at 20 min intervals and, after each tetanus, ^{31}P-NMR spectra were obtained. The intracellular pH shifted to alkaline direction after the first two tetani, and then reversely shifted to acidic direction as the tetanus was further applied. This suggests that the production of lactic acid does not occur upto the second 2-sec tetanus and does occur after the third. This is in accord with the conclusion obtained by our previous ^{31}P-NMR study of muscles poisoned with iodoacetic acid [Biochim. Biophys. Acta 931, 170-174 (1987)]. The present studies further suggested that the buffering power of frog skeletal muscle is about 40 mM/pH unit.

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A MODEL OF CROSSBRIDGE WITH BOTH A HOOKEAN AND A RUBBER-LIKE ELASTICITY IN MUSCULAR CONTRACTION.

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The proposed crossbridge (XB) model has a rubber-like elasticity which resides in a rod region of the XB and a hookean elasticity due to strain of the globular head of the XB. On attachment of the XB to the thin filament, the XB head undergoes a single tilting step, by which the rubber-like elastic element is stretched maximally, storing energy and producing a strain of the head. When a quick length change is applied to a contracting sarcomere, the strain of the head is instantaneously removed and subsequently the rubber-like element shortens, giving a new strain on the head. This process appears as a rapid tension recovery at a new sarcomere length. At any points on T_2 curve (Ford,Huxley & Simmons,1977), therefore, both the rubber-like and the hookean elasticities are balanced. The force-length relation of the rubber-like element using the T_2 curve quite resembled that of a typical rubber. The presence of the rubber-like elasticity together with the hookean elasticity solved to some extent the discrepancy between the observed number of the attached XBs in an isometric contraction and the theoretically expected one using T.L.Hill's idea (1975).

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SWELLING LIMITS OF FROG SKELETAL MUSCLE

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Reducing NaCl of bathing Ringer solution, frog skeletal muscle fibers swelled to some extent osmotically as if sarcolemma was perfectly semipermeable. Gravimetrically estimated swelling limits of whole muscles depended on their sarcomere length L. At longer L smaller swelling limits were attained at relatively high osmotic strength. For a given L, the upper limit of 1,0 lattice spacing of thick filaments, measured with X-ray diffraction method, was found at much higher tonicity than that of fiber volume, and was coincided with the spacing exhibited in mechanically skinned fibers. The cross sectional area of intact single fiber observed microscopically, keeping alive, did not show definite limitation for swelling over the range we examined. From these results, in whole muscle, it would be collagen fiber network and/or neighboring fibers that restrain swelling beyond its limitations. Further studies for tension borne by sarcolemma showed that, regardless to L, reducing the osmotic strength by more than half made the fibers cylindrical as they swelled. Stretching up to L = 3.8μm also rounded the fiber. At L < 2.8μm, resting tension decreased in hypotonic solutions. Conversely, increase in tension was observed at L > 2.8μm. These behavior could be explained by the model we proposed, which was made of stiff semipermeable bag containing a spring in it. The model was consistent with the structure of sarcolemma, and could account for the difference between resting tensions in chemically and mechanically skinned fibers.

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STRUCTURAL CHANGES OF THE MYOFILAMENT LATTICE IN TETANIZED FROG SKELETAL MUSCLE DURING THE FORCE ENHANCEMENT BY STRETCH.

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We have shown that the enhancement of isometric force in tetanized frog skeletal muscle fibers is associated with a decrease in stiffness, indicating that the enhanced force may result from a recruitment of some force-bearing system other than the cross-bridges. Subsequent time-resolved X-ray diffraction studies on tetanized muscle have shown that the enhanced force is accompanied by a decrease in the intensity of 1,1 equatorial reflection but not by a change in the intensity of 1,0 reflection, suggesting that the force enhancement results form a disordering of the 1,1 myofilament lattice caused by a shift of each thin filament from its trigonal position in the thick filament hexagonal lattice.

To explore the above possibility, tetanized muscle fibers were fixed with OsO_4 during the plateau of an isometric tetanus and during the force rise in response to a slow stretch. In accordance with our expectation, the myofilament lattice in tetanized fibers was found to be disordered by a slow stretch. Experiments are currently being done to obtain quantitative results on the electron micrographs.

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ANALYSIS OF FORCE ENHANCEMENT AFTER STRETCH IN INTACT SINGLE MUSCLE FIBERS OF THE FROG.

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Contractile tension in skeletal muscle is well known to increase above the isometric force level during and after stretch. Two possibilities are now being postulated about the mechanism of this phenomenon. One is that the phenomenon might be induced by the enhancement of the ability of each cross-bridge to sustain enhanced force, and another is that parallel elastic element, e.g. connectin, might be stretched and develop passive tension when a fiber is stretched. This experiment was conducted to examine the latter possibility by measuring the maximum velocity of shortening in two methods in intact muscle fibers of the frog at low temperature (2-3° C). A tetanized muscle fiber was quickly released in several amplitudes at various times before, during and after stretch and maximum velocities of shortening were compared. The maximum velocity was also measured in the segments marked by black dog hair by lowering the load to 0.03Po. No appreciable difference of the velocity was detected in all the measurements, suggesting that the parallel elastic element might not be involved in this phenomenon.

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EFFECT OF ETHYLENE GLYCOL ON MECHANICAL PROPERTIES OF MUSCLE CONTRACTION

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It has been shown that ethylene glycol(EG) reduces the Ca-ATPase activity of myosin, actomyosin ATPase activity and the affinity of myosin for actin. In the present study, we investigated the effect of EG on force, stiffness and velocity at zero load of glycerinated rabbit psoas muscle fibers. Measurements were made in the solutions containing various concentrations of EG at ionic strength of 0.2M, pH 7.0 and 10°C. Isometric force was reduced by increasing the concentration of EG. The force in 10 and 15% EG was about 80 and 50% of that in the absence of EG, respectively. The reduction of force was not due to an incomplete activation, though EG shifted the pCa-force relation to the right. The effect of EG on stiffness was less than that on force. Stiffness was almost unaffected by EG in concentrations up to 15% and reduced in higher concentrations. The stiffness in 20% EG was about 30% of that in the absence of EG. The velocity at zero load was reduced almost linearly as the concentration of EG was increased. The velocity at zero load in 10 and 15% EG was about 50 and 25% of that in the absence of EG, respectively. The effect of EG may be explained on the basis of the kinetics of ATP hydrolysis by actomyosin.

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ACTION OF DANTROLENE ON FORCE AND HEAT PRODUCTION IN MUSCLE FIBRES OF THE FROG.

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Force and heat production has been measured during tetani of isolated single fibres from the frog (Rana temporaria) anterior tibialis muscle treated with dantrolene sodium, usually at 50 uM concentration. The main effect of dantrolene on force development has been a great reduction in the rate of rise of force, with little effect on the force finally reached. A plateau of force may occur early in a tetanus followed by a further rise of force and a final plateau. Fibres microscopically observed during such contractions show no marked longitudinal redistributions of length, which are seen in damaged fibres. These effects of dantrolene are dose-dependent and reversible. The depressed rate of rise of force can be restored almost to normal either by increasing the stimulation frequency or by decreasing the interval between successive tetanic contractions. In contrast the rate of heat production is affected only slightly by dantrolene. These results suggest that dantrolene does not act by depressing calcium release, more probably its actions are due to increasing the calcium buffering.

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EFFECT OF TEMPERATURE ON REPRIMING OF THE LABILE MAINTENANCE HEAT IN BULLFROG SKELETAL MUSCLE.

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Maintenance heat production during isometric tetanus can be divided into two parts, the stable(h_b) and the labile(h_a/a) heats. It is known that the amount of the h_a/a is affected by an interval between two tetani; it is reduced in the 2nd tetanus immediately after the 1st one and is recovered by increasing the interval between the two (repriming of the labile heat). The time course of the repriming(E(t)) can be well described by the equation with two exponential terms; $E(t)=1-A\exp(-t/\tau_1)-B\exp(-t/\tau_2)$. We observed the effect of temperature on E(t) in semitendinosus muscles from bullfrog. Measurements were made at two different temperatures(14 & 4°C, or 9 & 4°C) on the same muscles. There was no significant difference in E(t) at different temperatures.

temperature(°C)	P(kNm^{-2})	h_a/a(mJg^{-1})	h_b($mJg^{-1}s^{-1}$)	A	B	τ_1(s)	τ_2(s)
14	225.5±55.9	24.3±4.4	50.4±5.63	0.75	0.23	7.19	69.9
4	179.0±43.9	14.4±2.82	16.3±1.68	0.65	0.34	6.41	285.7
9	203.3±14.4	18.7±3.72	31.0±1.86	0.57	0.43	2.48	147.9
4	173.4±13.9	18.4±3.67	15.9±1.03	0.69	0.31	8.20	336.7

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MECHANICS AND ENERGETICS OF MUSCLE CONTRACTIONS IN DYSTROPHIC (MDX) MICE.
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Mechanical and energetical properties of extensor digitorum longus (EDL) and soleus muscles from X-linked muscular dystrophic (mdx) mutant mice aged 4-6 weeks were compared to those of muscles from normal mice.

There was no difference between the force produced, speed of contraction and relaxation, and the heat production of soleus muscles from mdx and normal mice. However, it was found that in EDL muscles from mdx mice, force and heat production were much reduced, and relaxation was prolonged. To study the cause of these abnormalities in EDL muscles, heat and force were measured at various muscle lengths beyond optimum. Both twitch heat and tetanus heat rate were linearly related to the force and had non-zero intercepts (activation heat). Twitch activation heat and force related heat showed no difference between normal and mdx mice muscles. On the other hand, tetanus activation heat from mdx muscles was smaller than that from normal ones. These results suggest that the slowness of the relaxation of force is caused by the reduction of Ca-ATPase activity of salcoplasmic reticulum and the smaller force in mdx muscles may be due to the existence of degenerated fibers in the tissues.

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MUSCULAR DYSTROPHIC MICE: CENTRONUCLEATED MUSCLE FIBERS ARE OTHERWISE WITHIN THE OTHER FIBERS. TOTSUKA, T. AND URAMOTO, I. Dept. Physiol., Inst. Develop. Res., Aichi Prefect. Colony, Kasugai, Aichi 480-03

The centronucleated fibers are characteristically observed in skeletal muscles of dystrophic mice (C57BL/6J-dy dy/dy). These fibers are widely believed to be the regenerated fibers which are abortive and resistant to necrosis. If this is true, the central nuclei should be observable only in a peculier type of fibers similar to immature fibers. However, the present light-microscopic studies on cross sections (prepared with a cryotome) of the hindleg rectus muscles of dystrophic mice, demonstrated that the centronucleated fibers varied markedly on size, shape (apparent ellipticity) and degree of PAS staining. Moreover, some of "opaque" and "ghost" fibers (artifacts?) which were observed in specimens prepared accidentally in a less skillful manner, had central nuclei. Recently, the author found that some fibers had both central and peripheral nuclei in a cross section and that the tongue muscle fibers uninfluenced by the bone growth appeared normal (Proc Japan Acad 63B: 131-134). Thus far findings indicate that the central nucleation may be secondary to the age-related aggravation in bone-muscle imbalance.

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THE SPECIFIC PROTEIN DECREASED IN DISUSE ATROPHIED MUSCLE (3).
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Rat hindlimb suspension results in muscle atrophy, particularly, in the slow twitch soleus but the molecular mechanism is not well understood. We have found the specific protein component in soleus by one and two dimentional polyacrylamide gel electrophoresis, referred to as 24-kDa protein, which decreased after three days and continued to be depressed for 10 week's suspension. Passive stretch with suspension didn't induce muscle atrophy and maintained 24-kDa protein content. In order to know whether 24-kDa protein is synthesized and is related to myofibril protein, 24-kDa protein was purified from muscle extract through gel filtration, DEAE- and S-Sephacryl ionchromatography and anti 24-kDa protein antibody was made. Immunoprecipitation of 24-kDa protein with its antibody in vitro using [^{35}S]-methionine showed that 24-kDa protein is synthesized in the muscle cells and the rate of its synthesis is significantly smaller in the atrophied muscle (25%), however that in the stretched and suspended muscle was twice higher than that in control muscle after 1 week experiment. FITC-staining with anti-24-kDa protein antibody in glycerinated myofibril showed striations in myofibrils. From these results, this 24-kDa protein relates to myofibril might play an important role in the course of muscle atrophy.

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SUPPRESSING EFFECT OF BUTANEDIONE MONOXIME ON CONTRACTION AND HMM ATPase OF RABBIT MUSCLE. HIGUCHI, H. AND TAKEMORI, S. Dept. of Physiol., Jikei Univ. Sch. of Med., Minato-ku Tokyo 105

Effect of 2,3-butanedione-2-monoxime (BDM) on the isometric tension in skinned fibers and heavy meromyosin (HMM) ATPase activity in vitro in rabbit skeletal muscle was studied to clarify the molecular mechanism of action of BDM. The tension and ATPase were measured in the same solution (ionic strength 0.1M, 2mM MgATP, 0-20mM BDM, 2-20°C and pH 7.0). BDM reversibly inhibited not only the tension development activated by calcium ion, but also HMM ATPase. The inhibition effect on the relative HMM ATPase was, however, independent of addition of actin and troponin-tropomyosin-actin. The initial phosphate burst size at 20°C was about 1.6 mol per 1 mol HMM and was independent of concentration of BDM. These results suggest that the reduction of the tension is due mainly to the direct action of BDM on the myosin molecule and BDM affects the reactions after the formation of HMM-ADP-Pi complex.

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IMAGING OF INTRACELLULAR CA ION CONCENTRATION CHANGE IN AEQUORIN INJECTED SKELETAL MUSCLE FIBERS. KURIHARA, S., KONISHI, M., OKAZAKI, O., SUDA, N., Dept. of Physiol., The Jikei Univ. Sch. of Med., 3-25-8 Nishishinbashi Minato-ku, Tokyo 105

Measurement of intracellular Ca transient clarified the relation between $[Ca^{2+}]_i$ and tension. However, it is still not clear whether or not $[Ca^{2+}]_i$ gradient exists in a muscle fiber during activation by various interventions. In the present study, the light signal of aequorin in single frog skeletal muscle fibers was detected as an image using video-intensified microscopy system. Images were stored in the frame memory controlled by image processor and also recorded with video tape recorder. After injection of aequorin, tetanic stimulation (50 Hz) or caffeine (10 mM) was applied to the preparation. In tetanus, substantial inhomogeneity of light was not recognized. However, in caffeine contracture, the periphery of the fiber became bright and then the light spreaded into the center. Diffusion of caffeine was calculated but the inhomogeneity of the light could not be simply explained by the diffusion of caffeine from outside to inside the fiber.

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AN IMIDAZOLYL REAGENT RELEASES Ca^{2+} FROM SARCOPLASMIC RETICULUM. AOKI.T.[1], OBA,T.[2], AND HOTTA,K.[2] 1: Dept.Food Nutrit., Gifu Women's Junior Coll., Nagarafukumitsu, Gifu 502, and 2: Dept. Physiol., Nagoya City Univ. Med. Sch., Mizuho-ku, Nagoya 467.

Effect of diethylpyrocarbonate (DEP, an imidazolyl reagent) on calcium release and ATPase activity of sarcoplasmic retivulum (FSR) fragmented from bullfrog skeletal muscle was investigated. Calcium release was monitored by measuring calcium concentration of outside medium with calcium electrode. Following calcium loading to FSR by 4mM ATP for 30s, 0.1-1mM DEP was added. Release of calcium with various rate and amount was observed upon DEP addition. The maximum release was achieved after 40s-3min (1mM DEP). Ruthenium red (5μM) or increase of $MgCl_2$ (1→5mM) depressed the calcium release by DEP. Ca-ATPase activity in the presence of 2μM A23187 and 2mM ATP was depressed to 0.81, 0.92 or 1.00 of control by 1, 0.3 or 0.1mM DEP, respectively, after 1min. Inhibition by 1mM DEP attained almost steady level at 1min. 5μM ruthenium red did not decrease this inhibition (0.81 of control, by 1mM DEP 1min). Reduction of $MgCl_2$ (3→1mM) did not facilitate the inhibition (0.97 of control, by 1mM DEP 1min). These results indicate that: DEP releases calcium from FSR; DEP inhibits Ca-ATPase of FSR; but ATPase inhibition may not be responsible for calcium release.

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Movements of beads coated with single-headed myosin along actin-cables in Chara internodal cells [1]CHAEN, S., [2]TSUNOO, F*., [3]SHIMMEN, T*. AND [1]SUGI, H. [1]Dept. Physiol., Sch. Med., Teikyo Univ., Tokyo 173, [2]Dept. Biol., Japan Women's Univ., Tokyo 112, [3]Dept. Botany, Fac. Sci., Univ. of Tokyo, Tokyo 113

To examine the role of the double-headed structure of the myosin molecule in muscle contraction, movements of beads coated with single-headed myosin along actin-cables in Chara internodal cells were studied. Single-headed myosin was prepared by papain digestion of rabbit skeletal myosin. Addition of single-headed myosin preparation to the sample of 50% myosin and 50% pPDM myosin increased the beads velocity to 0.7 μm/sec which was larger than the expected value (about 0.37 μm/sec) from the contaminating double-headed myosin. Smooth movements of beads with single-headed myosin itself was observed when the ionic strength of the experimental solution was lowered. The present result suggests that each head of the myosin molecule has the potential ability to cause contraction, although the motion tended to be inhibited at the physiological ionic strength.

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ANALYSIS OF LOCAL MOVEMENTS OF INTACT SINGLE MUSCLE FIBERS OF FROG DURING AND AFTER CHANGE IN LOAD.

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To know the role of local movement during and after the change in load, segmental length change was measured in tetanized frog single fibers from the tibialis anterior muscle of Rana japonica at low temperature (2-4°C) by attaching fine carbon particles to the fiber surface to divide the fiber into several elementary segments of nearly equal lengths. The image of the whole fiber was observed under a Nikon dissecting microscope, and recorded with a high-speed video system (HSV-200, nac Inc.) at 200 frames/sec. Following small or moderate step increase in load (1.0-1.4Po) from isometric tension (Po), a fiber continued to lengthen with the velocity decreasing and the length of all the segments increased nearly equally. When large step increase in load (1.6-1.8Po), however, was applied, a fiber tended to show "give" phenomenon with the lengthening velocity rapidly increasing and only one of several segments was observed to lengthen remarkably. The latter phenomenon indicates that "give" is induced by slippage of cross-bridges of localized part of a fiber.

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ELECTRON MICROSCOPE STUDIES ON THE EXCITATION-CONTRACTION COUPLING IN THE SWIMBLADDER MUSCLE OF SEBASTICUS MARMORATUS.

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To demonstrate the intracellular Ca localization and its translocation during mechanical activity in the fast-contracting swimbladder muscle of a teleost, Sebasticus marmoratus, cytochemical studies with pyroantimonate and X-ray microanalsysis of cryosections were carried out. Ultrastructural observation of the fibers fixed with glutaraldehyde-OsO_4 revealed that the sarcoplasmic reticulum (SR) was well developed and the triads were located at the Z or A-I junction level. In the relaxed fibers, pyroantimonate precipitate was mainly localized in the terminal cisternae (TC) of the SR and on the N-line. While, in the fibers fixed during caffeine (50 mM) contracture, the pyroantimonate precipitate disappeared remarkably in the TC and increased in number at the A-band. The precipitate distribution at the N-line did not change. X-ray microanalysis revealed the presence of Ca in the precipitate. These results indicate that Ca in the TC is released into the myoplasm by caffeine during mechanical activity. Similar results on the intracellular Ca localization was obtained by quantitative X-ray microanalysis of the cryosections of the relaxed fibers. Experiments are in progress to demonstrate the intracellular Ca translocation during mechanical activity.

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EXCITATION-CONTRACTION COUPLING IN THE SWIMBLADDER MUSCLE OF SEBASTICUS MARMORATUS.
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Mechanical responses of the swimbladder muscle in a sound-producing fish, Sebasticus marmoratus, were studied. A single electric stimulus gave rise to an isometric twitch lasting 15 msec at 20°C. With repetitive stimuli, the tension showed a rapid spontaneous decrease. High external potassium caused only a small contracture tension at 4°C, but not at 20°C. These facts suggest that the rate of Ca^{2+} reuptake by the sarcoplasmic reticulum (SR) is very large. In the presence of 5 mM caffeine, complete tetanus occurred with repetitive stimuli, suggesting that the release of Ca^{2+} from the SR is facilitated by caffeine. On the other hand, the muscle did not respond to a single electric stimulus at low temperature. This result suggests that part of the excitation-contraction coupling processes is inhibited at low temperature, because the Ca^{2+}-activated tension in the skinned fibers is not affected by lowering of temperature. Further experiments are in progress to study the effect of temperature on the membrane potential to make clear the excitation-contraction coupling.

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ANALYSIS OF HINDLIMB SKELETAL MUSCLES IN THE DYSTROPHIC MICE(C57BL/6J-dy) AS THE MODEL OF NON-EXERCISE MUSCULAR HYPOTROPHY.
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Biochemical and histological changes of the hindlimb muscle fibers in normal(dy/?) and dystrophic(dy/dy) mice(5-6 and 8-9 wks, male, C57BL/6J-dy) were studied to elucidate the possible mechanism of non-exercise hypotrophy. The homogenate of muscle tissues was fractionated into cytosol(F-1), KCl-soluble(F-2) and KCl-insoluble(F-3). Concentrations of deoxyribonucleic acid(DNA), ribonucleic acid(RNA) and protein of muscle tissues were also determined. Values of [DNA] and [RNA] of hindlimb muscles in dy/dy mice were three times and twice higher than those in dy/? mice, respectively. Protein contents of muscle tissue in dy/dy mice were 15-20% lower than those in dy/? mice. Apparent cell volume of muscle fiber in dy/dy mice estimated from total protein/total DNA and muscle weight/total DNA, was one eighth and one third those in dy/? mice, respectively. The order of decrease of protein content in each muscle fraction was F-2 > F-3 > F-1 in dy/dy mice, indicating that the degree of the decrease of protein content is not identical with each fraction. The number of nucleus in dy/dy mice was twice larger than that in dy/? mice. The ratio of the centronucleus to total numbers of nucleus in dy/dy mice was ten times larger than that in dy/? mice. The value of the most frequent area of the cross section in dy/dy mice was 32-35% smaller than that in dy/? mice.

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FUNCTIONAL PROPERTIES OF THE INTER-MUSCULAR STRETCH RECEPTORS OF THE RAT MASTICATORY MUSCLES. YAMAMOTO, T., HADA, R. and SAKADA, S. Dept. Physiol., Tokyo Dental College, Masago, Chiba 260

In the masticatory muscles of rat, mouse and some other rodents, single train of stretch receptors extends from the lateral aponeurosis of M. masseter to the surface of M. pterygoideus medialis by way of the medial surface of M. temporalis. They are innervated by branches of N. buccalis, the fiber diameter of which are 8-12 μm. The trains were dissected out from rat masseter. Single axons were isolated within the distance of 1 mm from their terminals and laid across a 0.2 mm air-gap to record the afferent discharges during ramp-and-hold stretches. Static extension of the train to 104-112% in length resulted steady discharges of 30-70 impulses/sec. The static index, the frequency of discharges during the hold phase of stretch increased with increases of the extension up to 130%. The dynamic index, the difference between peak frequency and static index increased with stretch velocity up to 50 mm/sec according to a power function. The results suggest that these stretch receptors are sensitive to both the degree and the rate of inter-muscular distance change during mastication.

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PROPRIOCEPTIVE INFUENCE ON OCCURRENCE OF THE SILENT-PERIOD DURING RAPID GOAL DIRECTED VOLUNTARY MOVEMENT. SAWADA, Y., MIYAMOTO, S., AND AOKI, M.* Sch of Allied Health Professions and Dept. of Physiol., Sapporo Med. College*, Sapporo 060

For revealing the peripheral influences from muscle spindles of antagonists on the silent period, areas of each part of triphasic EMG (Ag1, S-P, and ANT) were measured under following two conditions in eight healthy subjects. The first condition is wrist flexion from three different starting positions (20 degree dorsiflexion, 10 degree dorsiflexion and 0), with 10 degree amplitude of movement. The second is flexion with six different amplitudes (5,10,15,20,25 and 30 degree) from 20 degree dorsiflexed starting position. Under the first condition, velocity (5/5) and acceleration (3/5) of movements were almost constant. Areas of Ag1 (5/5) and ANT (4/5) were almost constant and that of S-P slightly decreased. Under the second condition, velocity (6/6) and acceleration (6/6) linearly increased in proportion to increased amplitude of movements. Areas of Ag1 (6/6) responding to movements linearly increased. Areas of ANT (5/6) slightly decreased and areas of S-P (5/6) were constant in spite of the changes of amplitude of movements. These results suggested that activity of agonist MN pools was little influenced by proprioceptive inputs evoked by rapid goal-directed voluntary movements.

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ACTIVITY OF HUMAN SINGLE MOTOR UNITS DURING TREADMILL WALKING(3). OGAWA,Y., OKABE,H., MIYANO,S. AND YONEMOTO,K. Lab. Sports Med., Jikei Univ. Sch. Med., Chofu, Tokyo 182

In order to examine the activity of human single motor units of vastus lateral muscle during treadmill walking, the experiments were carried out on two healthy subjects. The change of knee joint was attained during walking using a goniometer, also. The speeds of treadmill ranged from 20m/min to 110m/min. The recruitment orders during walking were different from those at isometric ramp contraction. There was no change of the order between units which were recruited at considerable different tension at isometric ramp contraction. The order was variable among units whose tension of recruitment was similar. The instantaneous discharge rates of motor units (MUs) tended to be high with the increment of speeds of treadmill. Two kinds of MUs were observed about the knee joint angle when MUs fired. The one changed with the increment of speeds, the other fired in constant ranges without regard of speeds. It was suggested that the activity of MUs were effected by the change of knee joint.

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DIFFERENCE IN CONTRACTILE PROPERTIES BETWEEN SKELETAL MUSCLES CLASSIFIED BY HISTOCHEMICAL METHOD IN RAT AND MOUSE. KASUGA,N. AND UMAZUME,Y. Dept. of Physiol. Jikei Univ. Sch. of Med., Tokyo 105

A mechanically skinned single fiber of rat was devided into two parts, which were provided for measuring calcium activated maximum force P or shortening velocity V at no load and histochemical staining: ATPase and SDH methods were emploied for determining fiber types, SO, FOG, and FG. P was increased in proportion with the cross-sectional area, and slopes were not distinguishable between three types: P's per cross-sectional area were not different from eath other. V was 16-33% and 60-83% smaller in SO and FOG, respectively, than that in FG at any temperature (5-30°C) or any ATP concentration (0.05-10mM). Activation energy was independent of the types and Michaelis-Menten index was 0.10, 0.31 and 0.29 in SO, FOG and FG, respectively. Next we studied the time couse of twitch with varing composition in a bundle of fiber segments in mouse plantaris muscle. In the bundle containing only fibers of fast-twitch type, the proportion of FOG to FG was correlated with the time required for decaing from peak to one half of peak force.

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CHANGES IN HUMAN MOTOR UNIT FORCE THRESHOLDS FOLLOWING SUCCESSIVE WEAK MUSCLE CONTRACTIONS AND STRETCHES. HAYAMI, A.[1],SUZUKI, S.[2], SUZUKI, M.[3] AND WATANABE,S[4] [1]Japan Women's College of Physical Edu., [2]Dept. Sports Sci., Sch. Human Sci.,Waseda Univ.,[3]Kinjo Gakuin Univ.,[4]Dept. Physiol., Sch. Med., Kyorin Univ., Tokyo 181

Recent studies have shown that human biceps brachii motor units recruit at lower force threshold(Ft) after moderate (25% or 50%MVC) muscle contraction(Suzuki et al,Med.Sci.Sports Exercise,1988). This phenomenon may be reflected in the positively biased error in the reproduction of a criterion force after muscle contraction(Hutton et al,J.Physiol,1987). These findings are attributed in part to the postcontraction potentiation of the gamma loop, which can be cancelled by a muscle stretch. In the present study, Fts of biceps brachii single motor units (SMUs) were examined in two male subjects with or without intervening elbow extension. SMU Fts during successive weak contractions with interval of several seconds progressively decreased. However, SMUs showing decreased Fts following successive weak contractions tended to be reset towards the initial Ft level by a muscle stretch. Findings demonstrate how muscle stretch may promote lower myoelectric activity following exercise by acting on proprioceptive pathways.

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REFLEX DISCHARGES OF WRIST FLEXOR DURING BALL CATCHING MOVEMENT IN MAN. YONEDA, T., YANAGIHARA, D., KIMURA, M. & ISHIDA, A. Dept. Physiol., Sch.of Physical Edu., Juntendo University, Immba,Chiba 270-16

Reflex activity of wrist flexor musles(M1,M2) while catching a falling iron ball were studied. Six healthy adult men were employed. Subjects relaxed and performed the catching movement using three types of voluntary modes; " open-palm holding", "grasping", and "grasping and fingering". Surface e.m.g. were recorded on a magnetic tape and later those of fifty trials were averaged. The iron ball was released electromagnetically from 40 cm height. Kynetic energy of the falling ball caused the same level of muscle stretch in all three modes. Amplitudes of M1,M2 during open-palm holding were lower than those during the other two modes in open eye condition. In blindfold condition, M1 and M2 decreased further. It is suggested that the sense of vision might affect the neural mechanisms with respect to modulation of M1,M2 amplitudes. To study the progressive influence of catching experience on M1 and M2, 300 trials of ball catching were performed. However,in the present study it was not possible to show a clear difference of M1,M2 between the first stage(1-50 trials) and the final stage(250-300 trials).

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NEURAL EFFECTS ON INDUCTION OF COMPENSATORY HYPERTROPHY. OHIRA, Y., KURATA, H.
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Effects of denervation and deafferentation at L4 and L5 on muscle weight, protein content, and enzyme activity were studied in rats. Effects of them on induction of compensatory hypertrophy in soleus and plantaris muscles were also investigated when the synergistic gastrocnemius was tenotomized. Muscle atrophy was induced due to decreased protein content following both denervation and deafferentation. The degree of atrophy was greater following denervation than deafferentation. Denervation also caused a decrease in both mitochondrial and cytoplasmic enzyme activities. The EMG activity in soleus and plantaris, measured 3 days after the tenotomy, was greater relative to the pre-treatment level. Compensatory hypertrophy was induced only when the neural supply was intact. No compensatory effects were observed in muscle mass and enzyme activity in both denervated and deafferentated muscles. Data suggested that efferent neural information(s) has an important effect on the regulation of both morphology and function of skeletal muscles. Denervation affected more in mitochondrial than in cytoplasmic enzymes. It was also suggested that afferent information(s) plays a significant role for the regulation of muscle mass. It was further clear that both effernt and afferent nerve supplies have to be intact for the induction of compensatory hypertrophy in response to tenotomy of synergistic muscle.

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EFFECTS OF BODY POSTURE ON MOTOR UNIT FIRING PATTERNS. KURATA, H. and OHIRA, Y., Dept. Physiol. Biomech., Nat'l. Inst. Fit. Sports, Kanoya City, Kagoshima 891-23.

To study gravitational effects on muscle activity, action potentials in human lateral gastrocnemius and soleus muscles were recorded by using intramuscular and surface electrodes when a given tension was produced at either standing, supine, or 30° head-down tilt position. EMG amplitude of the soleus muscle was larger at standing position, but that of the lateral gastrocnemius muscle was larger at 30° head-down tilt position during ramp contraction up to 30kg of isometric ankle extension. EMG activity of the lateral gastrocnemius muscle was greater even at supine position when the leg blood flow was blocked by applying a cuff pressure of 200mmHg around the thigh. EMG activity of the lateral gastrocnemius muscle was decreased, and that of soleus muscle increased gradually during sustanance of force at 30kg for 60 seconds. Recruitment of motor unit with small spike amplitude preceded that with large amplitude at all of the three positions. Increasing motor unit activity in soleus muscle and decreasing activity in lateral gastrocnemius muscle were observed by changing body position from the 30° head-down tilt to the standing. It might be suggested that the increasing activity at standing position in slow-type motor unit of soleus is due to facilitation of motor system in association with the increased distribution of blood.

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THE CENTRAL AND PERIPHERAL CONTROL OF JAW MOVEMENTS IN THE JAPANESE TOAD.
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Inputs from the optic tectum (OT) and the intraoral [glossopharyngeal (nIX) and facial (nVII)] and perioral [trigeminal (nV)] sensory nerves are supposed to be involved in the jaw-muscle activation during 'snapping' 'rejecting' or 'avoiding' behavior (Takeuchi et al., 1986). As a step to understand the controlling mechanisms of jaw movements, we analyzed the intracellular responses of the jaw-muscle-controlling motoneurons (JMNs) to electrical stimuli applied to OT, nIX and nV in paralyzed Japanese toad. The OT stimulation evoked inhibitory postsynaptic potentials (IPSPs) as well as excitatory postsynaptic potentials (EPSPs) in JMNs. These PSPs were suggested to be polysynaptically evoked. Repetitive stimuli with stronger intensities and larger pulse numbers were needed to evoke the EPSPs than those needed to evoke the IPSPs, indicating that the threshold for activating the excitatory pathways is higher than that of inhibitory ones. The nIX and nV stimulation evoked three types of PSPs (i.e., EPSPs, IPSPs and mixture of EPSPs and IPSPs) which were suggested to be polysynaptically evoked. The proportion of JMNs in which the PSPs of three types were evoked was different between the cases of nIX and nV stimulation. The present results suggest that excitatory as well as inhibitory inputs to JMNs from the central and peripheral nervous systems are involved in the control of jaw movements during a variety of behavior.

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REGULATION OF LONGITUDINAL ANAL MUSCLE ACTIVITY THROUGH AUTONOMIC NERVOUS SYSTEM IN DOGS. Onoe, K., Tamura, K., Suda, S. and Takahira, H. Dept. of Physiology, Tokai University, School of Medicine, Bohseidai, Isehara, Japan. 259-11

Two kinds of electrical activities can be recorded by a bipolar electrode, inserted subcutaneously into anal sphincteric region, in decerebrate, deanesthetized dogs. The one is a sustained 'slow wave' with a rate of 0.5 Hz, being consistent with alterations of anal canal pressure, which was identified as the electrical activity of internal anal sphincter(IAS) in previous experiments. The other is a short-lasting 'spike burst', which can be identified as the electrical activity of longitudinal anal muscle coat(LAC), and the shortening of anal canal in consistent with 'spike burst' is recorded isotonically in the present experiment. It is interesting to note that IAS is regulated by autonomic outflows in reciprocal manner; sacral inhibition and lumbar excitation, on the other hand, LAC is regulated by identical outflows in synergic manner; both sacral and lumbar excitations. Further, it is also found that another smooth muscle sphincter located in pelvic viscera; the internal urethral sphincter, which has a periodic slow wave activity with a rate of 1 to 2 Hz, is controlled by autonomic outflows in synergistic manner, i.e. lumbar and sacral excitations with different transmitters. It is indicated that local regulation in effector system is dominant in these organs rather than centrifugal control.

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OPTICAL MAPPING OF POTENCY OF PACEMAKING ACTIVITY IN THE EMBRYONIC PRECONTRACTILE CHICK HEART USING A VOLTAGE-SENSITIVE DYE. KAMINO, K., HIROTA, A., KOMURO, H. and SAKAI, T. Dept. of Physiol., Tokyo Ika-Shika Dai., Sch. Med. Tokyo 113.

Regional gradient of pacemaker activity in the early embryonic precontractile chick heart was quantitatively assessed by means of simultaneous multiple-site optical recordings of changes in membrane potential, using a measuring system with a 10x10-element photodiode array which had a spatial resolution of 30 um. Absorption changes related to spontaneous electrical activity were recorded simultaneously from many contiguous regions in the area in which the pacemaker site was located in 7- to 9-somite embryonic hearts stained with a voltage-sensitive merocyanine-rhodanine dye(NK2761). The absorption changes related to slow diastolic depolarization were detected. The slope of the absorption change related to diastolic depolarization was largest in the pacemaking area, and gradually decreased toward the periphery. Thus, these results suggest that formation of a regional gradient of pacemaking activity results in the functional architecture of the pacemaking area in the early phases of cardiogenesis.

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PACEMAKING AREA AND CONDUCTION PATTERN OF EXCITATION IN THE BULLFROG SINUS VENOSUS AS REVEALED BY MULTIPLE SITE OPTICAL RECORDING OF SPONTANEOUS ACTION POTENTIALS. MOMOSE, Y., KOMURO, H. and KAMINO, K. Dept. of Physiol., Tokyo Ika-Shika Dai., Sch. Med. Tokyo 113.

Using a voltage-sensitive merocyanine-rhodanine dye (NK2761) and a multiple-site optical recording system with a 12x12-element photodiode array, spontaneous action potentials were monitored from multiple sites in the isolated sinus venosus from the bullfrog, and we have demonstrated the pacemaking area and spreading pattern of the excitation within the sinus venosus, under the condition of a low Ca^{2+}-bathing solution. Isochrone maps of conduction were constructed by timing the initiation of the spontaneous action potential-related optical signals. Excitatory waves appeared to conduct radially from the pacemaking area. The conduction velocity was estimated to be around 0.15 m/sec. The location of the pacemaking area in which the earliest optical signal was detected was not uniquely determined: there was great individual variation. In addition, we have found that the pacemaking area is approximately circular in shape and that it often shifts within the sinus venosus.

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EFFECTS OF HIGH K AND NI ON SYNCHRONIZATION IN THE RABBIT SINOATRIAL NODE. MIYAMAE, S., NAKANO, M., SUDO, S., OKAMUNE, S., GOTO, K. Dept. Physiol., Kanazawa Medical University, Uchinada, Ishikawa 920-02

The patterns of synchronization between the two external tissue segments were studied in a preparation of sinoatrial node strip placed in a three compartment bath. The electrical properties of the tissue in the gap segment were manipulated pharmacologically to study the patterns of synchronization between two pacemaker in the external segments. The gap segment of the sinoatrial node strip was superfused with Na-free solution (Na substituted by choline chloride or sucrose). In all cases (n=3), complete desynchronization was never achieved. When the gap segment was superfused with high K solution (Na substituted by K), the pacemakers in the external segments beat independently of one another. Further superfusion of the gap segment with high Ca solution (162.1 mM Na substituted by 117.4 mM Ca) produced a complete desynchronization of spontaneous discharges generated by the external pacemakers. On the other hand, superfusion of the gap segment with Ni (5 mM) produced a loss of 1:1 synchronization between the external pacemakers and a Wenckebach-like pattern developed. A complete desynchronization was never achieved. Our results show that complete desynchronization in the sinoatrial node results from the increase in intracellular free Ca concentration, which is known to abolish junctional conductance.

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AUTOMATISM, DEVELOPED AFTER REPLACEMENT OF POTASIUM BY CESIUM IN THE RABBIT SINOATRIAL NODE CELLS.
SUDO, S., MIYAMAE, S., NAKANO, M., OKAMUNE, S., TAKAHASHI, T. and GOTO, K.
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When external K (5.4 mM) was replaced by Cs (20 mM), an automaticity transiently disappeared within 15 min and thereafter, restored within 30 min. These process were analyzed by means of the action potential amplitude, APD50, prepotential amplitude and cycle length. After replacement of K by Cs, APD50 prolonged and prepotential amplitude decreased, and an automaticity disappeared. APD50 shortened from 163.2 ± 1.6 msec at 5 min after development of new automatism to 59.8 ± 0.8 msec at 35 min. Prepotential amplitude after restoration, was 9.6 ± 0.3 mV at 5 min and thereafter, became steady state (11.3 ± 0.3 mV). In restoration, action potential amplitude was depressed by 40 μM Ba (5.3%), 50 nM verapamil (11.9%) and 1 mM Ca (19%). APD50 was prolonged strongly by Ba (43.2%), but slightly by verapamil and low Ca. Prepotential amplitude was depressed by Ba (8.4%), but increased by low Ca (58%). Cycle length was prolonged slightly by Ba, verapamil and low Ca. These results suggest that the automaticity in Cs-replaced solution might result from a decrease in K conductance and an increase in Ca dependent slow inward current.

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INCREASE IN [Ca]i MAY MODULATE THE EXCITABILITY OF SA NODE SOAKED IN A HYPERTONIC SOLUTION.
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The frequency of spontaneous discharges of the sino-atrial node from guinea-pigs decreased with increasing the osmolarity of perfusate. The rate of reduction was larger when [Na]o is low and smaller when [Ca]o is high. Increasing the osmolarity more than 2.3 times of normal stopped the spontaneous beatings, however, in low [Na]o twice increase was enough to stop. Adding caffeine, dihydro-ouabain or monensin to the two times hyperosmotic solution stopped the spontaneous discharges. Quinine and amiloride could reactivate the spontaneity which had been arrested by the 2.3 times hyperosmolarity. When the osmolarity was increased to 2.3 times in either quinine or amiloride containing solution, the spontaneity never stopped. The transient membrane hyperpolarization induced by 9 mM RbCl after K^+-free superfusion was larger in an isotonic solution than in hypertonic solutions. These results suggest that increased [Ca]i after osmotic shrinkage may cause the suppression of spontaneous beatings.

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MODULATION BY INTRACELLULAR CA^{2+} OF THE HYPERPOLARIZATION ACTIVATED INWARD CURRENT IN RABBIT SINGLE SINOATRIAL NODE CELLS.
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The sensitivity to internal Ca^{2+} of the hyperpolarization activated inward current (Ih or If) in rabbit single sinoatrial node cells was investigated by the whole-cell voltage clamp method. When the patch pipette contained an internal solution of pCa 10, Ih decreased progressively by 74.8±3.3% (n=7). When the patch pipette contained pCa 7, the amplitude of Ih increased by 43.7±8.7% (n=5), and the activation curve shifted to a more positive potential. β-adrenergic agonists also modulated Ih, but the underlying mechanisms of their effects on Ih differed from those of the internal Ca2+. The former affected the Ih kinetics rather than its amplitude, whereas the latter acted on the Ih amplitude rather than on its kinetics.

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EFFECTS OF INTRACELLULAR Na AND Ca ON Na-Ca EXCHANGE CURRENT

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Na-Ca exchange current has been isolated recently by internal perfusion and whole cell patch clamp technique in single guinea pig ventricular cells (Kimura et al. 1986). By this method, we studied firstly the relation between internal Na (Na_i)-external Ca (Ca_o) exchange current and Na_i concentrations. Km value of Na_i was 20.7±6.9 mM and Hill coefficient was 2.03±0.2 (n=14). Secondly, in the relation between Na_o-Ca_i exchange current and Ca_i concentrations, Km of Ca_i was 0.6±0.24 μM and Hill coefficient 1.01±0.09 (n=8). Km of Ca_i and Na_i were both lower than those of Na_o (88mM) and Ca_o (1.43 mM; Kimura et al, 1987). Km of 0.6 μM for Ca_i indicates that Na-Ca exchange activity crucially depends on the physiological Ca_i. Thirdly, Na_i-Ca_o exchange requires Ca_i as an activator. This effect was found to have Km of 22 nM Ca_i and Hill coefficient of 3.7. The maximum activation at 50 nM suggests that the exchanger is fully available under physiological Ca_i.

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MEASUREMENT OF REVERSAL POTENTIAL OF Na/Ca EXCHANGE CURRENT IN SINGLE VENTRICULAR CELLS OF GUINEA-PIG.

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An increase of external Na^+ ($[Na]_o$) or Ca^{2+} ($[Ca]_o$) concentration induced an inward or outward current in ventricular cells under the condition of whole cell clamp combined with an intracellular perfusion technique. This current response decayed with time during the rise of $[Na]_o$ or $[Ca]_o$, while the I-V relation obtained by ramp pulses shifted. We confirmed that these changes resulted from the accumulation/depletion of Na^+ and Ca^{2+} within the cell. When the holding potential was set at the theoretical equilibrium potential of 3Na:1Ca exchange, the shift of the I-V relation was minimal. Under this condition, Ni^{2+} (an exchange blocker)-sensitive component of the current showed a clear reversal potential. The reversal potentials thus obtained were very close to the theoretical values in the range of $[Na]_o$ from 30 to 140 mM and $[Ca]_o$ from 0.2 to 20 mM. The result supports the view that the measured currents represent the Na/Ca exchange current, that its stoichiometry is 3Na:1Ca and that the ratio is independent of $[Na]_o$ and $[Ca]_o$.

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MECHANISMS OF INTRACELLULAR CALCIUM SENSITIVITY OF DELAYED RECTIFIER POTASSIUM CURRENT.

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Mechanisms of intracellular calcium (Ca_i) sensitivity of the delayed rectifier potassium current (I_K) were studied in isolated guinea-pig ventricular cells, using intracellular perfusion technique. Ca_i did not shift a instantaneous activation curve of I_K. An activation process of I_K consisted of fast decreasing, intermediate increasing, and slow increasing components. A deactivation process (tail current) of I_K consisted of fast decreasing and slow decreasing components. Ca_i did not change time constants of all components. Ca_i increased a ratio of the intermediate component to the slow component in activation process, and decreased a ratio of the fast component to the slow component in deactivation process. In an ensemble noise analysis, Ca_i increased a functional channel number of I_K, but not affected an unit amplitude of I_K. These results indicate that Ca_i shifted an equilibration between an open state and a closed state of I_K channels to a direction of the open state.

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THE EQUALLY CONDUCTIVE THREE SUBUNITS OF THE CARDIAC INWARDLY RECTIFYING POTASSIUM CHANNEL REVEALED BY CESIUM AND RUBIDIUM BLOCK.
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The open-state substructure of the inwardly rectifying potassium channels was investigated in isolated single cells of the guinea-pig ventricle using the cell-attached configuration of the patch clamp technique. Cs^+ (10-100 μM) or Rb^+ (20-100 μM) was added into the 150 mM K^+ pipette solution. In 17% of the experiments the inward currents fluctuated between four levels which corresponded to 0, 1/3, 2/3, and full size of the unit current amplitude, respectively. Probabilities of the open-channel current to stay at each sublevel at various conditions were well described by the binomial distribution, which indicated that each of three subunit is blocked (plugged) by the blocking ions independently of the others. The remaining 83% of the experiments, the current flickered between 0-level and full size of unit current amplitude without showing significant sublevels. In these channels blocking of one of the three subunits may induce simultaneous closure of the other two subunits.

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KINETICS OF THE INWARD RECTIFIER K CURRENT STUDIED BY THE OIL-GAP METHOD.
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The kinetics of the inward rectifier K current was studied using the oil-gap voltage clamp in the isolated guinea-pig ventricular cells. This current component was isolated as the difference between currents obtained at 14 and 0 mM K_o. To test contribution of the Mg-block to the inward-rectification (Matsuda., 1987), we varied internal Mg concentrations (2, 350 and 500uM). The rapid time-dependent increase of the inward current on repolarization from E_K+40 mV was not affected by Mg_i, indicating that this time course reflects an intrinsic channel kinetics. When the preceding depolarization was increased, however, the repolarizing pulse induced an initial jump in the current and the amplitude of the time-dependent current became smaller at 350-500uM Mg_i. This current jump was not observed at 2 uM Mg_i and may indicate the instantaneous unblocking. The findings confirm that most of the channels are in either closed states or blocked states during depolarization above E_K+50 mV.

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VOLTAGE-DEPENDENCE OF ISOPROTERENOL-INDUCED INCREASE OF CA CHANNEL AVAILABILITY IN CARDIAC MUSCLE.
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Single Ca-channel currents were recorded from cell-attached patches on guinea-pig ventricular cells using patch pipettes containing 50 mM-Ba and voltage steps to around 10 mV with a duration of 100ms were applied repetitively at 2 Hz from various holding potentials (HPs). The durations of available states (Ts) and unavailable states (Tf) were estimated as mean values from the number of consecutive non-blank and blank sweeps. At large negative HPs 100 nM isoproterenol(ISO) increased the channel availability (Ps) from 0.4 to 0.7 with a prolongation of Ts from 1.5s to 4 s and a shortening of Tf from 2 s to 1.5s. Ts was little affected with a depolarization of HP both in the absence and presence of ISO, while Tf was prolonged progressively with the depolarization of HP and was shortened slightly by ISO at each HP. Ps-V relationship was shifted to a depolarizing direction by 5-10 mV by ISO, i.e., ISO increases the availability more at depolarized HPs.

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OSCILLATORY CURRENTS IN THE ABSENCE OR PRESENCE OF EXTERNAL SODIUM IN Ca-LOADED SINGLE GUINEA PIG VENTRICULAR CELLS

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A possible involvement of nonspecific cation channel current to transient (inward) oscillatory current was investigated by loading a high Ca-low EGTA solution to single cardiac ventricular cells under whole cell voltage clamp. In the presence of external Na, loading 1 μM Ca induced transient current oscillation with contractile movement. This current did not reverse near 0 mV and was inward even at +40 mV, indicating that it is carried largely by Na-Ca exchange current. In the absence of external Na replaced by Li, loading 1 uM Ca from the pipette induced a small current oscillation at low external Ca in phase with movement oscillation. The current was inward at negative potentials and reversed at 0 mM with almost linear I-V relation, indicating that it is nonspecific cation channel current reported as single channel current in cardiac preparations (Colquhoun et al, 1981; Ono et al, 1987; Hill et al, 1988). The present result indicates that both Na-Ca exchange and Ca-activated nonspecific channel current are involved in the transient inward current.

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MEMBRANE POTENTIAL FLUCTUATIONS IN GUINEA PIG VENTRICULAR MYOCYTES UPON RESUMPTION OF OXIDATIVE PHOSPHORYLATION.

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Membrane potential and sarcomere length of guinea pig ventricular myocytes were simultaneously measured after a transient exposure to CN^-. 5 mM CN^- was applied for 30 to 70 min until the myocytes became inexcitable. On removal of CN^-, the myocytes exhibited periodic miniature membrane depolarizations from the resting potential level of -95 mV. When depolarizations were smaller than 5 mV in amplitude and longer than 500 msec in duration, they were accompanied by localized sarcomere shortening resulting in a "propagating contractile wave". Membrane depolarizations of larger amplitude and shorter duration were associated with a more uniform pattern of sarcomere shortening. Trains of electrical stimuli caused transient augmentation of membrane potential fluctuation and enhancement of synchronization of sarcomere shortening. These results suggest that non-uniform elevation of $[Ca^{2+}]_i$ at the resumption of oxidative phosphorylation may initiate membrane potential fluctuations leading to abnormal spontaneous excitation.

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Ca^{2+}-DEPENDENT TRANSIENT OUTWARD CURRENT IN RABBIT VENTRICULAR MYOCYTES.

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Rabbit ventricular myocytes exhibit two types of transient outward current (I_{to}), which are sensitive to 4-aminopyridine (4-AP) and to caffeine, respectively. The caffeine-sensitive I_{to} shows a rapid recovery from inactivation while the 4-AP sensitive one does a slow recovery. When rapid pulsation of 2-2.5 Hz were applied to the myocytes, the 4-AP sensitive I_{to} decreased its amplitude in the 2nd and following pulses but after 3-5th pulse the I_{to} regrowth appeared. The regrowth of I_{to} was not affected by 4-AP but was completely blocked by Co^{2+}, Sr^{2+} replacement for Ca^{2+}, external application of caffeine or ryanodine. An internal application of 20 mM EGTA also inhibited the I_{to} regrowth. These results indicated that the caffeine-sensitive I_{to} is Ca^{2+}-activated, and is produced by Ca^{2+}-influx via the slow channel and the Ca^{2+}-release from the SR. It contributes to ventricular repolarization at fast heart rate, while the 4-AP sensitive I_{to} does at slow heart rate.

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EFFECTS OF GRAYANOTOXIN ON Ca CURRENTS IN ISOLATED GUINEA PIG MYOCYTES. SAWANOBORI, T., KUGA, K.,HIRAOKA, M. Dept. Cardiovasc. Dis., MRI, Tokyo Med. and Dent. Univ., Tokyo 113

The effects of grayanotoxin (GTX) which increases the Na permeability, on Ca currents were examined using the whole cell clamp technique. In the presence of GTX at 10^{-5}M ventricular myocytes generated long lasting action potential without changes in resting potential. In the voltage clamp depolarizations from -40 mV GTX reduced peak inward currents (24% at 0 mV), suppressed the delayed outward K^+ currents (30% at 0 mV), tail currents (33% at +60 mV) and shifted the holding currents to inward direction (0.07 nA). Long exposure to GTX, tail currents changed to inward direction, developing oscillatory transient inward currents. The above changes were antagonized by TTX (30 μM). In the Na-free solution replaced by TEA and presence of TTX, slight reduction of Ca current was attributed to its "run down". In these conditions, kinetics of the Ca^{2+} current were not significantly changed after application of GTX. We confirmed that GTX has no direct action on Ca current but affected it through the Na^+-Ca^{2+} exchange mechanism after increased Na^+ permeability.

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INACTIVATION OF THE CARDIAC Na CHANNEL. MITSUIYE, T., KIMITSUKI, T. AND NOMA, A. Department of Physiology, Faculty of Medicine, Kyushu University, 812 Fukuoka, Japan.

The single guinea-pig ventricular cell dissociated by collagenase treatment was stretched across an oil-gap from a pool of K^+-free Tyrode solution to a pool of Cs^+ internal solution. Part of the cell in the internal solution was damaged by crushing a tip of glass capillary (oil-gap method). Through this open end fast voltage clamp of the cell membrane facing the external solution was achieved. It was shown that the inactivation of Na current (I_{Na}) proceeds with distinct delay. At potentials over the threshold of I_{Na} the delay was shortened corresponding the accelerated activation. The recovery from inactivation was much faster than that of inactivation, when compared at the same potential, and was fitted by a single exponential. Around the threshold potential (-50 to -40 mV) I_{Na} disappered, however, further depolarization (-10 mV) elicited Na current. This suggests that the decay of I_{Na} does not reflects inactivation of the overall Na channel. Coupled nature of Na inactivation with activation kinetics or non-homogenious population of Na channel may explain our results.

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A MECHANISM OF POSITIVE CONTRACTILE REBOUND AFTER REMOVAL OF ACETYLCHOLINE IN MAMMALIAN ATRIAL MUSCLE (IV). INATOMI, K., IMANAGA, I., TATEISHI, S AND YASUKOHTI, M.* Dept. of Physidol., Sch. of Med., Lab. of Human Biol*., Fukuoka Univ., Fukuoka 814-01

After removal of acetylcholine (ACh), contractile force was increased above the control value on the canine atrial myocardium. In the previous study, we reported this rebound phenomenon (R) was abolished by pretreatment of atropine, but was induced by addition of atropine during ACh application. Removal of carbamilcholine (CCh) did not induce R but addition of atropine during CCh induced R. In this study, during ACh(10^{-7} ∿10^{-5}M), CCh(10^{-7}∿10^{-5}M) and ACh(10^{-7}∿10^{-5}M) in presence of neostigmine (10^{-5}M), addition of atropine (10^{-7}∿10^{-5}M) increased the amplitude of R, and also shortened the time to peak R, in dose dependent manner. In CCh experiments, a good correlation was shown in relation between the amplitude of R and the time to peak R(r=-0.877). These results suggest that a rapid inactivation of m-AChR is playing an important role in Ca release from SR, since the rebound phenomenon is caused by accummulation of Ca ions in SR during muscarinic agonists (previous results).

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ISOPROTERENOL DECREASES SODIUM CURRENT OF MAMMALIAN VENTRICULAR MYOCYTES VIA INCREASED LEVELS OF CYCLIC AMP ONO, K., KIYOSUE, T. AND ARITA, M Dept. of Physiol., Med. Coll. of Oita, Oita 879-56

We studied the effects of isoproterenol (ISP), dibutyryl cyclic AMP (db-cAMP), and forskolin on the sodium current (I_{Na}) of guinea pig ventricular myocytes using tight-seal whole cell voltage clamp method. The $[Na^+]_o$ was decreased to 60mM by replacing NaCl with sucrose (temperature, 32~33°C). K^+ and Ca^{2+} currents were blocked by external and internal application of CsCl, TMA-Cl, 4AP and $CoCl_2$. Depolarizing clamp pulse (30msec) was applied at a rate of 0.2Hz from holding potential of -80mV. ISP (1μM) decreased the peak I_{Na} by 34% from 6.1±1.9nA (control, mean±SD) to 4.0±1.5nA (n=7). The inhibition was more prominent at less negative membrane potentials, and disappeared in the presence of a -blocker (atenolol 10μM). Dibutyryl cAMP (1-5mM) and forskolin (3μM) also depressed the peak I_{Na} reversibly; db-cAMP (5mM) shifted the inactivation curve of I_{Na} (h_∞-E_m relationship) to hyperpolarizing direction by 3.4± 0.3mV (n=4), in which the test pulse to -40mV was applied from various conditioning potentials of -80 to -50mV (duration, 4970msec). Results suggest that ISP inhibits the peak I_{Na} by altering gating mechanism of Na channels, and which is mediated by increased levels of cAMP.

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Overstretch-induced hyperpolarization in the ventricular muscle may be provoked by increased $[Ca^{2+}]_i$.

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We studied the effects of mechanical stretch on the resting potential(RP) and its modification by extracellular Ca, caffeine, ryanodine and D-600 in guinea pig ventricular papillary muscles. The stretch was imposed by manipulating a strain gauge over the range 90-140% of optimal muscle length(Lmax). The preparation was stimulated at 0.5Hz in Tyrode solution(K=5.4mM) with or without caffeine(10mM), ryanodine(1μM) and D-600(1μM). Stretch-related changes in ultrastructure was examined by electron microscopy. The RP depolarized by about 6mV at the length of 110-120% Lmax, while hyperpolarized by about 5mV at 130-140% Lmax(overstretch). The alterations were also found when $[K]_o$ was decreased to 1.35mM or increased to 21.6mM. However the stretch-related hyperpolarization was more marked in lower $[K]_o$. Caffeine, ryanodine and D-600 prevented this development of hyperpolarization. In 140% Lmax, the sarcomere lengthened by 21%, and the sarcoplasmic reticulum(SR) revealed marked conformational changes with some dilatation as compared to those in 90 and 120% Lmax. The results suggest that stretch-induced hyperpolarization may occur via increases in $[Ca]_i$ resulting from either increased Ca-influx or increased Ca-release from SR, upon overstretch of the muscle.

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PICROTOXIN REDUCES CONTRACTION OF FROG HEART MUSCLE. GUIBERT, R.* and TAKEDA, K.** Lab. Physiol. Cellulaire Cardiaque, U-241 INSERM, Univ. Paris-Sud, F-91405 Orsay, France (**Visitor from Lab. Physiol., Fac. Educ., Tottori Univ. Tottori 680)

Electrical and mechanical activity of atrial fibres of the frog (Rana esculenta) have been simultaneously recorded in normal Ringer solution using double-mannitol-gap method. With addition of 5 mM picrotoxin, action potential-induced peak twitch tension decreased in amplitude to less than one third within a few minutes. The tension recovered almost fully on return to normal solution after a short (4 min) exposure to picrotoxin, but the recovery was only partial after longer exposure. Some changes in the time course of the action potentials occurred with picrotoxin, but the correlation between the changes and induced tension could not be determined. Under voltage-clamp condition, peak tension for a given depolarization decreased (to ca. 80% in a fibre) in the presence of picrotoxin, but clear change in peak inward current was not noticed. The results have shown that picrotoxin inhibits the contraction of the atrial fibres, in contrast to its potentiating action on frog skeletal muscle fibres (Takeda, 1970, Zool. Mag. Japan 79, 334). It appears that main cause of the inhibition of the contraction of the atrial fibres is not an inhibition of Ca current.

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EFFECTS OF c-AMP ON MYOCARDIAL CROSS-BRIDGE DYNAMICS.

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To study the effects of c-AMP (1 mM) on the dynamic cross-bridge characteristics of steadily contracting heart muscle, we analyzed the transient segment-length changes (rather than the transient whole muscle length changes to avoid the contributions of the damaged ends of the preparation to the true mechanical properties) from the same initial segment-length in response to various amplitudes of step tension reductions in skinned (Triton X 100, 1% V/V) rat right ventricular papillary muscles. The segment-length transient responses comprised clear three different phases. The first phase is a rapid and minute shortening during the tension reduction, indicating that the series elasticity of the preparation is so stiff that functionally it can be ignored. The second phase is a slow further shortening and the third a slow lengthening. The segment-length isometric tension fairly decreased at pCa 5.4 but only slightly at pCa 4.4 (saturation concentration) with the administration of c-AMP. Regardless of the activation level, c-AMP decreased the amplitude and markedly shortened the duration of segment-length response in the second and third phase. The velocity of segment-length shortening measured from the second phase was clearly increased with the administration of c-AMP. These results suggest that c-AMP increases the rate of cross-bridge cycling in cardiac muscle.

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FAST X-RAY DIFFRACTION OF HEART MUSCLE.

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A papillary muscle, isolated from the right ventricle of the rat, was held isometrically at a sarcomere length of 2.1-2.2μm. The muscle was made to contract at 2Hz at room temperature (24°C). The equatorial X-ray diffraction pattern was recorded from the muscle using synchrotron radiation and a position-sensitive detector. This enabled us to follow the movements of myosin heads between the thick and thin filaments with a time resolution of 10ms. At the end of each diastolic phase, 20% of myosin heads were associated with thin filaments. The number increased as the tension developed during the systolic phase, reaching the maximum of 70% near the peak tension (150ms after stimulus). However, a detailed examination revealed that the increase in the number preceded the tension development by about 10ms. The number of myosin heads associated with the thin filaments started to decrease immediately after the maximum without forming any plateau. In this respects, the time course of the molecular change agreed with the intensity of the active state proposed for heart muscle.

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DOES BRETSCHNEIDER'S PREDICTIVE INDEX E_t REALLY PREDICT LEFT VENTRICULAR OXYGEN CONSUMPTION?

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E_t, composed of 5 parameters E_0 - E_4, is a predictive index for left ventricular oxygen consumption (VO_2), proposed by Bretschneider (1972). We examined its reliability in 9 excised cross-circulated dog hearts under controlled volume changes and inotropic interventions. In a total of 210 contractions, E_t showed fairly good correlation with VO_2 (R = 0.823). However, the regression lines in ejecting and isovolumic contractions were clearly separated from each other because E_2 containing ejection period became zero in isovolumic contractions. Five coefficients (k_0 - k_4) determined retrospectively by multiple regression analysis widely scattered among individual hearts, suggesting that the fairly good correlation observed between E_t and VO_2 was largely due to the correlation between E_3 containing dP/dt_{max} and VO_2.

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IRREGULARITY OF CYCLE LENGTH IN A SINUS NODE RHYTHM SLOWED DOWN. KAMIYAMA, A. AND SHIBAYAMA, R. Dept. of Physiol., Teikyo Univ. Sch. of Med., Itabashi, Tokyo 173

Various irregularities of the heart contraction rhythm are recognizde under the condition where the heart rate are slowed down. One of the mechanisms of these arrhythmias seems to be an abnormal rhythm in the sinus node pacemaker slowed down. To observe qualitatively change of the rhythms in slowed pacemaker frequencies, electrical activiteis were recorded from excised sinus node preparations of guinea pigs using both by a microelectrode and a suction electrode techniques. Pacemaker frequencies were slowed down by application of 0.5-2.0 mM Mn^{2+}. Cycle lengths of pacemaker potentials in the normal Tyrode's solution did not show any irregularity in the most cases, whereas irregular changes of the cycle length appeared in several preparations showing slowed rhythm. These irregularities after the application of Mn^{2+} were recognized at the range of 1500-3000 ms cycle length. The irregularity was more remarkable in a preparation surrounded by atrial muscle than in smaller sinus node preparation (within 1 x 1 mm). A cause of these irregularities could be cosidered as the desynchronization in the pacemaker cell activities.

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ISOPROTERENOL-INDUCED DECREASE IN MYOCARDIAL CONTRACTILE DURATION DOES NOT DEPEND UPON THE CHANGE IN INTERNAL SHORTENING. OKADA, T.
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The change in sarcomere length of rat right ventricular muscle was determined by laser diffraction technique. Under a muscle isometric condition, sarcomere shortened by 5-10% of its initial length: the internal shortening. When the muscle was stretched during contraction to minimize the internal shortening, i.e., the sarcomere isometric condition, the force development was augmented and the contractile duration was increased probably because of the diminished shortening-induced deactivation. It was hypothetized that when the inotropic state is elevated, the increased force development would increase the internal shortening and this might augment the shortening deactivation, resulting in shortened contractile duration more than that expected from improved SR function. To test this possibility, 1.6 uM of isoproterenol (ISO) was administered and the change in contractile duration was compared at muscle and sarcomere isometric conditions (n=3). Under a control condition, contractile duration at 50% of peak force increased by 26.7 ms when the contraction was switched from muscle isometric to sarcomere isometric. While under the influence of ISO, the increase in contractile duration was 25.7 ms. Thus, the presence of the internal shortening does not seem to affect the ISO-induced shortening of contractile duration.

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VENTRICULAR RELAXATION MODEL BY PHYSIOLOGICALLY LOADED PAPILLARY MUSCLE. OKUYAMA, H., NAKAJIMA, S.* and OCHI, R. Dept. of Physiol. and Dept. of Int. Med.*, Sch. of Med., Juntendo Univ., Tokyo 113

To examine mechanical relationships between ventricle and wall muscle, papillary muscles are assumed to behave as a wall muscle of a hypothetical cylindrical model of the left ventricle during both contraction and relaxation. As a loading condition of this ventricular model, Windkessel model is employed during ejection. On the other hand during filling, pressure difference between left atrium and ventricle creates flow through mitral impedance which is calculated from Yellin's data. Analogue computing circuit are used to generate ventricular pressure, aortic flow and pressure, mitral flow and atrial pressure. On both flows mitral flow is narrower than aortic flow, which is well known as rapid filling in the whole heart. When pressure in pulmonary vein is increased, maximal velocity of mitral flow is also increased. These signals (flow and pressure) well explain real pressure or flow. Therefore it is possible to measure some mechanical parameters of the muscle that might not be measured experimentally in whole heart.

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SCATTERED LIGHT INTENSITY FLUCTUATION STUDIES ON THE EFFECT OF OUABAGENIN AND BAY K 8644 IN THE CANINE VENTRICULAR TRABECULAE. KOBAYASHI, T.[1] AND BOSE, D.*[2] [1]Dept. of Physiol., Sch. of Med., Teikyo Univ., Tokyo 173 and [2]Dept. of Pharmacol., Fac. of Med., Univ. of Manitoba, Winnipeg R3E OW3

Intensity fluctuation of coherent light scattered by cardiac muscle strip during diastole (SLIF) is believed to be due to asynchronous wave-like cellular motion within the myocyte as result of sponteneous release of calcium from the sarcoplasmic reticulum (SR). Cardiac glycoside ouabagenin produces inotropy by increasing intracellular free Ca, and in toxic concentrations it produces abnormal aftercontractions due to oscillatory sponteneous Ca release from SR. On the other hand the Ca channel agonist Bay k 8644 also increases inotropy but at the same time impairs the ability of the Ca release from the SR after rest. This study was done to see if the effect of these inotropic agents on the power spectra of SLIF were different. Both frequency and amplitude of SLIF were increased after 1 uM ouabagenin but these changes were most marked after onset of toxicity followed by aftercontractions rather than during the positive inotropic response and were reversed 2 mM EGTA. In contrast, 1 uM Bay k 8644 decreased SLIF at all levels of inotropic response. These results suggest that SLIF is better indicater of toxicity due to inotrope in the form of abnormal oscillatory contractions rather than an increase in the contractile state.

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CONCENTRATION DEPENDENCE OF THIOCYANATE IONS ON THE CONTRACTION OF RAT PAPILLARY MUSCLE. SUGAYA, R., IWAMOTO, H. AND SUGI, H. Dept. Physiol., Sch. Med., Teikyo Univ., Tokyo 173

Effects of partial replacement of Cl^- in the Tyrode solution with SCN^- on the contractile force and the membrane potentials of rat papillary muscle were studied. Complete replacement of Cl^- caused a phasic enhancement and a following depression of the contractile force while the resting potential and the amplitude of the action potentials decreased monotonically, as we have already reported. Replacement with 50% SCN^- also enhanced the force but the following depression was less conspicuous. Similar reductions were observed in the membrane potentials. Replacement with 25% SCN^- also reduced the membrane potentials. However, the force enhancement was not followed by a depression but persisted until the solution was replaced by normal Tyrode. Thus the effect of 25% SCN^- was similar to that of NO_3^- (complete replacement) or Zn^{2+} (100 μM). The amplitude of the action potentials at a given depolarization level became progressively higher as the concentration of SCN^- reduced. The results suggest that the reduction in the resting potential and the depression of the action potentials or the force are independent actions of SCN^- and that the latter has a higher threshold.

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COMPARTMENTALIZED ATP AND ITS VARIATION UNDER ISCHEMIA IN RAT HEART. WATARI, H., SEO, Y., MURAKAMI, M., TAKAMI, H.*, MATSUDA, H.*, KAWASHIMA, Y.*, FURUYA, E.**, TAGAWA, K.**, Dept. Mol. Physiol., Natl. Inst. Physiol. Sci., Okazaki 444, *Dept. Surgery, Med. Sch., Osaka Univ., Osaka 553, **Dept. Physiol. Chem., Med. Sch., Osaka Univ., Osaka 530.

In order to examine subcellular compartmentalization of ATP and its relation to the energy depletion under iscehmia, ^{31}P-NMR was utilized in isolated perfused rat heart and the results were compared with that of chemical analysis. The signal of ATP and creatine phosphate in ^{31}P-NMR were standardized by the intracellular volume ratio measured by ^{23}Na-NMR to obtain each content. Under aerobic perfusion the ATP content determined by NMR (13.7 mol/gr. dry wt.) was significantly lower than that by chemical analysis (22.4 mol/gr. dry wt.), while the creatine phosphate content measured by two methods coincided with each other. Under ischemia at 33 C, ATP signal in ^{31}P-NMR decreased progressively and completely disappeared at 16 min of ischemia. At this point, however, myocardial ATP of 5.7 mol/gr. dry wt. was still detected by the chemical analysis. It was concluded that there were two comparments of intracellular ATP in the heart, detectable and undetectable by ^{31}P-NMR spectroscopy, and that the ATP in the former compartment which seemed to be cytosolic free form of ATP diminished earlier than that in the latter compartment under ischemia.

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A NEW ^{39}K-NMR APPROACH TO MEASURE MYOCARDIAL INTRACELLULAR POTASSIUM WITHOUT SHIFT REAGENT. KUKI,S., MATSUDA,H., TAKAMI,H., KAWASHIMA,Y., SUZUKI,E.*, MURAKAMI,M.*, WATARI,H.* First Dept.of Surg., Osaka Univ. Med. School, Osaka 553, and *Dept. of Mol. Physiol., Natl. Inst. for Physiol. Sci., Okazaki 444

It has been reported that myocardial intracellular potassium ion (Ki) can be detected by ^{39}K-NMR, but its sensitivity is not satisfactory even in use of chemical shift reagents. In this study we found that the T_1 of Ki was less than 10 msec, and the T_1 of extracellular potassium ion (Ke) was several times longer than that of Ki. This new approach was applied to Langendorff perfused rat hearts to measure Ki without shift reagent using a modified inversion recovery method in which the extracellular resonance was nulled and almost all of the only intracellular resonance was obtained at this null point of Ke. Using rat hearts subjected to anoxia and following reoxygenation, the Ki was measured by ^{39}K-NMR, while the potassium flux was detected by the ion analysis of coronary effluent during the same intervention. The changes of intracellular potassium obtained by ^{39}K-NMR agreed with those by the ion analysis.

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SODIUM CHANNEL CURRENT IN THE VENTRICULAR CELLS OF EMBRYONIC RAT HEART. HINO, N. AND KOIZUMI, K.* Dept. Physiol. and Dept. Anat.*, Sch. Med., Juntendo Univ., Hongo, Tokyo 113

The characteristics of the sodium current (I_{Na}) in the single ventricular cells isolated from 14-day-old embryonic rat hearts were studied by the patch-pipette whole-cell clamp recordings. The internal and external solutions contained Na^+ of 20mM and 135mM, respectively. I_{Na} was activated by depolarizations positive to -45mV from a holding potential of -85mV, and its peak amplitude was obtained at about -15mV with a current density of 0.25mA/cm^2 (n=15). The reversal potential of +50mV estimated from the currents during the depolarizations or its tail currents agreed with that predicted from the Nernst relation. The steady-state inactivation was examined using 0.3sec pre-pulses followed by a depolarization to -20mV. I_{Na} decreased on pre-pulses positive to -65mV. Half activation and inactivation potentials calculated according to the m^3h model were -33.3mV for m and -48.9mV for h. These values were 15∿40mV more positive than those in the adult cells. It is suggested that the Na^+-dependent action potentials in embryonic cells with low resting potentials (∿-60mV) can be generated by the voltage-shift in the Na channel kinetics at this stage.

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THE SENSITIVITY OF CULTURED CHICK EMBRYONIC VENTRICULAR CELLS TO NOREPINEPHRINE OR cAMP. TOYOTA, H., MATSUMURA, M. AND OHKITA, Y. Dept. Physiol., Kawasaki Med. Sch., Kurashiki, Okayama 701-01

Studies were carried out to investigate the actions of norepinephrine (NE) and of cAMP on the chick ventricular cells cultured from 9-10 day and 17-19 day embryos. The membrane potential was recorded with an ordinary microelectrode and contraction was detected as the change in diameter of the cell aggregate. NE was applied either locally from a thin glass pipette placed close to the cells or small volume of concentrated NE solution was dropped into the medium to make the desired final concentration. When electrically stimulated, the cell aggregate showed the negative relationship between the strength of contraction and the stimulation rates; the higher the stimulation rate the smaller contraction. NE augmented the spontaneous contraction of 18 day embryo. The cells of 10 day embryo were very little sensitive to NE when it was applied by the dropping method. It is probable that the cells were desensitized to NE. Intracellular injection of cAMP by iontophoresis produced slight hyperpolarization without noticeable change in the spontaneous beating rate or the shape of action potential. However, both NE and cAMP were effective on the plateau if it was previously reduced or shortened with nifedipine. The recovering action on the reduced plateau was more marked in 17 day than in 9-10 day embryonic ventricular cells.

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MECHANISMS OF β-ADRENERGIC ACTION OF DELAYED RECTIFIER K+ CURRENT IN GUINEA-PIG VENTRICULAR CELLS.

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We investigated the mechanism of β-adrenergic agonist on the delayed rectifier K^+curent (I_K) in guinea-pig ventricular cells using the whole-cell clamp method. Isoproterenol(ISO) increased I_K amplitude without changing its voltage dependency. The increasing effect was observed even in the presence of 10 mM EGTA in the pipette, suggesting that the effect of ISO was not modulated significantly by the intracellular Ca^{2+}. Dose-response relation between ISO and I_K amplitude yielded a half maximal effect at 1.8×10^{-8} M. Forskolin (10^{-5} M) increased I_K amplitude to a similar extent as that produced by 10^{-6} M ISO. Internally applied 5×10^{-5}M c-AMP and 5×10^{-6} M catalytic subunit of A-kinase (C-subunit) also increased I_K to a similar extent. Phorbor esters are known to increase I_K by activating C-kinase. The effect of a phorbor ester (10^{-8} M) on I_K was still observed after application of a maximal dose of forskolin (10^{-5} M) or C-subunit(5×10^{-6} M), suggesting that these two substances affected I_K additively.

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EFFECTS OF CATECHOLAMINE ON MYOCARDIUM OF SHRs' FOLLWING DEVELOPMENT. NAKATA.T., SATO, S., SEKIYA,S.*, TSUTSUMI,T.*, OSADA,H.*, Dept. of Clinical Physiol. Kanagawa Prefectural College, Yokohama 241. *Div. of Cardiology, Showa Univ. Fujigaoka hospital Yokohama 227.

The purpose of the present study was about possible relation between catecholamines (CAs) and left ventricular hypertrophy(LVH) on SHRs. In this study, we observed responses and effects of l-isoproterenol(l-ISO) and dl-norepinephrine(dl-NE) on the action potential duration of 50% of repolarization(APD50) in WKYs and SHRs.

The hearts(left ventricle:LV) were excised and isolated from embryonic rats(gestation age of 18,20 days),newborn rats(age of 3,5,10 days) and adult rats(age of 10weeks). The LV was electrically stimulated at frequency of 1 Hz. APs were recorded with micro-electrode method in the Tyrode solution kept at 37°C. Each drug was cumulatively added to the normal Tyrode solution to the concentration of $1x10^{-9}\sim1x10^{-5}$ g/ml.

When concentration of l-ISO and dl-NE was changed to $1x10^{-5}$ from $1x10^{-9}$ g/ml, the both rdugs induced elongating of LV-APD50 with the dose-dependence. Pertaining to LV responses to the drugs in vitro, SHRs showed slightly longer prolongation tendency of LV-APD50 than WKYs. But both drugs induced shorting tendency of LV-APD50 with high concentration from age of 10 days and adults. Of interest was that the responses of CAs changed following development. However, it was not clearly elucidated whether these effects lead to LVH.

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A NEW APPARATUS TO MEASURE SIMULTANEOUSLY INNER AND OUTER DIAMETERS UTILIZING THE X-RAY SENSITIVE IMAGE SENSOR.

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We have designed and constructed a new diameter gauge, utilizing a high resolving power and stability of the X-ray sensitive image sensor. The present device consists of the following three parts: (1) an X-ray generator, a visible light source and a control circuit, (2) an X-ray image sensor and (3) a video signal processing circuit for the X-ray and the visible light. The distinct feature of the new apparatus is summarized as follows. (1) Contact-free measurements of blood vessel inner, outer diameters, and wall thickness are possible. (2) The resolving power of the gauge is 25 μm in principle. (3) The inner diameter measurement by the X-ray is made 6.66 seconds, and outer diameter is continuously made during the time when the measurement by using of the X-ray is not performed. (4) The measurement result of the diameter can be monitored digitally and be recorded in the analog formed. A few results of its preliminary application to renal arteries were also demonstrated.

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ELECTRICAL IMPEDANCE-CUFF TECHNIQUE FOR THE NONINVASIVE MEASUREMENT OF ARTERIAL PRESSURE, BLOOD FLOW AND ARTERIAL ELASTICITY.

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A new plethysmograph, called "electric impedance-cuff", was designed for the indirect measurement of blood flow, arterial pressure and compliance in human limb arteries. The device comprises a compression chamber filled with electrolyte solution and a tetrapolar electric impedance plethysmograph whose electrodes are placed inside the chamber; the former for controlling transmural pressure (Pt) and the latter for detecting limb volume, arterial volume and its pulsatile variation (Δ Va). Systolic and mean arterial pressure were determined by detecting respectively the appearance and maximum point of the pulsatile impedance variations during the gradual increase in the chamber pressure. Diastolic pressure and pulse pressure (ΔP) were calculated from these pressures using conventional equations. Compliance defined as $\Delta V/\Delta P$ was obtained at various Pt levels controlled by the compression pressure. Limb blood flow was also measured using this technique combimed with a conventional venous occlusion method.

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THE THEORETICAL ANALYSIS OF THE BLOOD FLOW VELOCITY DISTRIBUTION IN THE VESSEL.

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The blood flow velocity distrúbution was analyzed theoretically based on the linear Navier Stokes equation. The flow velocity decreased with the increase of the Womersleys parameter in the phase of n*t=0 and pai/2. Such changes were evident fór larger radius Ra.and near the central axis of the artery. The each frequency components of the flow velocity increased with the increase of the Ra at any position of the cross section of the artery.

The normalyzed blood flow velocity u/uc showed complex dependency on the frequency and Ra. A distinct differences of the frequency dependency existed between 0.075cm Ra 0.175cm and 0.2cm Ra 0.3cm. With respect to the Ra dependency of the blood flow velocity a certain maximum flow velocity existed for each frequency and position of the cross section of the artery. The radius dependent changes of the flow velocity was also affected by the changes in the viscosity of the blood. It aslo showed a certain maximum flow velocity for each frequency and position of the cross section of the artery.

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A SPECTRAL ANALYSIS OF FLOWING BLOOD IN A MICROVESSEL.

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We have constructed an apparatus for obtaining an absorption spectrum of flowing blood in microvessel. This system consists of an inverted microscope, a grating, and a photon counter. The transmitted light is guided with a light fiber(ϕ=400μm) from microscope to the grating. This light is diffracted with the grating and the number of photons are counted as a function of wave length.

The characteristics of this system are as follows. 1) The measurable smallest area is about 5μm diameter. 2) The objective area can be set easily. 3) The sensitivity 10^3 - 10^6 photon counts/sec. 4) Its spectral range is 350 - 750 nm.

We have developed an algorithm of data analysis for the system, and measured the absorption spectra of hemoglobin solution and RBC suspension. 1) The visible spectra of hemoglobin at various concentrations is recorded. 2) After calculation of the light scattering, the spectra of flowing RBC can be obtained. 3) The degree of O_2 saturation of hemoglobin or RBC can be calculated.

Applying this system to a microvessel of rat mesenterium, we can measure 1) RBC concentration and 2) the change of O_2 saturation of flowing blood in a microvessel (diameter $\geq$ 8μm).

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The Effect of Minimal Atherosclerotic Plaque on the Spatial Distribution of Wall Shear Stress - A Model Study - T. Yamaguchi* and S.Hanai.
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Low wall shear stress (WSS) regions are specific arterial locations prone to atherosclerosis. However, it is likely that the WSS distribution pattern changes markedly when atherosclerotic wall irregularities affect arterial geometry. Very few studies on exact shear stress distribution patterns following the appearance of an atherosclerotic lesion have been reported. We measured model WSS distribution pattern using an electrochemical method. There was a striking and complex change in the WSS distribution around the small model plaque, even when the reduction in area produced by the obstacle was only an order of magnitude of several percent. The WSS value increased to twice or greater than twice the Poiseuille flow value. Our results suggest that the changes in WSS induced by the appearance of an early atherosclerotic lesion may markedly alter the course of the disease.

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MECHANISMS OF SYSTEMIC ARTERIAL PRESSURE OSCILLATION. MIYAKAWA, K. 2nd Dept. Physiol. Shinshu Univ. Sch. Med., 3-1-1, Asahi-machi, Matsumoto, 390

Systemic arterial pressure oscillation (SAPO) caused by side pressure exertion procedure can be sustained by an active mechanism for each descent of SAP in addition to the same for each ascent. During the oscillation Type II and Type I vasomotor neurons discharge reciprocally in the medulla, while sympathetic and vagus nerves discharge in the same way in the periphery, respectively. The heart is innervated by both sympathetic and parasympathetic nerve fibers, while the peripheral arterioles lack such symmetry in innervation. Accordingly they are provided with no mechanism of active distension. The vagus discharge produces bradycardia and slow contraction of the left ventricle which results in a decrease of dp/dt. It converts the activity of left ventricle into squeezing style of push of blood toward periphery. It is very effective for overcoming the viscosity accompanying distension of the arterioles which remains constricted after the stop of sympathetic discharge. In this regard, the left ventricle under vagus discharge can be regarded as an active dilator of peripheral arterioles.

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HEMODYNAMIC CHANGES CAUSED BY SKIN STIMULATION. IGARASHI,K., TAKEO,T.*, HOSHINA,Y.*, SUGA,S.* and NIKARA,T.* National Sanat. Iwaki Hosp., Namioka 038-13, Dept. of Physiol., Hirosaki Univ. Sch. of Med.* and Physiol. Lab., Sch. Allied Med. Sci.*, Hirosaki 036

In the present report, the hemodynamic changes by the skin stimulation with dry towel rubbing were studied from the standpoint of autonomic nervous tone. The subjects were naked upper trunk and chestwall, back were rubbed during about 5-10 minutes by examiner. Before and after skin stimulation, arterial blood pressure, heart rate, stroke volume, cardiac output, total peripheral resistance were noninvasively measured by the pulse wave and Korotkoff sound graph recorder (PARAMA, TOKYO). The systolic pressure, mean pressure, heart rate, and cardiac output were slightly increased, whereas diastolic pressure, cardiac index and total peripheral resistance were almost unchanged after skin stimulation. From the above mentioned results, it is suggested that skin stimulation may act inhibitory to vagus center intervening in bulbar pathway.

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PULSE WAVE PROPAGATION VELOCITY IN THE ARTERY UNDER VARIOUS CONDITIONS. OKAI. O., and MAKINO, K., Dept. of Clin. Physiol., Kyorin Univ. Sch. of Health Sci., Miyashita 476, Hachioji, Tokyo 192.

We proposed the theoretical study of pulse wave propagation velocity (PWPV). This is attributable to the effects of blood viscosity and arterial viscoelasticity resulting in frequency dispersion and selective attenuation. We proposed the theoretical study of PWPV, emphasizing arterial wall compliance and viscosity i.e., viscous properties of blood are included in a viscoelastic vessel wall representing the analogous electrical cable model, distributed parameter one, which is rewritten to the three component model, lumped parameter one; a new concept of PWPV has been established on the basis of the simplified model. Using this concept we have investigated the relation between PWPV and other circulatory parameters under various conditions, especially direct electrical stimulated ones to the aorta. The effects of the stimulation are increased with decreasing frequency. An decrease in compliance is observed during stimulation, suggesting the lack of nervous control because the same decrease in compliance occurs under final condition to death.

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EFFECTS OF SYMPATHETIC VASOCONSTRICTOR NERVE ON CALF BLOOD FLOW DURING STATIC MUSCLE CONTRACTION. SAITO, M., †MANO, T. AND †IWASE, S. Toyota Technological Institute. Nagoya 468, †Res. Inst. Environ. Med., Nagoya Univ. Nagoya 464-01

To confirme the function of sympathetic vasoconstrictor nerve on blood flow in the resting limbs during static muscle contraction, calf blood flow(CBF) determined by strain gauge method and sympathetic nerve activity supplying the calf muscle(MSNA) recorded by microneurography were analyzed simultaneously in seven healthy subjects before, during and after a 2-min static handgrip(SHG). CBF increased at the initial phase of SHG and thereafter decreased gradually until the end of SHG. After SHG, CBF recovered to the resting value before SHG. MSNA expressed as total activity (bursts x burst amplitude) for 30 sec before SHG decreased rather than the resting value and this lower value remained for 30 sec after the start of SHG, followed by gradual increase until the end of SHG. After SHG, MSNA decreased quickly, but was slightly higher than that of the resting value. Although there was no significant correlation between CBF and MSNA at rest and during the recovery, there was a significant correlation between these two variables during SHG. These results indicate that the decrease in CBF during SHG is induced predominantly by a calf muscle vasoconstriction due to the increase in MSNA. Contrarily, a brief increase in CBF at the inital phase during SHG may result from the decrease in MSNA transitionally before and after the start of SHG.

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MYELINATION OF AFFERENT FIBERS OF THE AORTIC BAROREFLEX ARCH. YAMASAKI, M., SHIMIZU, T. Dept. Physiol., Fukushima Medical College, 1 Hikari-ga-oka, Fukushima 960-12

The postnatal development of the aortic nerve in rabbits, the result of which has been reported in part, was functionally and structually studied in more detail. In anesthetized rabbits at different ages, we first measured the arterial pressure of the right common carotid artery with a pressure transducer and heart rate by a cardiotachometer and then counted the number of myelinated fibers in aortic nerves under the light microsope. The nerve was also examined by the electron microscope. For the histological examination, a fresh sample of the nerve was taken out of the animal after perfusing with modified Karnowsky's solution, postfixed with 1% osmic acid, and embedded in Epon 812. The number of myelinated fibers increased rapidly until 4 weeks after birth and reached to the mature level around 8 weeks. The thickness of myelin sheath (y) significantly correlated with the diameter of axon (x) in myelinated fibers ($y=0.03x+0.26$, $n=693$, $r=0.51$, $p<0.01$). There was also a significant correlation between the number of myelinated fibers (y) and the basal mean arterial pressure (x) ($y=9.31x+92.7$, $n=13$, $r=0.88$ $p<0.01$) during the developmental period. The results support the previous suggestion that postnatal myelination of aortic nerve fibers in rabbits is depend on the magnitude of the basal arterial pressure.

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PARTICIPATION OF OPIOID RECEPTOR ON NEURAL TRANSMISSION IN THE CELIAC GANGLION DURING BAROREFLEX. HORIUCHI, J., TERADA, N. AND TAKEUCHI, T. Dept. Physiol., Yamanashi Medical College, Tamaho, Yamanashi 409-38

This study was designed to elucidate responses of pre-ganglionic (pre-NA, splancnic nerve activity) and post-ganglionic activities (post-NA, renal nerve activity) in altering blood pressure with pharmacological method in anesthetized rabbits. Changes in pre- and post-NA during baroreflex were compaired between before and after local administration of naloxone (20 μg/kg) into the celiac ganglion. Local administration of methionine-enkephalin (0.1∼10.0 μg/kg) only reduced post-NA (-9.0±1.0∼-41.2±4.7%, mean±S.E.), and this reduction was inhibited by the administration of naloxone into the ganglion. Both pre- and post-NA increased with the pharmacological hypotension and these increases didn't be influenced by the administration of naloxone. In contrast, both pre- and post-NA decreased with the pharmacological hypertension, but the post-NA was significantly inhibited by the administration of naloxone in baroreceptors intact rabbits. The inhibitory effect induced by the administration of naloxone disappeared after the carotid sinus nerve denervation. These results suggest as follows. Opioid receptor in the sympathetic ganglion exerts an inhibitory action on neural ganglionic transmission. This inhibitory action participates in the efferent sympathetic nerve activity decreases caused by baroreflex, especially by carotid sinus reflex.

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INHIBITION OF BAROREFLEX VAGAL BRADYCARDIA BY DISTENSION OF VISCERAL HOLLOW ORGANS IN RATS. NOSAKA, S. AND MURATA, K.※ Dept. Physiol., Mie Univ. Sch. Med., Mie 514

Arterial baroreflex, a major mechanism to maintain circulatory homeostasis, is offset under circumstances such as defense area activation and somatosensory excitation. Here, we report the influence of visceral afferent activation on the baroreflex, especially on its heart rate component. In chloralose-urethane anesthetized, succinyl-choline immobilized and artificially ventilated rats, the aortic depressor nerve was electrically stimulated while propranolol being continuously infused, to elicit baroreflex hypotension (BH) and vagal bradycardia (BVB). Hydrostatic distension of the esophagus, stomach, jejunum and urinary bladder with Ringer solution, was found to inhibit the baroreflex, especially BVB with a threshold below 5 mmHg. Lung inflation by increasing inspiratory volume suppressed BVB as well. Thus, it may be generalized that distension of visceral hollow organs inhibits arterial baroreflex. Spinal cord transection at C_1 was found to abolish BVB inhibition by esophageal, gastric and jejunal distension. Low frequency, but not high frequency, stimulation of the splanchnic (Spl) nerve strongly suppressed BVB as well as BH, whereas the subdiaphragmatic vagus did not inhibit the baroreflex when stimulated. Finally, Spl afferent discharges were found to increase in response to gastric and jejunal distension. In conclusion, baroreflex inhibition due to distension of the upper digestive tract is largely mediated by sympathetic unmyelinated afferents.

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DOES THE CAUDAL VENTROLATERAL MEDULLA PARTICIPATE IN THE ARTERIAL BARORECEPTOR REFLEX ? KOSHIYA, N., SAEKI, Y., TERUI, N., and KUMADA, M. Institute of Basic Medical Sciences, University of Tsukuba, Tsukuba, Ibaraki 305, Japan

In urethane-anesthetized rabbits, we examined whether neurons in the caudal ventrolateral medulla (CVLM) participate in the arterial baroreceptor reflex. The medulla was split at the midsagittal plane to disrupt projections from baroreceptor afferents to the contralateral medulla. In such preparations, baroreceptor reflexes arising from individual baroreceptor nerves and tonic sympathetic nerve activity remained intact. A unilateral parasagittal section between the nucleus tractus solitarius (NTS) and the CVLM (from obex to 2 mm caudal to it and 2 mm lateral from the midsagittal plane) abolished the reflex response of renal sympathetic discharges to stimulation of aortic nerve A-fibers of the manipulated side (n=4). Furthermore, a unilateral local injection of kainic acid (2-5 nmol) into the CVLM abolished the arterial baroreceptor reflex of the injected side (n=4). These interventions preserved the field potential of the ipsilateral NTS, the sympathoexcitatory response evoked by electrical stimulation of the ipsilateral rostral ventrolateral medulla and the sympathetic response to stimulation of the contralateral aortic nerve. These results are consistent with the hypothesis that neurons in the CVLM subserve the arterial baroreceptor reflex.

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PERIPHERAL EFFECTS OF ANP ON BAROREFLEX CONTROL OF HINDLIMB VASCULAR BEDS. KAWADA,M., YOSHIDA,H., MORITA,H., UEMURA,N.,MOTOCHIGAWA,H.,KAJIMOTO,S., MATSUSHITA,K., HOSOMI,H. Dept. Physiol., Kagawa Medical School, Miki, Kita, Kagawa 761-07

ANP has been reported to inhibit baroreflex control of arterial pressure. The aim of this study was to examine peripheral effects of ANP on baroreflex control of dog hindlimb vascular beds. In the first protocol, we perfused the vascularly isolated hindlimb of one dog with blood from another and mesured the quick mild hemorrhage induced reflexogenic increase in perfusion pressure (ΔHPP) before and during the infusion of ANP (0.3 μg/kg/min, 20min, i.v.) to the donor dog. The ANP infusion to the donor dog did not affect ΔHPP. This result indicated that ANP did not affect responsiveness of hindlimb vascular beds. In the second protocol, we used the same procedure as in the first protocol except that ANP (0.3 μg/kg/min, 20min, i.v.) was infused to the recipient dog. We evaluated the effect of ANP on ΔHPP and overall open-loop gain (G) of the baroreceptor reflex system with the quick mild hemorrhage. The ANP infusion to the recipient dog did not affect ΔHPP, but G significantly decreased from 7.5 ± 0.8 to 3.9 ± 1.1 (mean $\pm$ SE, n=6). This result indicated that ANP did not influence the neural control via baroreceptor reflex system on hindlimb vascular beds. Thus, we concluded that ANP could interfere with baroreflex control of arterial pressure but not with baroreflex control of hindlimb vascular beds.

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CHANGES IN SYSTEMIC AND PANCREATIC CIRCULATION IN CONSCIOUS DOGS WITH ACUTE PANCREATITIS. NAKAYAMA, S., TSUKAMOTO, Y., SAITOH, Y., 1st. Dept. Surg., Kobe Univ., School of Med., Kobe 650, MORITA, H., NISHIDA, Y., MOTOCHIGAWA, H., KAWADA, M ., MATSUSHITA, K., NAMEKATA, K., HOSOMI, H. Dept. Physiol., Kagawa Medical School, Kagawa, 761-07

The aim of this experiment was to study changes in systemic and pancreatic circulation in conscious dogs with acute pancreatitis. Pancreatitis was induced by retrograde injection of 10% or 30% Sodium Desoxycholate into the pancreatic duct through a tube inserted into the main pancreatic duct. Cardiac output (CO), gastroduodenal artery flow (GDAF) and superior pancreaticoduodenal vein flow (SPDVF) were monitored for a week. In "10%" group (n=9), CO, GDAF and SPDVF decreased by 54, 36 and 60% of each control in 12 hours following inducing pancreatitis. In "30%" group (n=12), these decreased more than those of "10%" group. GDAF/CO increased by 47%, SPDVF/CO decreased by 37% in "10%" group, while both decresed in "30%" group. These findings suggest that increase in GDAF/CO in "10%" group is due to increased vascular permeability in the pancreas, while decrease in GDAF/CO in "30%" group is due to hemorrhage and necrosis in the pancreatic tissue. One to seven days after inducing pancreatitis in both groups, CO and GDAF returned close to the control, but SPDVF did not return. These data probably mean that decrease in pancreatic venous flow is due to severe inflammation and degeneration in the pancreatic tissue.

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PLASMA ATRIAL NATRIURETIC PEPTIDE(ANP) LEVEL AND MOLECULAR FORMS IN CANINES WITH ACUTE HEART FAILURE INDUCED BY EXPERIMENTAL MITRAL REGURGITATION(MR). K.Satoh, T.Masuda, Y.Masaki, K.Ando, N.Hasegawa, F.Marumo, and R.Kikawada, Kitasato Univ., Japan.

To examine the ANP secretion from the atrium, the concentration of plasma ANP were measured and its molecular forms were determined in 13 healthy canines during and after acute heart failure(HF) induced by experimental MR. A basket catheter was inserted into the left atrium via the pulmonary vein and fixed at the mitral valve. MR can be made by extending the tip basket wire and recovery from MR is immediately possible by closing it. Blood samples were obtained several times from the right atrium during and following MR. Plasma ANP concentrations were measured by RIA and ANP molecular forms were determined by reverse HPLC and GPC. Plasma ANP concentration were 59.8±30.9 pg/ml before MR, 102.1±73.0 during acute HF induced by it, and 36.4±18.6 after it . The left atrial pressure(AP) were 8.3±2.9mmHg before MR, 28.3±7.9 during acute HF, and 10.9±4.7 following MR. Plasma ANP concentration was significantly correlated to Left AP(r=0.77~0.98). Both low and high molecular weight ANP peak were noted before MR. Low molecular weight ANP peaks consisting of alpha-ANP increased far more than the high molecular weight ANP peaks. In conclusion,ANP secretion from the atrium to respond rapidly to change in AP. The main ANP molecular form may thus be alpha-ANP produced in the rapid increase in ANP secretion due to quick increase in AP.

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PLASMA ATRIAL NATRIURETIC PEPTIDE(ANP) LEVEL AND MOLECULAR FORMS IN CANINES WITH ACUTE HEART FAILURE INDUCED BY EXPERIMENTAL AORTIC REGURGITATION(AR). T.Masuda, K.Satoh, Y.Masaki, K.Ando and F.Marumo Kitasato Univ., Sch. Med. 1-15-1 Sagamihara Kanagawa 228

To examine the effects of acute change in left atrial pressure(LAP) on ANP secretion from the atrium, ANP concentration and molecular forms in the plasma of 14 healthy canines were observed during and after experimental AR. A basket catheter inserted into the left ventricle from the apex through the pericardium and fixed at the aortic valve. Experimental acute AR can be made by extending the tip basket wire, and recovery from AR is immediate by closing it. Blood samples were obtained several times from the right atrium during and after AR. Plasma ANP concentrations were measured by RIA and ANP molecular forms determined by reverse HPLC and GPC. The Plasma ANP concentration and LAP were 47±23 pg/ml and 7.3±2.2 mmHg before AR, 149±93 and 23.4±7.0 during acute heart failure and 52±32 and 10.7±3.4 following AR. Plasma ANP concentration and LAP induced by AR were found to be significantly correlated(r=0.82~0.96) in each dogs. Both low and high molecular weight ANP peaks were noted in plasma before AR. However, low molecular weight ANP peaks consisting of alpha-ANP increased far more than the high molecular weight ANP peaks during AR. In conclusion, ANP secretion from the atrium immediately responds to change in LAP induced by experimental AR, and main molecular form of ANP may be alpha-ANP due to rapid secretion of ANP induced by increase in LAP.

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REVERSIBILITY OF CIRCULATORY AND RESPIRATORY FUNCTIONS AFTER THE GLOBAL BRAIN ISCHEMIA. NAGAYAMA, T., SHIMIZU, T., Dept. Physiol., Fukushima Medical College, 1 Hikari-ga-oka, Fukushima 960-12

We measured simultaneously the femoral arterial pressure (AP), heart rate (HR), common carotid blood flow and respiratory movements to study the reversibility of these phenomena after the global brain ischemia sustained for various durations in anesthetized mature rabbits. The ischemia was produced by occluding permanently both vertebral arteries in advance and clamping temporarily both common carotid arteries. In 25 animals, 112 trials of carotid occlusion sustained variously for 10 to 280 sec were performed. In all the trials of occlusion shorter than 100 sec, all the phenomena recovered to these control values after release of the occlusion and in all the trials of occlusion longer than 250 sec, no phenomena recovered. In the trials between 100 sec and 250 sec occlusion, 53 recovered cases and 22 irreversible cases were observed. In irreversible cases, without the resumption of the normal breathing, AP fell down markedly during occlusion in spite of the similar HR change to that of recovered cases. The reversibility of circulatory and respiratory functions after the global brain ischemia may be restricted by not only the duration of the ischemia but also the tolerance against hypoxia in the individual brain stem. The irreversibility may be accelerated also by characteristics of peripheral organs.

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THE ACTIVITY OF AORTIC BARORECEPTORS DURING BRAIN ISCHEMIA. MATSUMOTO, S., SHIMIZU, T., YAMASAKI, M., KANNO, T., NAGAYAMA, T., Dept. Physiol., Fukushima Medical College, 1 Hikari-ga-oka, Fukushima 960-12

In 14 anesthetized, spontaneously breathing rabbits, changes of the whole aortic nerve activities and aortic baroreceptors in response to brain ischemia were studied in relation to the reflex bradycardia. When the blood supply to the brain was completely interrupted, the mean values of HR during bilateral aortic nerve (BAN), left aortic nerve (LAN) and right aortic nerve (RAN) activation were 76, 161 and 225 beats/min, respectively. Under the same preparations, the values of mean arterial pressure (MAP) during BAN, LAN and RAN activation were 152, 155 and 154 mmHg on the average, respectively. The results indicate that cardiac vagal effects of LAN and RAN activation are additive and HR fall responses to LAN and RAN activation are significantly different from each other. In addition, the magnitude of reflex bradycardia provoked by the brain ischemia-induced aortic nerve activation is probably dependent on the total activity by additional recruitment of the fibers being silent during normal AP as well as the total impulse frequency of aortic baroreceptors.

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CIRCULATORY REGULATION OF THE RABBIT CEREBRAL CORTEX TISSUE DURING CEREBRAL ISCHEMIA. TAKEUCHI, T., HORIUCHI, J. AND TERADA, N. Dept. Physiol., Yamanashi Medical College, Tamaho, Yamanashi 409-38

The role of respective internal carotid and vertebral arteries was studied in the maintenance of the parietal cortical tissue blood flow (CTF) in the rabbit brain. Effects of graded reduction of internal carotid artery blood flow (ICF) on CTF and systemic arterial pressure (SAP) were also studied. Effect of occlusion of an artery to the brain on CTF was the same in either side of the hemisphere. Significantly higher reducing rate was obtained in CTF after occlusion of the bilateral internal carotid arteries (81.9±3.7% of control, mean±SE) than that of the bilateral vertebral arteries (99.6±0.4%). Blood supply to the brain was well maintained only by the left internal carotid artery (96.2±1.3%) but did not maintain well only by the left vertebral artery (64.6±7.1%). Calculated regression equations were $Y=-53.8\log X-201$ ($r=-0.931$) between ICF(Y) and SAP(X), and $Y=55.3\log X-6.6$ ($r=0.968$) between ICF(Y) and CTF(X). The both equations shaped a sort of mirror image. Thus the relation between SAP(Y) and CTF(X) fitted a linear regression equation of $Y=-0.94X+192$ ($r=-0.931$). Calculated regression equation $Y=105\log X-109$ having a lower correlation coefficient of 0.884 was obtained between CTF(Y) and internal carotid artery pressure(X). Denervation of cervical sympathetic trunks did not show any significant changes in the values described above.

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COMPARISON OF VENTILATORY AND HEART RATE RESPONSES TO HYPOXIA AND HYPERCAPNIA IN PATIENTS WITH BILATERAL CAROTID BODY RESECTION. HONDA,Y., HASHIZUNE,I. AND KIMURA,H. Department of Physiology, School of Medicine, Chiba University, Chiba 280.

Six patients with bilateral carotid body resection (BR), eight with unilateral resection (UR) and three patients of similar age and pulmonary function (C) were studied. Ventilatory and heart rate (HR) responses were examined during progressive eucapnic hypoxia and steady state hypercapnia with and without hypoxia.

1. In progressive hypoxia test, HR response of the BR was higher than UR and C whereas the opposite tendency was seen in the ventilatory response.
2. In steady state hypercapnia test with hypoxia, HR was depressed in the C, but such suppression was significantly less in the BR and UR. Again, the opposite was true in the ventilatory response.

Thus, in the presence of hypoxic stimulation, the BR invariably revealed HR acceleration with lack of ventilatory augmentation. These results may have been ascribed to withdrawal of the bradycardic and hyperpneic effects of the carotid chemoreceptors.

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THE DEPRESSOR EFFECT OF CATECHOLAMINE NEURONS GRAFTED INTO THE THIRD VENTRICLE OF THE BRAIN IN CONSCIOUS RATS. HASHIMOTO, R. AND KIMURA, F., Dept. Physiol., Yokohama City Univ. Sch. Med., Yokohama 236

We examined the systemic blood pressure (BP) in conscious rats grafted with neural tissues including A-6 group noradrenaline (NA) or A-10 group dopamine (DA) neurons into the third ventricle at the level of preoptic-anterior hypothalamic region. Measurement of BP and heart rate (HR) with tail-cuff method was made every 10 days before and after grafting. Both NA and DA neuron-rich graft caused significant depressor effects, ranging between 20 and 50 mmHg, in the normotensive and salt-loaded hypertensive Wistar rats used as the recipient. Such hypotention began at 10 to 20 days after grafting and continued stably during the period of BP measurement for 70 days. It was noticeable, however, that the depressor effects caused by NA neuron-rich graft was greater than those by DA neuron-rich one. HR in these grafted animals also decreased by 25 to 50 bpm. The results indicate that catecholaminergic transmission in the forebrain participates in the control of cardiovascular function with its hypotensive action.

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CEREBRAL VASODILATOR AREA IN THE BRAIN STEM RETICULAR FORMATION OF CAT. MAEDA, M., MATSUURA, S. Dept. Physiol., Osaka City University Medical School, 1-4-54, Asahi-machi Abeno-ku, Osaka 545

In cats anaesthetized with urethane and chloralose, the sites of brain stem reticular formation (RF) which relate with cerebral vasodilatation evoked by electrical stimulation were identified. The arterial pressure (AP), intracranial pressure (ICP), local cerebral blood volume and other respirocardiovascular parameters were monitored. As a control, stimulation was performed in cats without spinalization and vagotomy (S & V). After S & V, stimulation to 108 out of 262 sites in arterial pressor area that usually evoked ICP rise in the control produced an increase in ICP despite no rise in AP. The sites were in three principal regions: the central part of the pontine RF, the dorsal medullary RF, and the central part of the medullary RF. Stimulation to 32 out of 62 sites in the arterial depressor area produced an increase in ICP with no change in AP after S & V. The response was mainly concentrated in the paramedial and ventral medial region of the medullary RF. Since AP and respiration are constant after S & V, the change in cerebral blood volume due to vasodilatation momentarily reflects the change in ICP. It is concluded that activation of cell bodies or fibres within these regions produces cerebral vasodilatation.

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EFFECT OF TRH ON BLOOD FLOW OF SENSORY CORTEX IN ANESTHETIZED RATS, INANAMI, O.[1], MEGURO, K.*[2], OHNO, K.*[3] & SATO, A.[1], [1]Dept. Physiol. Tokyo Metropol. Inst., Tokyo 173. [2]Dept. Anesthesiol., Tokyo Metropol. Geriatric Hosp., Tokyo 173. [3]Dept. Neurosurgery, Tokyo Med. and Dent. Univ. Tokyo 113.

The effect of an intravenous administration of thyrotropin releasing hormone (TRH) on the regional cerebral blood flow in the sensory cortex was studied in halothane-anesthetized adult Wistar rats. The regional cerebral blood flow was continuously monitored with the laser Doppler flowmetry. The cerebral cortical blood flow increased dose-dependently following administrations of 3×10^{2} ug/kg and 3×10^{3} ug/kg TRH. The systemic blood pressure also increased simultaneously. The TRH-induced increases in the cerebral blood flow existed, after maintaining the systemic blood pressure at a constant level via a pressure reservoir system. After atropinization, the TRH-induced increased responses of blood pressure did not change significantly, but the responses of the cerebral blood flow were attenuated almost 50%. It was suggested that the cholinergic vasodilative system contributed to the TRH-induced increase in blood flow of sensory cortex.

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MAINTENANCE OF BRAIN BLOOD FLOW DURING HEMORRHAGIC HYPOTENSION IS NOT MODULATED BY A REFLEX INCREASE IN PLASMA VASOPRESSIN IN RATS. NAKAI, M., YAMANE, Y.*, Natl. Cardiovasc. Ctr. Res. Inst., Suita, Osaka 565; *2nd Dept. of Int. Med., Kansai Med. Univ., Moriguchi, Osaka 570

Vasopressin is known to dilate isolated brain arteries by stimulating the endothelium of these vessels. We therefore investigated whether or not a reflex increase in plasma vasopressin level during hemorrhagic hypotension favored the autoregulatory dilatation by stimulating the endothelium, thereby maintaining the brain blood flow. In anesthetized, artificially ventilated rats, brain blood flow was determined with radiolabeled microspheres. We found an excellent maintenance of blood flow throughout the brain regions in the hypotensive state, and such maintenance of flow was not modulated at all by a supramaximal i.v. dose of the vasopressin antagonist, or by a sympathectomy. The magnitude of the brain blood flow during hemorrhageic hypotension was entirely independent of the plasma vasopressin level, which ranged from 118 to 973 pg/ml. We conclude that the brain ciruculation can maintain its blood flow in hemorrhagic hypotension without any apparent contribution from a reflex increase in plasma vasopressin.

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VASOPRESSIN MICROINJETED INTO NUCLEUS TRACTUS SOLITARII AUGMENTS ARTERIAL BAROREFLEX CONTROL IN THE RABBIT. YAMAZAKI, T., NINOMIYA, I. Dept. of Cardiac Physiol., National Cardiovascular Center, Osaka 565

The role of arginine vasopressin (AVP) within nucleus tractus solitarii (NTS) in central cardiovascular control was investigated by microinjection of AVP (30ng) in the anesthetized rabbit. In intact arterial baroreflex system, AVP microinjected into NTS had no significant effect on arterial pressure (AP) and renal nerve activity (RNA). When carotid sinus baroreceptor region was isolated and maintained with constant pressure, microinjection of AVP caused an increase in AP and RNA. Further, to determine the influence of AVP on the arterial baroreflex function, we examined the hemodynamic responses to bilateral carotid occlusion with aortic and vagal denervation. Increases in AP and RNA were enhanced by microinjection of AVP. The reflex gain of AP and RNA were increased when compared with control. Based on these results, we conclude that AVP microinjected into NTS modified the arterial baroreflex system in the rabbit.

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ADRENAL SYMPATHETIC NERVE ACTIVITY AND PLASMA CATECHOLAMINE DURING HAEMORRHAGE. NABUCHI, A., MATSUKAWA, K., AND NINOMIYA, I.. Department of Cardiac Physiology. National Cardiovascular Centre, Research Institute, Suita, Osaka, Japan.

Adrenal sympathetic nerve activity (AdSNA) and plasma catecholamine were measured before and after haemorrhage in anesthetized cats. The haemorrhage volume ranged from 10% to 30% of estimated total blood volume was performed by 2%/min. and 10%/min via the femoral artery. An increase of AdSNA and a decrease of arterial pressure occured after haemorrhage and they reached the peaks at the end of haemorrhage. The increase in AdSNA depended upon the magnitude of haemorrhage. Epinephrine and norepinephrine measured at the end of haemorrhage were also increased from 0.17 ± 0.13, 0.55 ± 0.28 to 0.50 ± 0.28, 1.25 ± 0.55 (ng/ml) respectively with 20% of haemorrhage. The correlation between AdSNA and epinephrine ($r=0.69$) was significantly larger than that between AdSNA and norepinephrine ($r=0.04$). These results suggested that plasma epinephrine was determined by AdSNA during haemorrhage whereas plasma norepinephrine was regulated by AdSNA and other factors.

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QUANTITATIVE ANALYSIS OF BAROREFLEX EFFECT ON SYMPATHETIC NERVE ACTIVITY TO THE HEART BEFORE AND AFTER ATROPINE IN THE AWAKE ANIMAL.

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We measured simultaneously sympathetic nerve activity to the heart (CSNA) and kidney (RNA) and arterial pressure (AP) in awake cats at rest and analysed quantitatively mean AP-CSNA and AP-RNA relationships. When AP was increased by norepinephrine iv, CSNA and RNA reduced proportionally to a rise in AP. The gain of baroceptor-sympathetic system, estimated from mean AP-CSNA and AP-RNA relations, was 2.31 and 1.84 to the heart and kidney, respectively. Baroreflex control of CSNA was greater than that of RNA. We examined influences of atropine iv on the baroreflex control of CSNA and RNA. Under atropinization, inhibition of CSNA and RNA by a rise in AP was prolonged after recovery of AP. The AP-CSNA and AP-RNA relationships changed into a remarkable clockwise hysteresis loop. These data suggested that the baroreflex control of CSNA and RNA were nonuniformly modified under atropinization in the awake cat at rest.

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SYMPATHETIC TONE AND BLOOD CATECHOLAMINE CONCENTRATIONS.

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For radioenzymatic assay of noradrenaline (NA) and adrenaline (A) concentrations, arterial blood was withdrawn with an indwelling catheter from spontaneously hypertensive rats (SHR) and normal rats (NR) in the conscious state. At rest both NA and A were significantly higher in SHR than in NR (NA: 319±170(12) vs. 153±31(10) pg/ml plasma, mean±SD(number of rats), $p<0.01$ by U-test; A: 265±126 vs. 120±90, $p<0.01$). They were significantly lower in SHR after lumbar sympathectomy (NA: 185±55(12), $p<0.05$; A: 103±48, $p<0.003$) than intact SHR. This was consistent with the previous observation that ganglionic blockade decreases hindquarter vascular resistance in SHR but not in NR, which suggests the presence of an abnormal tone in the hindquarters of SHR.

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FUNDAMENTAL EXPERIMENT OF CEREBRAL VASOSPASM USING CEREBROVASCULAR SMOOTH MUSCLE CELL IN CULTURE (PART 1).

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The effect of vasoactive agents on the vasoconstriction of vascular smooth muscle cells (VSMCs) in culture was measured by a differential interference microscope to investigate the prolonged vasoconstriction in vasospasm following subarachnoid hemorrhage. VSMCs were obtained from the basilar artery of the rabbit by enzyme-dispersed method. Contraction of VSMCs was expressed as decreased percent in cell area which was calculated by a video-analyze system. VSMCs exhibited a dose dependent graded response to vasoactive agents. The maximum decreased percent induced by hemolysate was 94% of that induced by serotonin and almost similar to that induced by norepinephrine. The result of this study was similar to that of chamber study using ring segments of cerebral arteries by other investigators. Thus contraction model using VSMCs in culture is useful for detecting pharmacological effect of vasoactive agents and morphological change of VSMCs.

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RELAXANT EFFECTS OF PROSTAGLANDIN $F_{2\alpha}$ ON ISOLATED MONKEY CEREBRAL ARTERIES.
KAWAI, Y. AND OHHASHI, T. Dept. Physiol., Shinshu Univ. Sch. Med., Matsumoto 390.

Effects of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) on isolated monkey cerebral arteries were investigated. Low concentrations of $PGF_{2\alpha}$ (up to 10^{-8}M) caused a dose-dependent relaxation in basilar and vertebral arteries, whereas high concentrations of $PGF_{2\alpha}$ (higher than 10^{-6}M) produced a contraction in the same preparations. The $PGF_{2\alpha}$-induced relaxation was not modified by pretreatment with propranolol (10^{-7}M), atropine (10^{-7}M), nor cimetidine (10^{-6}M). Removal of the endothelium by mechanical rubbing markedly suppressed or abolished the $PGF_{2\alpha}$-induced relaxation, but did not attenuate a relaxation induced by sodium nitroprusside (SNP). The $PGF_{2\alpha}$-induced relaxation, but not the SNP-induced one, was significantly reduced by pretreatment with aspirin (5×10^{-5} M). Addition of prostaglandin I_2 (PGI_2) mimicked the effect of a low concentration of $PGF_{2\alpha}$ on monkey cerebral arteries.

These results suggest that a low concentration of $PGF_{2\alpha}$ causes relaxation in monkey cerebral arteries which is dependent on the presence of endothelium. The $PGF_{2\alpha}$-induced relaxation may be associated, at least in a part, with the release of endogenous prostaglandins.

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HETEROGENEITY IN THE DENSITY OF THE AMINERGIC INNERVATION OF CANINE PULMONARY VEIN. MATSUKI, T. AND OHHASHI, T. Dept. Physiol., Shinshu Univ., Sch. Med., Matsumoto 390

The present study was undertaken to examine regional differences in the density of aminergic innervation of canine intra-(IPV) and extra-pulmonary veins (EPV). Transmural electrical stimulation (1-50 Hz in frequency, 5 msec in pulse width and 15 V in nominal voltage) was adopted to intramural nerve fibers in isolated venous preparations. The stimulation produced brief contractions in EPV and IPV ring preparations. The frequency-contraction curve in EPV was sigmoid-shaped, being significantly greater than that in IPV. The contractions were completely blocked by pretreatment with 10^{-7}M tetrodotoxin and significantly attenuated by phentolamine and guanethizine in a dose-dependent manner. The dose-response curves of exogenous noradrenaline, however, were similar in IPV and EPV preparations. Aminergic nerve fibers demonstrated histochemically by glyoxylic acid technique were observed more densely in EPV. The results suggest that there exist regional differences in aminergic innervation in canine pulmonary veins; EPV are innervated more densely than IPV.

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EMF CAN INHIBIT ARTERIOLAR VASOCONSTRICTION INDUCED BY NORADRENALIN, ANGIOTENSIN II AND VASOPRESSIN. OKADA, J. AND MIURA, M., Dept. Physiol., 1st Div., Gunma Univ. Sch. Med. Maebashi 371

The aim of this paper is to elucidate the influence of a high-frequency burst-typed electromagnetic field (EMF) on the blood flow. The Xenopus laevis (albino) was anesthetized with urethane (2.5 g/kg, i.p.), the local web blood flow was determined by the diameter of several fixed points of the arteriols. After a vasoconstrictor agent (such as 2 μM noradrenalin, 0.1 μM angiotensin II and 0.5 μM vasopressin) was added to perfusion medium, the web arteriols were exposed to EMF (9 mG, 10MHz) for 60 or 100 min. The EMF was generated by passing a current through a 10-turn coil wired to a burst-typed EMF generator. The diameter of arteriol was measured by video measuring gauge and the obtained numerical data were calculated by personal computor for statistical analysis. The results were: (1) Action of any vasoconstrictor agent was inhibited by EMF radiation. (2) Inhibition appeared 10 min after onset of EMF radiation and lasted 70 min after cessation of EMF radiation. (3) Inhibition was facilitated when perfusion medium was replaced by high Ca^{2+}solution. (4) Inhibition was transiently abolished when perfusion medium was replaced by low Ca^{2+}solution. These results suggest that such an inhibitory mechanism may be due to a slow outflow of Ca^{2+}across the membrane of a muscle fiber

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CARDIAC COOLING DID NOT AFFECT THE MECHANICAL ENERGY EFFICIENCY OF CONTRACTILE MACHINERY IN DOG LEFT VENTRICLE. SUGA, H., FUTAKI, S., and TANAKA, N. Dept. Cardiovasc. Dynamics, National Cardiovasc. Ctr. (NCVC) Res. Inst., 5 Fujishirodai, Suita, Osaka 565

Our theoretical consideration has shown that the mechanical energy efficiency is inversely related with the slope of the relation of left ventricular O_2 consumption (Vo_2) on total mechanical energy measured by systolic pressure-volume area (PVA) (Suga et al.: Circ. Res. 53: 306-318, 1983). Myocardial cooling is expected to increase this efficiency by decreasing the myosin ATPase activity (Q_{10} = 3) and hence slowing the cross-bridge cycling rate. However, in the left ventricle of excised, cross-circulated canine hearts paced at a fixed rate, cooling from 36°C to 29°C did not change the slope of the Vo_2-PVA relation despite an increase in ventricular contractility by 46% in terms of Emax (slope of the end-systolic pressure-volume relation). The mechanical energy efficiency remained unchanged at about 40%. Intriguingly, the Vo_2-axis intercept or Vo_2 for both basal metabolism and activation did not significantly increase with Emax unlike catecholamines and calcium. (Partly supported by a MESC grant B61480102 and a MHW grant 60C-3)

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OPTIMAL CONTRACTILITY FOR MINIMAL MYOCARDIAL OXYGEN CONSUMPTION GENERALLY EXISTS AT LOWER END OF WORKING RANGE OF CONTRACTILITY. TANAKA, N.*, FUTAKI, S., SUGA, H. Dept. of Cardiovascular Dynamics, National Cardiovascular Center Research Institute, 5-Fujishirodai, Suita, Osaka 565

We studied myocardial oxygen consumption (MVo_2)-contractility relation in right-heart-bypassed dog hearts (n=10) while heart rate, cardiac output, mean aortic pressure, and hence, cardiac work were kept constant. We gradually changed a contractility index Emax by dobutamine or propranolol infusion. When Emax was increased from control by dobutamine, MVo_2 increased monotonically. On the contrary, when Emax was decreased by propranolol, MVo_2 decreased except for one heart, in which MVo_2 decreased at first and then increased slightly. In this heart, the optimal contractility for minimal MVo_2 for the constant cardiac work was obtained as the nadir of the MVo_2-Emax relation curve. However, in the other the hearts, the optimal contractility was recognized as the lower end of the obtained Emax range. This finding is partly inconsistent with our prediction from the previous theoretical study (Tanaka et al: Am J Physiol 254: 1988, in press).

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EFFECTS OF ACIDOSIS AND ALKALOSIS ON CARDIAC FUNCTIONS IN THE DOG. DOI,K., UCHIDA,K., SHIBUYA,I. AND NIIZEKI,K. Dept. Physiol., Sch. Med., Yamagata Univ., Nishinomae, Yamagata, 990-23.

The effect of CO_2 inhalation(10% CO_2 in air) on cardiac functions was studied in anesthetized Mongrel dogs(n=15). Right ventricular and arterial pressures were continuously monitored with catheters introduced from the femoral artery. Mixed venous and arterial blood were sampled every 5 min, and cardiac output($\dot{Q}$) was estimated using the direct Fick's method. During CO_2 inhalation, the animals showed a bradycardia and the increased $\dot{Q}$, stroke volume, right ventricular pressure and cardiac work,i.e.,enhanced cardiac contractility. Vagotomy in both sides did not influence cardiac functions durring CO_2 breathing, suggesting that vagal reflex is not essentially responsible for the CO_2-induced bradycardia and increased contractility. Lactic acid(LA) infusion, which caused the same degree of fall in pH but no change in Pco_2, elicited the similar responses as those observed in CO_2 inhalation. Thus, the effects of CO_2 breathing and LA infusion on cardiac functions appear to be solely attributed to the effect of H^+. An administration of propranolol depressed cardiac contractility, but did not affect the acidosis-induced bradicardia. These results suggest that, during acidosis, bradicardia and enhanced contractility are produced due to H^+ and partly activation of βreceptor. On the othe hand, alkalosis due to hyperventilation made an opposite effect on heart.

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BUFFER VALUE AND DIFFUSION COEFFICIENT OF CO_2 IN HEART MYOGLOBIN SOLUTION. UCHIDA, K., NIIZEKI, K. AND DOI, K. Dept. Physiol., Sch. Med., Yamagata Univ., Nishinomae, Yamagata, 990-23

The role of myoglobin (Mb) in acid-base balance and CO_2 transport has been studied in a Krebs-Ringer bicarbonate solution of horse heart Mb (Sigma, M 1882). The CO_2 content and pH were measured as a function of P_{CO_2} and Mb concentration in the range of 0.11 to 4.0 mM. The buffer value (β) was determined from the slope of the plots of HCO_3^- concentration against pH. At the normal Mb concentration in cardiac cells 0.2 mM, β was 7.4 mEq/pH, which was about one tenth of that in red blood cells. The diffusion coefficients of CO_2 molecule and HCO_3^- (D_{CO_2} and D_{HCO_3}) were determined by comparing observed pH-time curves with calculated ones. The pH changes in a thin layer of Mb solution (75 μ) were measured by pH-sensitive fluorescence of 4-methylumbelliferone. The P_{CO_2} change in the layer was obtained from the numerical analysis of a diffusion equation and then converted to the pH change with the observed linear relation between $\log P_{CO_2}$ and pH. Both the D_{CO_2} and D_{HCO_3} were decreased with increasing Mb concentration, and at 0.2 mM, the values were 9.9 and 16×10^{-5} cm^2/sec, respectively. The D_{CO_2} and D_{HCO_3} values were about 30 and 100 times as high as the corresponding values in red blood cells. The observed high diffusion coefficients seem to be favorable for the CO_2 transport in cardiac cells.

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BETA 1- AND BETA 2-ADRENOCEPTOR-INDUCED NEGATIVE CHRONOTROPIC EFFECT IN SPONTANEOUS CONTRACTIONS OF BOVINE MESENTERIC LYMPHATICS. WATANABE, N. AND OHHASHI, T. Dept. Physiol., Shinshu Univ. Sch. Med., Matsumoto 390

Effects of many kinds of beta-adrenoceptor agonists on spontaneous activity in isolated bovine mesenteric lymphatics were investigated in order to classify pharmacological subtypes of the receptors in lymphatic smooth muscles. Administration of isoproterenol (ISP) caused dose-dependent decrease in the rhythm of the spontaneous contractions. Pretreatment with metoprolol, selective beta 1-adrenoceptor antagonist, and propranolol, non-selective beta-adrenoceptor antagonist, inhibited the ISP-induced negative chronotropic effects, respectively. The inhibitory effect of propranolol was more potent than that of metoprolol. Dobutamine, a selective beta 1-adrenoceptor agonist, produced the negative chronotropic effects, which were inhibited by pretreatment with 10^{-7}M metoprolol or 10^{-7}M propranolol. On the other hand, salbutamol and procaterol, selective beta 2-adrenoceptor agonists, also caused the negative chronotropic effects, which were not inhibited by pretreatment with 10^{-7}M metoprolol but with 10^{-7}M propranolol. These results suggest that there may be both beta 1- and beta 2-adrenoceptors on the pacemaker cells of bovine mesenteric lymphatics and the stimulation of these receptors produces a deceleration in the rhythm of spontaneous contractions.

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THE RELATIONSHIP BETWEEN CARDIAC ARRHYTHMIAS AND SLEEP STATES IN THE 3RD GENERATION RATS FED IN THE CONTANT LIGHT. NOJIMA,K.,*OTSUKA,K.,**TAKATSUJI,H.,SAITO,H.,SETO,K., Dept.Physiol.,**Med.Res.Lab., Kochi Medical School, *Internal Medicine, Tokyo Women's Medical College, Kohasu Oko-cho Nankoku City, Kochi 781-51

We have already reported the arrhythmogenic properties of paradoxical sleep in male Wistar rats. The purpose of this study is as follows : (1) whether or not, there is the similar relationship between sleep states and occurrence of arrhythmias in the constant light schedule. (2) whether or not, constant light schedule alters the frequency of arrhythmia occurrence. Eleven male Wister rats were used for this study. Locomotor activity was recorded continuously for 14 days. Environmental temperature and humidity were kept on constant as 23 °C and 55%, respectivery. After the recording of locomotor activity ambulatory ECG-EEG monitoring was done continuously for 7 days. There observed a circadian rhythm in locomotor activity : the period was 24.9 ± 0.5 hour. Bradyarrhythmia(BA) episodes were observed most frequently during paradoxical sleep the same sa the observation under the light-dark illumination schedule. The incidence of BA episodes and the duration of them showed no significant changes. Circadian rhythm in BA was also observed under the constant light, while the diurnal pattern was altered. It may be possible to speculate the participation of the dark period on the appearance of the characteristic circadian pattern of BA observed in the light-dark schedule.

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IN VIVO STUDIES OF PIAL VASCULAR PERMEABILITY TO SODIUM FLUORESCEIN: ABSENCE OF ALTERATIONS BY BRADYKININ, HISTAMINE, SEROTONIN, OR ARACHIDONIC ACID. Watanabe, M., Tyuma, I., Rosenblum, W.I. Dept. Physiol. Sch. Med., Osaka Univ.. Osaka 530

We studied pial vessels in mice, examining under mercury light the permeability of sodium fluorescein. Topical application of hypertonic solution of NaCl caused leakage of fluorescein. However, putative chemical mediators of leakage, such as histamine, serotonin, arachidonic acid, and bradykinin, all failed to increase permeability to the dye. Apparent increase in permeability only accompanied endothelial damage caused by the dye + light combination, as indicated by productioin of local platelet aggregates. The technique is useful, provided inadvertent endothelial injury is recognized and avoided. The data in mice suggest that pial vessel may not perticipate in the permeability changes reportedly produced in parenchymal brain vessels by several of the mediators we tested.

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EFFECTS OF VASOACTIVE SUBSTANCES ON LYMPHATIC SMOOTH MUSCLES IN ISOLATED CANINE THORACIC DUCT. TAKAHASHI, N. AND OHHASHI, T. Dept.Physiol., Shinshu Univ. Sch. Med., Matsumoto 390

The present study was undertaken to investigate responses of canine thoracic ducts to vasoactive substances and attempted to elucidate regional differences. Cylindrical preparations, 7 mm long, were dissected from the isolated thoracic ducts and placed in 10 mℓ organ baths perfused with Krebs solution. Changes in tension were detected by means of isometric transducers. Addition of epinephrine (Epi), norepinephrine (NE), histamine (His), prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), and 5-hydroxytryptamine (5-HT) caused a dose-dependent contraction. The decreasing order of the contractile responses was as follows; Epi>NE>His=$PGF_{2\alpha}$>5-HT. On the other hand, acetylcholine (ACh), histamine (His), adenosine (ADO), isoproterenol (ISP), and ATP caused a dose-dependent relaxation, among which ACh induced the most prominent relaxant response. ACh and His caused not only relaxation but also contraction in most preparations. However, there was no significant regional difference in the responsiveness of the thoracic duct to vasoactive substances. Further studies will be needed to evaluate the effects of vasoactive substances in regulation of lymph transport through thoracic duct in vivo experiments.

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ULTRASONIC MEASUREMENT OF SMALL VESSEL DIMENSIONS BY M.E.M. CEPSTRUM. MINAMIYAMA, M. AND YAGI, S.*, Dept. Vascular Physiol., National Cardiovas. Center Research Insti., Suita 565, *Dept. Electri. and Electron. Engineer., Sophia University, Tokyo 102

For exact measurement of diameter and wall thickness of a small vessels, a developed computer algorithm for time delay extraction from a composite echo signal was introduced. This is fundamentally Cepstrum Method but has sufficient accuracy for this evaluation by combining with Burg's Maximum Entropy Method.

The r-f echo signal from a nominal 10 MHz, 6 mm diameter, middle internal focus PZT transducer was then digitized into time series at 30 MHz sampling rate with 10-bit resolution. For the normalization of the echo spectrum the response function of the measurement system was experimentally derived as Fourier Transform of the echo signal from a spherical steel target. The normalized log-spectrum of the echo signal of the vessel was truncated by the effective bandwidth of the response function and then the time delay carrier of its frequency series was estimated by the Maximum Entropy Method. The time delay is directly translated in separation between reflectors because the velocity fluctuation is very small in living soft tissues.

The estimated values indicated the fairly good agreement with the real dimensions of small arteries, which were directly measured under the microscopic examination.

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MEASUREMENT OF MICROVASCULAR BLOOD PRESSURE USING A SERVONULLING MICROPRESSURE SYSTEM.

HANAI, S., NISHIO, Y.*, NIIMI, H. and SUZAKI, T.*, Dept. Vascular Physiol., National Cardiovascular Center Research Institute, Suita 565, and *Tateisi Institute of Life Sciences, Kyoto 616

We applied the servonulling technique and directly measured blood pressure in the microvascular beds of the mesentery of rats (Wister (WR) and spontaneous hypertensive rats (SHR)). The frequency response (0-30Hz) and the accuracy (0.5%) of the measuring system (WPI 900) were verified in a test chamber.

Pressure measured in the microvessels of SHR showed features different from WR. In the arterioles of diamater more than 30μm, SHR pressure was significantly higher than WR pressure. The arteriolar pressure of SHR fell steeply down to normal level in the capillary. In the small arterioles (20-15μm) and the venules (15-80μm), pressure distribution in SHR was almost the same with that in WR. It is suggested that higher systemic pressure may influence local pressure of small arterioles.

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FREQUENCY ANALYSES OF PRESSURE PULSE WAVE IN THE AORTA OF WHHL RABBITS.

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Frequency analyses were made of pressure pulse waves in the aorta of WHHL rabbits with inherited hyperlipidemia and premature atherosclerosis. After intravenous injection of pentobarbital(25mg/kg), pressure pulse waves were simultaneously measured at both the aortic arch and the abdominal aorta by microtip catheter type pressure transducers and fed into the technical computer through the data recorder to obtain frequency spectra, phase velocities and transfer functions. Frequency spectra of each pulse wave were mainly composed of the first to third harmonic components. The amplitude of the first harmonic showed a large increase with advancing age in contrast to a slight increase in amplitude of the second and third harmonics. Therefore, the peaking phenomenon appearing in the pulse wave of the atherosclerotic aorta may be due to the increased amplitude of the first harmonic. Phase velocity of the first harmonic was higher than those of the second and third harmonics and increased with advancing age. The ratio of wave height at the abdominal aorta to that at the aortic arch was greater than 1.0 regardless of harmonic number and age. This supports the increased amplitude of the pulse wave travelling along the aorta.

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A NEWLY DEVELOPED SYSTEM FOR MEASURING AUTONOMIC NERVE ACTIVITY AND ARTERIAL BLOOD PRESSURE DURING EATING IN FREE-MOVING CATS.

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We developed a new system for continuously recording autonomic nerve activity and arterial blood pressure (AP) during eating in unrestrained cats. A pressure catheter was inserted into the carotid artery and electrodes for recording renal nerve activity (RNA) or aortic nerve activity (ANA) were implanted under pentobarbital anesthesia. After recovery from anesthesia, the cat was brought into an experimental box (1x0.7x1m) and the catheter and electrodes were connected to a pressure transducer and an amplifier mounted on the back of the cat. Using a small multichannel telemeter(size:12x14cm, weight:240g), RNA, ANA and AP were measured in free-moving state. Eating was evoked by presenting food with a specially designed rotary solenoid. RNA and AP increased during eating. ANA increased proportionally with the rise in AP. The results indicate that RNA participates in cardiovascular adjustment associated with eating behavior in free-moving cats, and that ANA transmits information about changes in AP during eating to central nervous system.

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RED CELL FILTRATION WITH NUCLEPORE AT LOW PRESSURE *SHI-JIA GAO, S. YAMAGUCHI AND H. NIIMI, National Cardiovascular Center Research Institute, Suita 565, Osaka and *Institute of Hematology, Chinese Academy of Medical Sciences, Tianjin, China

Red cell (RBC) filtration at low pressure has not been intensely studied yet, although the shear stress produced by such low pressure differences is comparable to those in microvessels. We examined the RBC filtration at low pressure differences (mainly 17 mmH_2O): the blood suspension was driven by gravitational force of the suspension. In some experiments, additional negative pressures (-30,-50,-70 and -100 mmH_2O) were applied to the suspension. Based on the height-time curve, We analyzed the pressure-flow relationship using the relative resistance of the suspension to the buffer. (i) The resistance of the RBC suspension changed with pressure but that of the buffer remained constant. (ii) The relative resitance without negative pressure greatly increased when pressure decreased but the relative resistance with negative pressures did not increase so much. Filtration tests at the level of physiological shear stresses in microvessels (about 2--5 mmH_2O pressure difference) was better in sensitivity than those at adding negative pressure.

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EFFECTS OF VASOACTIVE PEPTIDES ON THE FLOW RESISTANCE THROUGH VASA VASORUM IN ISOLATED CANINE THORACIC AORTA. YOSHINAKA, Y. AND OHHASHI, T. Dept. of Physiol., Shinshu Univ. Sch. Med., Matsumoto 390

In this study, we attempted to evaluate effects of vasoactive peptides on the resistance through vasa vasorum in isolated canine thoracic aorta.

Angiotensisn II (Ang II, 10^{-9} - 10^{-6} M) and vasopressin (10^{-9} - 10^{-6} M) increased dose-dependently the flow resistance. Pretreatment with saralasin (10^{-8} - 10^{-7} M), a specific antagonist for the Ang II receptor, reduced dose-dependently the Ang II-induced response. On the other hand, pretreatment with aspirin (2×10^{-4} M) potentiated the response to Ang II. Bradykinin (10^{-11} - 10^{-7} M), substance P (10^{-9} - 10^{-7} M), calcitonin gene-related peptide (10^{-9} - 10^{-7} M) and vasoactive intestinal peptide (10^{-8} - 10^{-6} M) decreased dose-dependently the flow resistance through vasa vasorum. Atrial natriuretic peptide (more than 10^{-6} M) decreased slightly the flow resistance. These results suggest that peptides may play some roles in the regulation of the circulation in vasa vasorum through canine thoracic aorta and that Ang II has not only a vasocontracting effect but also a vasodilating effect, which may be related to endogeneous prostaglandin cascades.

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RESPONSIVENESS OF ISOLATED CANINE SPINAL BRANCH OF INTERCOSTAL ARTERY TO VASOACTIVE SUBSTANCES. SHIRAI, K., KAWAI, Y., OHHASHI, T., AND KIYONO, S.* Dept. Physiol. and Anesthesiol.*, Shinshu Univ. Sch. Med., Matsumoto 390

In the present study, we attempted to examine effects of vasoactive substances on isolated canine spinal (outer diameter : 400 - 600 μm) and muscle branches (o.d.: 800-1000 μm) of intercostal arteries. A cylindrical preparation (2 mm wide) was dissected from each artery and suspended in an organ bath perfused with Krebs solution (pH 7.4, 37°C). Changes in tension induced by vasoactive agents were detected by isometric transducers. Addition of 5-hydroxytryptamine (5-HT), norepinephrine (NE), epinephrine, dopamine, angiotensin II (AG II), and vasopressin caused dose-dependent contractions in both branches, among which AG II produced the most remarkable contraction in each arterial preparation. On the other hand, acetylcholine (ACh), sodium nitroprusside (SNP), ATP, ADP, adenosine and isoproterenol produced dose-dependent relaxations in both branches precontracted by NE. Each preparation of both branches was most sensitive to ACh. Histamine caused slight relaxation and contraction in the muscle branch but only slight relaxation in the spinal branch. These results suggest that there were few difference in responsiveness to vasoactive substances excepting for histamine between the spinal and muscle branches of isolated canine intercostal artery.

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THE CARDIOVASCULAR RESPONSES EVOKED FROM THE LATERAL NODULUS-UVULA OF THE CEREBELLAR CORTEX IN DECEREBRATE AND ANESTHETIZED RABBITS.

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The lateral nodulus-uvula of the cerebellar cortex has been electrically stimulated (6 sec train, 25-1000μA, 0.1 msec, 200Hz) and changes in renal sympathetic nerve activity (SNA), systemic blood pressure (BP), blood flow to the kidney (RAF) and hindlimb (FAF) were recorded in either decerebrate or anesthetized rabbits. Under decerebrate condition, the nodulus-uvula stimulation with weak current (25-200 μA) evoked a transient inhibition of SNA, a transient increase of RAF, a decrease of FAF and a fall in BP. Stimulation of the identical area with a strong current (200-400 μA) evoked a transient excitation of SNA, a transient decrease of RAF, an increase of FAF and an increase in BP. Under α-chloralose and urethane anesthesia, the stimulation of an identical area evoked the same cardiovascular responses as in the decerebrate rabbit, although a stronger current was required. Hexamethonium infusion abolished these cardiovascular response in both decerebrate and anesthetized rabbits. These data suggest that this cardiovascular response elicited by nodulus-uvula mediated through the sympathetic nerve fibers, and the anesthesia might change the excitability of the cells or nerve fibers in the cerebellar cortex.

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EFFECT OF ELECTRICAL STIMULATION OF THE CEREBELLUM ON PHRENIC NERVE ACTIVITY

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The purpose of this study was to examine both effects of electrical stimulation of the cerebellum on the respiratory and cardiovascular systems. The experiment was done in a rabbit paralyzed with gallamine under urethane anesthesia. The animal was mounted on the stereotaxic apparatus. Bipolar electrode was used to stimulate the cerebellum. Systemic blood pressure (SBP), heart rate (HR) and phrenic nerve activity (PNA) was monitored. Condition of electrical stimulation (15V, -20Hz, 0.1 msec for 20 seconds) was applied. The electrical stimulation of the fastigial nucleus (FN) caused to change in SBP but not in HR. PNA was augmented by stimulation of FN; increase of the frequency of grouped discharge and impulses in each grouped discharge of PNA. These results suggest that cerebellum including the FN has a role of modulating cardiovascular regulation as well as respiratory control.

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EFFECTS OF α-hANP ON THE HEPATIC CIRCULATION IN CONSCIOUS DOGS.

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The aim of the present study was to investigate effects of α-hANP on hepatic circulation in conscious dogs. Dogs were chronically instrumented by doppler flow probes around the hepatic artery and portal vein, an electromagnetic flow probe around the ascending aorta, and catheters in the descending aorta and superior vena cava. At least two weeks after instrumentation, we measured arterial plasma ANP concentration (ANPa), systemic arterial pressure (SAP), heart rate (HR), cardiac output (CO), portal veinous plasma flow (PVF) and hepatic arterial plasma flow (HAF) before and during the infusion of ANP (0.3 μg/kg/min, 30min). ANPa increased from 214 ± 15 pg/ml to 4.26 ± 0.70ng/ml (mean ± SE,n=5). SAP decreased by 13 ±3 % (n=13). HR increased by 15 ± 3 % (n=13). CO, PVF, HAF and total hepatic flow (THF=PVF+HAF) decreased by 9 ±4, 12 ± 7, 15 ±5 and 13 ± 5 % (n=11), respectively. However, the ratio of decrease in THF to decrease in CO did not change. These results indicated that ANP did not have direct effects on hepatic circulation.

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EFFECTS OF ELECTRICAL STIMULATION OF THE SCIATIC NERVE ON THE CAROTID SINUS BAROREFLEX ARTERIAL PRESSURE CONTROL SYSTEM. NAMEKATA, K., MORITA, H., NISHIDA, Y., MOTOCHIGAWA, H., KAWADA, M., NAKAYAMA, S., TSUKAMOTO, Y., KAJIMOTO, S., MATSUSHITA, K. AND HOSOMI, H. Dept. Physiol., Kagawa Med. Sch., Kagawa 761-07

We examined effects of sciatic nerve stimulation on an open-loop gain (G) of the carotid sinus baroreflex arterial pressure control system in 16 pentobarbital anesthetized dogs. G was estimated from arterial pressure changes after a quick mild hemorrhage (2 ml/kg in 1-2 seconds) through a catheter inserted into the abdominal aorta. After the bilateral vagus and unilateral carotid sinus nerves were cut, we estimated G during stimulation of either the right or left central cut end of the sciatic nerve. G was not significantly altered by electrical stimulation of the ipsilateral sciatic nerve (3.0±0.3 to 2.6±0.3). On the other hand, G was decreased from 3.0±0.3 to 1.9±0.3 by electrical stimulation of the contralateral sciatic nerve ($p<0.05$). The decrease in G was blocked by pretreatment with morphine (0.5 mg/kg). Electrical stimulation of the sciatic nerve decreased mean arterial pressurre by 25±8 mmHg, which was also blocked by pretreatment with morphine. These results suggest that electrical stimulation of the sciatic nerve modulates the baroreflex system and that there are differences between the modulatory effects induced by ipsilateral and contralateral stimulations.

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EFFECTS OF INCREASE OF ARTERIAL PRESSURE ON THE CIRCULATION TIME. KANNO, T., SHIMIZU, T. Dept. Physiol., Fukushima Medical College, 1 Hikari-ga-oka, Fukushima 960-12

To study the hemodynamics during the acute brain ischemic hypertension, the circulation time (CT) in the large vein (LV), pulmonary circulation (PC) and large artery (LA) was measured at various constant arterial pressure (AP) levels by the dyedensitometer, and the blood velocity (BV) in LV and LA was calculated. In a total of 20 anesthetized rabbits, both vertebral arteries and one carotid artery were occluded. AP recorded at femoral artery was elevated to various constant levels by decreasing stepwise the other carotid arterial flow. There was a tendency that CT increased in LV and decreased in LA as AP level increased, and therefore, BV showed the reverse result. The average CT in PC increased to 2.9±0.6 sec from 1.9±0.2 sec of the control for the first time when the mean AP increased to 130 mmHg. Following the complete interruption of the cerebral blood flow, AP level was elevated as high as twice of the control. CT increased and BV decreased significantly in each vascular system. The percent prolongation of CT was 344±291 % in PC, 302±204 % in LV and 215±115 % in LA, and percent decrease of BV was 63±23 % in LV and 59±21 % in LA. From the result, changes of the CT and BV will be mainly due to redistribution of blood volume which relates to the degree of increase of the afterload to the left ventricule, decrease of the cardiac output at various AP levels and difference of compliance of each vessel.

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EFFECTS OF METHYLPREDNISOLONE AND PHENTOLAMINE ON CANINE SPLENIC BLOOD VOLUME HARA,K.*, KOYAMA,S., AIBIKI,M., KANAI,K., and MIYAKAWA,K. Shinshu University School of Medicine, Department of Anesthesiology and Phsiology, Division 2, Matsumoto, Nagano 390

We determined effects of methylprednisolone (MPS, 30mg/Kg iv), phentolamine (0.2mg/Kg, intrasplenic) on changes in splenic blood volume (SBV) in dogs. Splenic venous pressure (SVP) was measured. The spleen was isolated vascullary and was placed into the water-sealed box. Changes in the water in the box was weighted and displayed. Both decreased response on SBV and increased response on SVP to the stimulation and norepinephrine (NE, 0.2 ug/kg, intrasplenic) were diminished by the pretreatment with phentolamine, indicating that the force of splenic blood empty is mediated throught alpha adrenergic stimulation. The nerve stimulation after MPS showed to decrease SVB significantly and trended to increase SVP. These effects of MPS on SBV were lower than that of phentolamine. Capacity of blood pooling into the spleen during occlusion of the splenic vein was trended to increase following phentolamine, but to decrease after MPS. These results may suggest that MPS has a potency of loss of the elasticity with alpha blocking effect.

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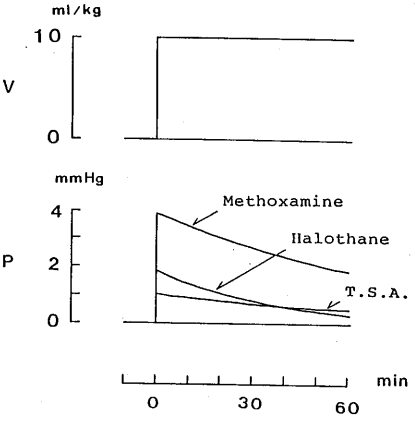
EXPLORATION OF MECHANISM OF DEPRESSOR RESPONSE TO RAPID INFUSION OF BLOOD INTQ AORTA BY MEANS OF FACTOR ANALYSIS ON TIME SERIES.
HATAKEYAMA, I., KATAKURA, T, and NISHIDA, S. Dept. Physiol., Kitasato Univ. Sch. Med., 1 Kitasato, Sagamihara 228

We have reported that rapid infusion of a small quantity of blood (5-15ml) into aorta caused a transitory drop of systemic arterial pressure in the rabbit. In 29 rabbits the SAP changes during 54 minutes from the outset of the infusion were sampled with period 2s. Principal component analysis (PA) as well as image factor analysis (FACTA) were applied to the time series data thus obtained. The contribution ratio indicated that the system can be explained by three factors. The first function loading (FL) obtained by PA increased linearly during the infusion and maintained almost a constant value. The second FL also increased during the infusion but decreased gradually after stop of the infusion. The third FL began to decrease on outset of the infusion and turned to increase about 25 seconds after the start of infusion. These results and the results obtained by FACTA suggests that the SAP change concerns with three factors: venous return (blood volume), arterial windkessel and active depressor mechanism.

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CAPACITANCE VESSELS ARE REGULATED BY AUTONOMIC NERVOUS SYSTEM. Shigemi,K., Morimoto,T., Itoh,T., Chihara,E., Natsuyama,T., Hashimoto,S.*, Tanaka,Y. Depts. Physiol. and Anesthesiol., Kyoto Pref. Univ. Med., Kamigyoku, Kyoto 602.

We studied the effects of total spinal anesthesia (TSA) and pure alpha receptor agonist (methoxamine) on vascular compliance and delayed compliance (stress relaxation) in splenectomized dogs. From the cahnges in blood volume (determined continuously by the dilution method of ^{51}Cr labeled erythrocytes) and central venous pressure consequent to the fluid infusion, vascular compliance was calculated based on the unit response of Maxwell's viscoelastic model. Using the compliance values obtained under different experimental conditions, changes in central venous pressure in response to a step change in blood volume were calculated and shown in the figure. These results suggest that both vascular compliance and delayed compliance (stress relaxation) are regulated by the autonomic nervous system.



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EFFECTS OF ACUTE PULMONARY HYPERTENSION ON INTERNAL DIAMETER OF SMALL PULMONARY ARTERIES IN ANESTHETIZED CATS. SHIRAI, M., NINOMIYA, I, and SADA, K. Dept. of Cardiac Physiol., National Cardiovascular Center Research Institute, Fujishiro-dai, Suita, Osaka 565, Japan

Increases in pulmonary arterial pressure (PAP) were made by altering the volume of air within a balloon inserted into the left atrium, and the changes in internal diameter (ID) of small pulmonary arteries (100-600 μm ID) were analyzed using an X-ray TV system. The ID of the arteries significantly dilated during the PAP increase of 12 and 20 mmHg, but not during the increase of 6 mmHg. The percentage ID dilatation was significantly larger during the 12 mmHg increase (20%) than during the 20 mmHg increase (12%), and it was minimal in the arteries of 200-300 μm ID . After the rapid balloon deflation, the ID response of the arteries varied from dilatation to constriction, whereas PAP immediately returned to the control value. The ID constriction was maximal in the arteries of 200-300 μm ID, and it continued for several minutes after the balloon deflation. We concluded that an active constriction occurred locally in small pulmonary arteries in response to acute pulmonary hypertension caused by the balloon inflation in the left atrium.

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EFFECT OF TAURINE ON SYMPATHETIC NERVE DISCHARGE IN THE SPONTANEOUSLY HYPERTENSIVE RAT. KIMURA, N., KATO, F., TAKANO, K., AND HUKUHARA, T., Jr. Department of Pharmacology II, The Jikei University School of Medicine, Minato-ku, Tokyo 105.

Effect of taurine on spontaneous efferent discharge of the greater splanchnic nerve was studied in the spontaneously hypertensive rats (SHR) and Wistar-Kyoto rats (WKY) anesthetized with urethan-chloralose. Changes in the splanchnic nerve discharge were evaluated by means of power spectral analysis. The intraventricular injection of taurine (300 μg/rat) significantly decreased the arterial blood pressure and heart rate in SHR. The total activity of the splanchnic nerve discharge, which was estimated by power spectral analysis, decreased to 64±11% (N=6, mean±SD) of the control level in SHR and decreased to 91±5% (N=3) of the control level in WKY at 10 min after the intraventricular injection of taurine. In the power spectrum of the splanchnic nerve discharge of SHR, a peak corresponding to the cardiac-related activity (4 to 7 Hz) was specifically abolished by the intraventricular injection of taurine, although the respiratory-related activity (0.7 to 2 Hz) and other components remained with a slight decrease. These results suggest that taurine-sensitive sites exist in the central neural mechanisms controlling the vasomotor activity and baroreceptor reflex.

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VOLUNTARY EXERCISE DECREASED BLOOD PRESSURE AND BRAIN INDOLEAMINE CONTENTS IN SPONTANEOUSLY HYPERTENSIVE RATS. MATSUI, H., OKAMURA, K. AND NOMURA, M. Dept. Physiol., Sch. of Med., Fujita-Gakuen Health Univ. Toyoake, Aichi 470-11

The antihypertensive effect of exercise using a bicycle ergometer is useful for human hypertensive patients. As a model of exercise in hypertension, 14- to 15-week-old spontaneously hypertensive rats (SHR) were tasked on a wheel running test for 6 days (6-D-SHR) or 9 days (9-D-SHR). The blood pressure (BP) and heart rate (HR) were significantly reduced in the 6-D-SHR. Pre-exercise HR was 430 (beats/min) and BP was 185 (mm Hg) and post-exercised HR was 300, and BP 160. On the other hand, 9-D-SHR did not show remarkable changes. In 6-D-SHR, monoamine contents in diencephalon were almost the similar but insignificant changes in non-running SHR, except 5-hydroxyindole acetic acid (5-HIAA). In 9-D-SHR, serotonin and 5-HIAA were remarkably decreased. These decreases were significantly correlated with the resting BP after exercise. Consequently, the serotonergic nervous system is considered to regulate cardiovascular function in the diencephalon.

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INTERRELATIONSHIP BETWEEN UNIT ACTIVITY OF THE NUCLEUS LOCUS COERULEUS AND ARTERIAL PRESSURE IN SPONTANEOUSLY HYPERTENSIVE RAT. HARA, K., KAWAMURA, H., HATANO, M., et al., 2nd Dept. of Int. Med. Nihon Univ. Sch. of Med. 30-1, Oyaguchi-Kamimachi, Itabasi-ku, Tokoy, Japan

We demonstrated previously that arterial pressure elevated when nucleus locus coeruleus (LC) was stimulated electrically, and that it was hyporesponsive in mature SHR. To evaluate this hyporesponsiveness, we investigated the extracellular unit activities (UA) in SHR LC with physiological and pharmacological alteration of arterial pressure. The mean arterial pressure in SHR was higher than WKY. The heart rate was not different between the two strains. The UA of the LC in both strains increased when the arterial pressure was lowered with papaverin-HCl or venesection. It decreased when arterial pressure was elevated with saline or phenylephrine. The %change of UA in SHR LC was less than that of WKY with respect to alteration of arteiral pressure. Therefore, these results suggest that the LC in SHR appears to be lessresponsive to the alteration of arterial pressure, compared to WKY. These responses were readily reversed by bilateral vagotomy. We have found that various peripheral inputs to the LC were mediated via vagal afferents.

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ANALYSIS OF ERYTHROCYTE DEFORMATION UNDER OSCILLATORY SHEAR STRESS (III). KON, K. MURAKAMI, J. AND SHIGA, T. Dept. Physiol., Sch., Med., Ehime Univ., Ehime 791-02

The time dependent erythrocyte deformation was observed under oscillatory shear stress using a rheoscope. When shear stress was sinusoidally modulated between 8 and 32 dyn/cm^2 by varying the velocity of cone rotation with a pulse motor, the extent of cellular deformation altered as erythrocytes followed the change in shear stress. At a low modulation frequency (less than 1.8 Hz), intact cells perfectly responded to the change in shear stress. Above 2 Hz, the extent of deformation during rising phase was less than that measured at a low modulation frequency. While, during descending phase, the extent of deformation was not affected by the modulation frequency. Therefore the cellular deformation could not respond to the rapid increase in shear stress at the rising phase in the shear stress cycle. The impairment of cellular response to the oscillatory shear stress appeared in following cases: (i) increasing of intracellular hemoglobin concentration, (ii) cross-linking of cytoskeletal proteins, (iii) altering of total Ca content of erythrocytes. These results suggest that the cellular response to the oscillatory shear stress is determined by both the intracellular viscosity and the integrity of cytoskeletal proteins.

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RHEOLOGICAL STUDY OF ERYTHROCYTES IN A PATIENT WITH UNSTABLE HEMOGLOBIN DISEASE (Hb YOKOHAMA). S. Hasegawa, K. Arai, M. Iino, N. Uyesaka and Y. Shinagawa.
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Rheological characteristics of erythrocytes in a patient with unstable hemoglobin disease (Hb Yokohama : [β31 (B13) Leu→Pro]) were investigated. Splenectomy had been performed on this patient. Most of the erythrocytes of the patient contained spherical inclusions, namely, Heinz bodies. Remarkable decrease in osmotic fragility, however, was observed in this patient. On the contrary, the patient's erythrocytes produced striking increase in mechanical fragility studied by the impact-force method. Measurement of viscosity revealed the increase in blood viscosity of the patient due to erythrocytes not to plasma component. The perfusion of the bullfrog's hind limbs with erythrocyte suspension of Hb Yokohama produced marked decrease in rate of flow when the perfusion was performed using glutaraldehyde fixed hind limbs. Similar results were obtained from filterability test using nickel mesh which was a new micropore filter produced by a photofabrication technique (Anegawa, T. et al., Clin. Hemorheol., 1988, in press). The present study demonstrated clearly that the decreased deformability of patient's erythrocytes, which might be due to the formation of Heinz bodies, caused the increase in blood viscosity and in resistance to blood flow through vascular network, and that an increase in mechanical fragility indicated intravascular hemolysis *in vivo*.

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PRESSURE-FLOW RATE RELATIONSHIP OF ERYTHROCYTE SUSPENSION INVESTIGATED BY PERFUSION OF NICKEL MESH. K. Arai, T. Anegawa*, S. Hasegawa, M. Iino, H. Shio* and N. Uyesaka.
Dept. of physiol., Nippon Medical School, Bunkyo-ku, Tokyo, JAPAN. *Dept. of Neurol., Faculty of Medicine, Kyoto Univ., Sakyo-ku, Kyoto, JAPAN.

The rheological characteristics of nickel mesh filtration were evaluated from a pressure (P) - flow rate ($\dot{Q}$) relationship of erythrocyte suspension using a slight modification of vertical-tube method (Uyesaka, N., Jpn. J. Physiol., 1988, in press). Nickel mesh is a new pored membrane produced by a photofabrication technique (Anegawa, T. et al., Clin. Hemorheol., 1988, in press). The perfusion of nickel mesh with several stages of echinocytes or stomatocytes produced a decreased flow. The perfusion with erythrocyte suspensions at several osmolality demonstrated osmolality related change in flow. The perfusion with erythrocyte suspension made by different viscosity produced decrease in flow with the rise of the viscosity of suspending medium. Flow decreased with increasing hematocrit value and the total volume of cell suspension through nickel mesh. In this experiment, quantitative data concerning plural cell effect and reversible plugging effect on filterability of erythrocytes were obtained. These effects on the filterability of erythrocytes were also theoretically analyzed. It was reconfirmed in the present experiment that nickel mesh was preferable to nuclepore membrane from a quantitative and reproducible point of view.

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EFFECT OF CONTRAST MEDIA ON RBC DEFORMABILITY. Usuki, N.[1], Minakuchi, K.[1], Onoyama, Y.[1], Nagasawa, T.[2] and Kinoshita, Y.[2]
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We studied the effects of contrast media on the deformability and morphology of RBC using Iopamiron300, Omnipaque300, DIPconray220, 76% Urografin, Amipaque and Biliscopin, which we adjusted to physiological osmolarity, physiological pH, both or neither. RBC and a contrast medium were mixed and incubated for 10 min or else observed immediately. The deformability of RBC was measured by laser diffractometry and the morphological changes were examined by phase contrast microscopy. Iopamiron and Omnipaque, when adjusted to physiological osmolarity, produced more morphological change than DIPconray and Urogurafin, when adjusted to phvsiological osmolarity, and all four contarst media reduced the deformability of RBC. Amipaque and Biliscopin, which we adjusted to physiological osmolarity or not, produced many echinocytes, but decreased the deformability of RBC only slightly. The results suggested that decreases in RBC deformability caused by contrast media depend not only on the osmolarity of the contrast media and on the morphology of RBC, but also on other unknown factors.

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SOLUTE EXCHANGE BETWEEN PLASMA AND PERICARDIAL SPACE: AN INCREASED TRANSPORT RATE OF MEDIAL SIZE MOLECULES. KIKUCHI, Y. and OHSHIMA, N. Dept. of Biomed. Eng., Inst. of Basic Med. Sci., Univ. of Tsukuba, Tsukuba 305

Studies were made on transport of solutes from plasma to pericardial space by analyzing the composition of the pericardial fluid and plasma obtained from rabbits. Components separated by means of a high performance liquid chromatography (gel permeation) ranged from 200 to 800,000 in molecular weight (M.W.). Relative concentrations of plasma solutes in the pericardial fluid determined from the chromatograms did not decrease monotonously with increasing M.W. but were found to form a broad peak from about 1,000 to 7,000 in M.W. (the values often exceeded 1, i.e. those solutes were more concentrated in the pericardial fluid). In order to further assess such peculiar dependence on M.W. of the equilibrium distribution of solutes, their transport rates from plasma to pericardial space were determined by measuring increases in concentration in an isotonic solution introduced into the pericardial space. Higher transport rates even in comparison to lower M.W. solutes were obtained for those medial M.W. solutes in accord with the equilibrium distribution. Similar results were also obtained for intravascularly injected FITC-dextran molecules. A possible mechanism and also a possible physiological role of the increased transport rate for medial M.W. solutes were suggested.

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EFFECT OF TEMPERATURE ON THE VELOCITY OF ERYTHROCYTE AGGREGATION. MAEDA, N., SEIKE, M. and SHIGA, T. Dept. Physiol., Sch. Med., Ehime Univ., Shigenobu, Onsen-gun, Ehime 791-02

The velocity of the aggregation of human erythrocytes under a constant shear rate was examined in the range of 5-43°C with a rheoscope combined with a video-camera, an image analyzer and a computer. (1) With increasing temperature, the velocity of erythrocyte aggregation induced by fibrinogen and immunoglobulin G increased. However, the relationship between the velocity of erythrocyte aggregation and the temperature was different among these plasma proteins. (2) In 70 % autologous plasma, the velocity of erythrocyte aggregation was minimum at 15-18°C, and increased at both higher and lower temperatures. But the velocity was nearly constant above 30°C. (3) The shape of erythrocyte aggregates formed in 12 μmoles/l fibrinogen (containing 770 μmoles/l albumin) and in 70 % autologous plasma was similar each other, and developed into three-dimensional (complicatedly piled and branched) aggregates below 15-18°C and into one-dimensional aggregates (i.e., "rouleaux") above 15-18°C. However, the shape of aggregates formed in 27 μmoles/l immunoglobulin G (containing 770 μmoles/l albumin) was three-dimensional in all temperature ranges. (4) The physiological meaning of the temperature dependency of erythrocyte aggregation was discussed.

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ROLE OF THROMBIN IN He-Ne LASER-INDUCED THROMBUS FORMATION IN THE RAT MICROCIRCULATION. YAMAMOTO,J., IIZUMI,H., HIROTA,R., SHIMONAKA,K., HORIE,N. AND OKAMOTO,U. Faculty of Nutrition, Kobe-Gakuin University, Kobe 673

Thrombus formation is dependent on such factors as blood components, blood vessels and blood flow. Therefore, it is worthwhile studying the mechanism of thrombus formation at the site of their interactions. The present paper describes the role of thrombin in thrombus formation in microcirculation ex vivo. Wistar male rats weighing 300 to 400 g were anesthetized by sodium pentobarbital (i.m.) and the mesenteries were exteriorized into Tyrode solution at 37°C. The thrombus was observed by the irradiation of He-Ne laser (spot diameter 15 μm; power 15mW) after the administration of Evans blue (20 mg/kg, i.v.) in arterioles (20-25 μm in diameter) and venules (27-32 μm). The process of thrombus formation was recorded and analyzed by a microscope-VTR system.

The primary thrombus formation in arterioles and venules was prolonged by commercial heparin as well as by MD 805, a synthetic thrombin inhibitor with high specificity. Minimal inhibitory concentrations of heparin and MD 805 were estimated to be between 5 - 10 x 10^{-5} M, suggesting that thrombin plays the important role in the primary thrombus formation in arterioles as well as in venules.

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RELEASE OF HISTAMINE FROM PAF-ACTIVATED PLATELET OF RABBITS. KAKINOHANA, O., MIYAZAKI, I., KOSUGI, T., Ist Dept. Physiol., School of Medicine, University of the Ryukyus, 207 Uehara, Nishihara-cho, Okinawa 903-01

The role and significance of platelet itself was not clear at present time although these of platelet activating factor (PAF) has been well known in allergy. In this paper, we tried to clarify the direct relationship between PAF and platelet in allergic reaction. Platelet of rabbits was used in this experiment and washed platelet was prepared following Watanabe's method. Determination of released histamine from platelet was procedured by means of Shore's method. After washed platelet (platelet count : $30 \times 10^4/\mu l$) was centrifuged at 3000 r.p.m., 15 minutes, histamine content in the supernatant was 2.4 ± 0.2 μg/ml (Mean ± standard deviation, n=10). Furthermore, after PAF (3.4×10^{-7} M) activated washed platelet and this mixture was centrifuged, histamine content of this supernatant was 3.8 ± 0.25 μg/ml. Histamine (3.8 ± 0.25 μg/ml) derived from washed platelet could contract the ileum of guinea pig in the same manner of histamine hydrochloride (10^{-6}M). Cimetidine and pyrilamine could inhibit the contraction of histamine derived from platelet. From these results, it was suggested that histamine from PAF-activated platelet had an important role in allergic reaction.

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CHANGES OF PLATELET FUNCTION AFTER THE INTRAVENOUS ADMINISTRATION OF HABU VENOM IN RABBITS. MIYAZAKI, I., KAKINOHANA, O., KOSUGI, T., Ist Dept. Physiol., School of Medicine, University of the Ryukyus, 207 Uehara, Nishihara-cho, Okinawa 903-01

We have demonstrated that thrombin-like enzyme, metalloprotease, platelet aggregating substance and inhibitor of platelet aggregating substance contained in crude venom of Habu (Trimeresurus flavoviridis) from the result of biochemical study in vitro. In this paper, we studied in vivo the effect of Habu venom to platelet function, fibrinogen content in the circulating blood of rabbits. The results obtained from this experiments were as follows : 1) Platelet count in PRP in crude venom-administrated group was significantly lower than that in thrombin-administrated group at 15 minutes and 30 minutes after these administration ($P < 0.05$). 2) The activity of platelet aggregation induced by collagen and ADP in supernatant-administrated group was significantly lower than that in precipitate-administrated group at 15 minutes and 30 minutes after these administration ($P < 0.05$).
From these results, it was clarified that venom of Habu could inhibit the function of platelet in the circulating blood of rabbits and this inhibitory activity contained in the supernatant fractionated with 50% saturated ammonium sulfate.

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INHIBITORY MECHANISM OF PLATELET AGGREGATION BY GARLIC OIL AND ITS COMPONENT. OSHIBA, S., SUZUKI, H.*, SAWAI, H. and ARIGA, T.* Dept. of Physiol., Nihon Univ. Sch. of Med., Itabashi, Tokyo 173 and *Dept. of Nutrition & Physiol., Sch. of Agric. and Vet. Med., Setagaya, Tokyo 154

We have found that methyl allyl trisulfide (MATS) in the essential oil of garlic is the most potent inhibitor to platelet aggregation. In the present study, we attempted to clarify the inhibitory mechanism of garlic oil and its active principle, MATS on platelet aggregation. Quantitative analysis of arachidonic acid (AA) metabolites by HPLC showed that garlic oil markedly suppressed both respective pathways of cyclooxygenase and lipoxygenase. MATS inhibited similarly these enzymes. In the AA releasing steps in platelet membrane, garlic oil acted stimulatively. Release of AA from membranous phosphatidylcholine moiety was increased. But that from the other phospholipid moieties were unchanged by garlic oil. It is concluded that inhibition of platelet aggregation by garlic oil is caused by the suppression of enzymatic catalysis of AA, resulting of reduction of thromboxane A_2 generation.

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METABOLIC FATE OF ACID STABLE TRYPSIN INHIBITOR. SUGIKI, M., YOSHIDA, E., SUMI, H., TSUSHIMA, H., MARUYAMA, M., MATSUOKA, Y., IKEDA, R., MORIMOTO, N., ETO, Y., HAMAI, K., HAYASHI, M., HAMASUNA, S., MIHARA, H. Dept. Physiol., Miyazaki Medical College, 5200 Kihara, Kiyotake, Miyazaki 889-16, Japan.

The clearance, organ distribution and metabolic pathway of acid stable trypsin inhibitor (ASTI) were investigated using ^{125}I-labeled preparations. Human urinary trypsin inhibitor (UTI), an ASTI in urine, with a mol. wt. of 67,000, was labeled with ^{125}I by the chloramine T method. Experiments were performed in 55 male mice by intravenous injection of the ^{125}I-labeled UTI. The radioactivity disappeared rapidly from the plasma with a half life of 4 min for the initial part of the curve. Gel filtration of plasma samples showed that UTI was present in the plasma as the free form. The radioactivity was accumulated to a greater extent in the kidneys than in the other organs. 73% of the administered radioactivity was recovered in the urine within 12 hr after injection. Gel filtration of urine samples taken 30 min after the injection showed that approximately 50% of the radioactivity in the urine appeared at the same elution volume as ^{125}I-UTI in the plasma. Affinity for trypsin was observed in this peak fraction. These findings indicated that UTI in the plasma was excreted in the urine in its intact form. The basic kinetics and fate of ASTI in the plasma were thus clarified. Moreover, it was confirmed that the origin of UTI was ASTI in the plasma.

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EFFECT OF LOW MOLECULAR WEIGHT HEPARIN ON FIBRINOLYSIS. OKADA, K., TANAKA, N., TANAKA, H., UESHIMA, S. AND MATSUO, O. Dept. Physiol., Kinki Univ. Sch. Med., Osakasayama 589

Low molecular weight heparin (LMWH) enhanced the plasminogen activation with tissue-type plasminogen activator (t-PA). Further, LMWH enhanced the synthetic chromogenic substrate, H-D-Ile-Pro-Arg-pNA (S-2288) amidolysis of plasma. In the present report, the plasma factor which is responsible for the enhancement of S-2288 amidolytic activity with LMWH. The purification procedures were of the precipitation with $(NH_4)_2SO_4$, was purified heparin-Sepharose affinity chromatography, and high performance affinity chromatography with Zn-chelate 5PW. The plasma factor was recovered in the precipitate with 30% saturated $(NH_4)_2SO_4$. In the heparin-Sepharose affinity chromatography, the enhancement was observed in the eluted fraction with 0.5MNaCl. When this fraction was applied to Zn-chelate 5PW, the enhanced activity was observed in the unbound fraction and the eluted fraction with 0.035M Glycine. The purification factor of enhanced S-2288 amidolytic activity with LMWH was about 1,000. The immunoelectrophoresis revealed the precipitate line in the γ-region.

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STUDY ON THE FIBRINOLYTIC ENZYME IN THE HEPATOBILIARY SYSTEM (XVII) —A PLASMINOGEN ACTIVATOR RELEASED BY THE CELL LINE DERIVED FROM HUMAN LIVER— OSHIBA, S., IMAI, H., TAKAO, K., SAWAI, H., IMAI, S., *ARIGA, T. AND *SEKI, T. Dept. of Physiol., Nihon Univ. Sch. of Med., Tokyo 173, *Dept. of Nutr. and Physiol., Nihon Univ. Coll. of Agric. and Veter. Med., Tokyo 154

The plasminogen activator (PA) released from primary cultured rat hepatocyte has been recognized to be identical with a biliary PA, Bilokinase in terms of its enzymatic properties. In the present investigation, we dealt with some cell lines derived from human liver, and some of the enzymatic properties of PA from HuH-7 and KN7-7 were eluciated in comparative way with those of UK and t-PA. HuH-7 and KN7-7 cell lines were observed to produce high active PA releasable into culture medium. The molecular weights of the two kinds of PA of HuH-7 were 72,000 and 50,000, and the molecular weight of single PA of KN7-7 was 50,000. The affinity to fibrin of PA from HuH-7 as well as that of KN7-7 were extremely high. The activities of these PA on fibrinolysis were not inhibited by UK anti-body, but inhibited by melanoma t-PA anti-body. Namely, the PA from HuH-7 and KN7-7 demonstrated the main characteristics of so called t-PA.

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PURIFICATION AND CHARACTERIZATION OF FIBRINOLYTIC ENZYME OF RAT MAST CELLS. OKADA, T., YAMANOUCHI, H., WAKAMATSU, S., NAKAMURA, Y. and SUGIE, I. Dept. of Physiol., Aichi Medical University, Nagakute, Aichi, 480-11

Rat mast cells purified with a modified coil planet centrifuge at an average purity of 97% showed little damages in electron microscopy, and released about 60% of histamine in response to the specific antigen(DNP-Ascaris). Mast cell lysate caused lysis of both plasminogen rich and free fibrin plates, and the fibrinolytic activity of 10^6 cells was comparable to that of 0.5 CU of plasmin. Fibrinolytic enzyme was partially purified with AG 1-X2, DEAE Sephadex A-25 and heparin Sephadex CL6B columns. The preparation caused lysis of both types of fibrin plates, esterolysis of BTEE and amidolysis of S-2586. These activities were completely suppressed by DFP or TPCK. Therefore, it is suggested that rat mast cells release chymotrypsin like enzyme in allergic reaction and probably participate in local fibrinolysis at the site of acute inflammation.

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PLASMINOGEN ACTIVATOR RELEASING FACTOR OF BOVINE ANTERIOR PITUITARY. SAKAI, J., SHIONO, H., NAKASHIMA, A., OKADA, T. and SUGIE, I. Dept. of Physiol., Aichi Medical University, Nagakute, Aichi, 480-11

In order to study hypothalamic-hypophysial regulation of fibrinolysis in systemic circulation, t-PA release from blood vessels of perfused rat hind legs was measured after the injection of extracts from bovine pituitary. The release of plasminogen activator was detected when the perfused leg was stimulated with the extract from anterior pituitary, so we tried to purify plasminogen activator releasing factor(PARF) by gel filtration with Sephadex G-25 and G-10 columns. Two PARFs with molecular weight below 3,000 were identified and they showed different potency in the t-PA release from vessels of rats or cats. This difference between species remains to be elucidate. Current studies are aimed at identifying these factors(PARFs).

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ACTIVATION MECHANISMS OF PLASMINOGEN BY STREPTOKINASE. Takada, Y., Sugawara, Y. and Takda, A. Department of Physiology, Hamamatsu University, School of Medicine, 3600 Handa-cho, Hamamatsu-shi, Shizuoka-ken, Japan 431-31

Glu-plasminogen (Glu-plg) was incubated with an equimolar amount of streptokinase (SK) and the formation of SK-plg complex or SK-plasmin complex was studied by using autoradiography. When Glu-plg was incubated with an equimolar amount of SK, the hydrolysis of S-2251 was mainly due to SK-plg complex, since autoradiograph of the incubated mixture of Glu-plg and SK showed that less than 2 % of SK-plg complex was converted to SK-plasmin complex. When Glu-plg was incubated with an equimolar amount of SK in the presence of fibrinogen or fibrin, the hydrolysis of S-2251 was enhanced, and the formation of plasmin was accelerated. Lys-plasmin was mainly formed in the presence of fibrin or fibrinogen. In conclusion, in the absence of fibrinogen or fibrin, SK-plg complex acts as an activator of plasminogen, and SK-plg complex is slowly converted to SK-Glu-plasmin complex. In the presence of fibrin or fibrinogen, SK-plg complex is quickly converted to SK-Lys-plasmin complex.

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KINETIC ANALYSIS OF POTENTIATION OF PLASMINOGEN ACTIVATION BY STREPTOKINASE IN THE PRESENCE OF FIBRIN OR ITS DEGRADATION PRODUCTS. SUGAWARA, Y., TAKADA, Y. and TAKADA, A. Dept. of Physiol. Hamamatsu University, School of Medicine, 3600 Handa-Cho, Hamamatsu 431-31

When Glu-plasminogen(Glu-plg) was activated by various amounts of streptokinase (SK), K_m of the hydrolysis of S-2251 by the mixture of Glu-plg and SK did not change, but V_{max} increased with an increase in the amount of SK. Since low concentrations of SK-plg complex do not result in its conversion to the SK-plasmin complex by mutual activation, these results seem to suggest that the SK-plg complex may be a better activator when S-2251 is used as a substrate.

When Glu-plg was activated by SK in the presence of fibrin(ogen) or its degradation products (potentiating agens), K_m did not change with increase in the concentration of each potentiating agent, but V_{max} increased. The effects of potentiating agents on the k_{cat} values of these activators were in order of fibrin fibrinogen D E.

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RESTORATION OF WHITE BLOOD CELL COUNT WITH CARNOSINE (CAR). YAMAGUCHI, Y., SUDA, T., KAWASAKI, K.*, NAGAI, K. Department of Pathophysiology, Dental Research Center, School of Dentistry, Nihon University

CAR is a physiologically active agent that restores homeostasis by promoting tissue repair, modulating immune responses, and enhancing non-specific immune reactions. The present study revealed that CAR and its component amino acid β-alanine (ALA) correct leukocytopenia induced under various conditions. The white blood cell count decreased to 24% after the administration of the anti-cancer agent MMC (1 mg/kg) for 7 days, but it increased to 76% and 66%, respectively, when 100 mg/kg CAR and 40 mg/kg ALA were administered. The white cell count, reduced to 30% after the administration of 50 mg/kg 5-FU, was increased to 53% and 47%, and that reduced to 45% after γ-irradiation was increased to 69% and 55%, respectively, by the administration of CAR and ALA.

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CADMIUM AND ERYTHROPOIESIS. SAKATA, S., ENOKI, Y., KOHZUKI, H., SHIMIZU, S., OHGA, Y., NAKATANI, A. AND MATSUDA, M. Second Dept. Physiol., Nara Medical University, Kashihara, Nara 634

Effects of cadmium (Cd) on in vitro and in vivo erythropoiesis in rats were studied by a methylcellulose colony assay. Cd suppressed the in vitro CFU-E growth and this inhibitory action was not annihilated by increasing doses of erythropoietin (EPO). Cd did not influence ^{59}Fe incorporation into the cells, and the Cd dose-responsive inhibition curve of living cell number was similar to that of CFU-E. These results suggest that CFU-E suppression by Cd is not due to the blocking of either EPO action or iron incorporation, but due to its direct cytotoxic effect. Oral Cd administration to rats induced a typical iron deficiency anemia (IDA). Marrow CFU-E density and also plasma EPO titers increased as plasma iron was decreased by Cd drinking. Parenteral iron administration during Cd drinking period could prevent the development of IDA and the increase of both CFU-E and plasma EPO. There was a hyperbolic correlation between CFU-E and plasma iron or transferrin saturation. These results demonstrate that oral Cd administration produces bone marrow hyperplasia at the CFU-E level due to iron deficiency.

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COMPARISON OF THE COMPLEMENT SENSITIVITY OF ERYTHROPOIETIC PRECURSORS (BFU-E) IN PATIENTS WITH PNH AND NORMAL INDIVIDUALS. MATSUDA, M. and TERASAWA, T. Dept Physiol. Tohoku Dental University, Koriyama, Fukushima 963

To clarify the regulatory mechanisms related to the differentiation of complement sensitive cells from erythropoietic precursor cells (BFU-E) in paroxysmal nocturnal hemoglobinuria (PNH), the complement sensitivities of erythropoietic precursor cells and erythroblasts cultred from BFU-E were evaluated by a modification of complement lysis sensitivity test using trypan blue dye exclusion test in 6 patients with PNH. Significant inhibitory effects of erythroid bursts formation in PNH were not observed in 3 out of 4 patients. The hypersensitivity to complement was observed in the erythroblasts cultured from BFU-E in PNH bone marrow, in comparison with the concentrations of 1/100 diluted human complement for 50% lysis in normal controls (42.3 ±4.5 ml,n=4) and PNH patients (13.5 ± 8.4 ml, n=6). Furthermore, significant correlation was found between the relative proportions of complement sensitive cells in peripheral blood and of hypersensitve erythroblasts cultred from BFU-E in patients with PNH ($p<0.001$). These findings suggest that the expression of complement sensitivity occure during the couse of erythroid cell maturation and the production rates of complement sensitive cells are already programmed at the level of BFU-E.

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TEMPORAL PATTERN OF PLASMA ERYTHROPOIETIN (EPO) RESPONSE TO HYPOXIC HYPOXIA IN MICE. SHIMIZU, S., ENOKI, Y., SAKATA, S., OHGA, Y., KOHZUKI, H.

Temporal patterns of the plasma EPO response were examined in mice with normal or cyanate-induced high oxygen affinity of blood under two different grades of hypoxic hypoxia. A hemopoietic inhibitor present in murine plasma which might interfere with the EPO assay was found to be effectively removed by pretreatment of the plasma with chloroform and dialysis. When normal mice (8-10 weeks old, P_{50} = 42.4 ± 1.1 Torr) were exposed to moderate (0.46 atm) and severe (0.26 atm) hypoxia, plasma EPO values elevated significantly (4.1 and 5.2 times) with the peak after 72 hours and 36 hours, respectively, followed by a gradual decrease. As compared with normal mice, the EPO response in the cyanated animals (P_{50} = 30.1 ± 1.5 Torr) were much depressed under the moderate hypoxia but a little enhanced under the severe hypoxia, the peak values amounting to 1.6 and 6.9 times the pre-hypoxic level after 48 hours of hypoxia, respectively. The different temporal patterns of normal and cyanated mice suggest that higher oxygen affinity of blood makes the tissues less hypoxic under moderate hypoxia.

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EFFECTS OF SODIUM LOAD ON RENAL NERVE ACTIVITY AND RENAL FUNCTION IN CONSCIOUS RABBITS. MORITA, H., NISHIDA, Y., MOTOCHIGAWA, H., KAWADA, M., MATSUSHITA, K., KAJIMOTO, S., NAMEKATA, K. AND HOSOMI, H. Department of Physiology, Kagawa Medical School, Ikenobe, Miki, Kagawa 761-07

We examined responses of renal nerve activity, urine flow, and urinary Na^+ excretion to hypertonic NaCl infusion in chronically instrumented conscious rabbits with unilateral renal denervation. Infusion of 20% NaCl at 0.2 ml/min for 30 min increased plasma osmolality by 27 ± 5 mosmol/kg, plasma Na^+ by 16 ± 3 mEq/l, and decreased hematocrit by 5.1 ± 0.6%. These changes were accompanied by a 5.8 ± 2.3 mmHg increase in mean arterial pressure and a marked 82 ± 7% decrease in renal nerve activity. Urine flow and Na^+ excretion increased gradually and peaked at the end of infusion. The innervated kidney excreted 20 ± 3 ml urine and 5.3 ± 0.7 mEq Na^+ for the subsequent 60 min. On the other hand, the contralateral denervated kidney excreted only 4 ± 2 ml urine and 2.0 ± 0.6 mEq Na^+, significantly less than those of the innervated kidney. In rabbits with sinoaortic baroreceptor denervation plus vagotomy, NaCl infusion also decreased renal nerve activity (64 ± 8%). These results suggest that hypertonic NaCl infusion elicits a marked decrease in renal nerve activity which is not mainly due to baroreflexes and that the decrease in renal nerve activity plays an important role in the augmentation of renal function.

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TYMPANOPLASTY ENHANCES WATER DIURESIS IN HUMANS.
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We sometimes encounter the phenomenon of increased urinary volume increases during the tympanoplasty operation. The purpose of this study is to investigate whether or not tympanoplasty increases urinary flow rate (UFR) and by what mechanism UFR increases. Thirteen surgical cases were divided into two groups: a tympanoplasty (T) group (n=7) and a control (C) group (n=6) including minor operations in the eyes or four extremities. All patients were anesthetized with enflurane and nitrous oxide, and infused with lactated Ringer solution at 3 ml/kg/min. UFR increased from 1.1 to 3.4 ml/kg/min, and urine osmolality decreased from 450 to 140 mOsm/kg during the operation in T group, while they did not change in C group. These results indicate that tympanoplasty markedly enhances water diuresis. Systolic arterial pressure decreased, and plasma osmolality did not change during the operation in T group. Plasma aldosterone or atrial natriuretic peptide level did not change during the operation. Plasma vasopressin level, however, increased from 0.9 to 19.0 pg/ml during the operation in C group, while it did not change in T group. These results suggest that tympanoplasty-induced diuresis was not due to pressure diuresis or hypoosmolality but due to suppression of AVP secretion by unknown mechanisms.

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VASODILATORY ACTION OF ATRIAL NATRIURETIC PEPTIDE ON CANINE GLOMERULAR AFFERENT ARTERIOLES IN VITRO. OHISHI, K., HISHIDA, A., HONDA, N., The First Dept. of Medicine, Hamamatsu Univ. Sch. of Medicine, 3600 Handa-cho, Hamamatsu 431-31

A single afferent arteriole was dissected from the superficial or jaxtamedullary cortex of the canine kidney and perfused with the single glomerular perfusion technique. In superficial afferent arterioles, norepinephrine(NE $1x10^{-6}$M) significantly increased arteriolar resistance. Synthetic human atrial natriuretic peptide(hANP) provoked afferent arteriolar dilation and attenuated the NE-induced increase in arteriolar resistance within $1x10^{-10}$to $1x10^{-6}$ M concentrations. This vasodilatory effect was significantly potentiated by 2-o-propoxyphenyl-8-azapurin-6-one(M&B 22,948 , $4x10^{-12}$M), a cGMP phosphodiesterase inhibitor, probably due to a sequential interaction of synergistic drugs. Also, the $1x10^{-4}$M concentration of 8-BrcGMP or DBcGMP lessened NE-induced arteriolar constriction, but DBcAMP did not. Similarly, hANP attenuated NE-induced vasoconstriction in the jaxtamedullary afferent arterioles. The findings suggest that ANP has a direct vasodilatory action on canine superficial and jaxtamedullary glomerular afferent arterioles, and that this ANP-induced vasodilation is mediated by enhanced cGMP synthesis.

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MECHANISMS REGULATING DRINKING IN THE QUAIL, COTURNIX COTURNIX JAPONICA. TAKEI, Y. Dept. Physiol., Kitasato Univ. Sch. Med., 1-15-1 Kitasato, Sagamihara, Kanagawa 228

Drinking was induced in water-replete quail after (1) intravenous injection of hypertonic solutions of NaCl or sucrose but not of urea, (2) hemorrhage, (3) intravenous or intracerebral injection of angiotensin II. This result show that cellular dehydration, extracellular dehydration, and angiotensin II are major dipsogen in the quail as has been reported in mammals. The minimum dipsogenic increase in plasma osmolality was only 0.64%, while 12.5% of blood have to be withdrawn to cause reliable drinking. Thus, the quail was more sensitive to dipsogenic action of cellular dehydration but less sensitive to extracellular dehydration than in mammals. Dipsogenic potency of angiotensin II in the quail was comparable to that of mammals. Drinking was also induced in the quail after more than 4 h of water deprivation. Blood volume decreased, plasma angiotensin II increased, but plasma osmolality did not change after 4 h of water deprivation. The level of blood volume was held rather constant after more than 4 h of water deprivation, but plasma angiotensin II and plasma osmolality increased thereafter. These results show that homeostatic control of plasma osmolality is of primary importance over the volemic control, and that dipsogenic potency of the osmotic mechanism was greater than that of the volemic mechanism in the quail.

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EFFECTS OF MESOTOCIN IN THE INTACT BULLFROG AND IN THE PERFUSED BULLFROG KIDNEY. UCHIYAMA, M., MURAKAMI, T., Dept. of Oral Physiol., School of Dentistry at Niigata, The Nippon Dental Univ., 1-8 Hamaura-cho, Niigata 951

Renal and blood pressure responses to mesotocin (MT) were studied in the bullfrog (Rana catesbeiana). Effects of MT were also investigated in the perfused bullfrog kidney. Under the condition that the conscious animal was placed in a plastic box containing tap water, aortic blood pressure was measured and urine was collected directly from the ureters. In a simultaneous recording of the blood pressure and urine flow rate during hormone treatments, diuresis was sustained though the blood pressure was unchanged. Diuresis was accompanied by increases in GFR, Na excretion and free water clearance. On the other hand, MT injection did not give distinct influence on the urine-to-plasma inulin ratio nor on the relative free water clearance. In perfused kidney experiments, MT infusion from the artery increased GFR, urine flow rate and sodium excretion and slightly increased outflow. MT given through the renal portal perfusion did not show any consistent effects. These results suggest that MT induces the glomerular diuresis rather than the tubular one.

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DIURESIS INDUCED BY HEAD-OUT WATER IMMERSION IN THE ELDERLY. TAJIMA, F., SAGAWA, S., IWAMOTO, J., MIKI, K., AND SHIRAKI, K. Dept. Physiol., Sch. Med., Univ. Occup. and Environ. Health, Kitakyushu 807.

After overnight food and fluid restriction, seven healthy old (62 to 74 yr) and 8 young (21 to 28 yr) men were examined before, during, and after 3-h head-out immersion (HOI) in thermoneutral water (34.5±0.5°C). Although HOI induced a reversible increase in urine flow in all subjects, the response was faster and greater in magnitude in the elderly compared with the young. Na excretion and osmolal clearance also followed a response pattern identical to that of urine flow; thus the HOI-induced diuresis was entirely osmotic. Endogenous creatinine clearance increased in the elderly at the 2nd h of HOI, suggesting an age-related modification in the hemodynamics in the kidney. Mean arterial pressure significantly increased ($P<0.05$) during HOI in the elderly, which also indicated a different response of peripheral circulation to HOI in the elderly. Control level of plasma atrial natriuretic factor (ANF) was nearly twofold greater in the elderly compared with the young. The HOI induced a nearly fourfold increase in ANF in the elderly, whereas that for the young was threefold. Both plasma aldosterone and ADH responses to HOI were attenuated in the elderly compared with the young, which had no correlation with urine flow or Na excretion. It is concluded that the elderly release more ANF at a given cephalad volume expansion compared with the young, but the vasodilative reaction to ANF is attenuated in the elderly.

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Role of sympathetic nerve activity in natriuresis during head-out water immersion in conscious dogs. Miki, K., [b]Hayashida, Y., and Shiraki, K., Dept. of Physiol., [b]System Physiol., Sch. of Med., Univ. of Occup. and Environ. Health, Kitakyushu 807.

The role of renal sympathetic nerve activity (RSNA) in natriuresis and diuresis induced by head-out water immersion (WI) was studied in 8 female conscious dogs. The stainless steel electrode for the measurement of RSNA and catheters for the measurements of systemic arterial (Pa) and central venous (Pv) pressures were instrumented chronically in the dogs. After a 60-min control in air, 120-min WI in thermoneutral condition (37 ^{o}C) was carried out, followed by a 60-min recovery in air. The WI caused an immediate reduction of RSNA by 45% ($p<0.05$) and sustained the lowered level during the period of WI. Urine flow and Na excretion increased significantly ($p<0.05$) by 180% and 100%, but creatinine clearance did not change significantly during WI. A stepwise increase in Pa (by 10 mmHg) and Pv (by 10 mmHg) was observed during WI. In a separate study, renal denervation was made 2-4 weeks before the experiment in the same dogs (6 out of 8 dogs). No significant changes in urine flow and Na excretion during WI while Pa and Pv increased by 10 mmHg and 10 mmHg, respectively. We may conclude that the decrease in RSNA observed during WI plays a major role in natriuresis in the dog.

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EXPERIMENTAL UREMIC NEUROPATHY IN RATS WITH ACUTE RENAL FAILURE. SHIBAHARA, N , YASUTA, H., ONISHI, S., OKADA, S., HAMADA, K., MIYAZAKI, S., NAKAGAKI, I* & SASAKI, S.* Depts. of Urology and *Physiology, Osaka Med. Coll., Takatsuki, Osaka 569.

The objective of the present study was to elucidate possible mechanisms of human uremic neuropathy. This was done by studying moter nerve conduction velocities, axopasmic electrolyte concentration and myelinated fibers diameter in the sciatic nerves of rats with acute renal failure. The axoplasmic Na, K and Cl concentrations were measured by electron probe X-ray microanalysis using freshly freeze-dried thin sections.

The results were as follows ; 1) The sciatic motor nerve conduction velocity of acutely uremic rats had significantly decreased compared with that of control rats. (29.2 ± 3.1 m/sec. vs. 37.1 ± 1.9 m/sec. n=20, mean ± S.D. ; p 0.01). 2) Axoplasmic Na concentration of these rats had significantly decreased compared with the controls. (6.0 ± 0.7 mmol/Kg wet weight vs. 12.7 ± 1.4 mmol/Kg wet weight, n=10, mean ± S.D.; p 0.05). 3) Myelinated fiber diameter of these rats had significantly decreased compared with the controls.

These results suggest that the decrease of the Na permeability and of the myelinated fiber causes the decrease of the sciatic nerve conduction velocities. In the acute uremic state, toxic metabolities may interfere with the Na permeability of nerve axoplasmic membranes.

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DAUGHTER BRANCH OF TERMINAL AIRWAY IN HILUM REGION. UYEDA, M. TANIFUJI, S.*, MATSUI, E.** AND INOUYE, A. Dept. of Physiol. and **Radiol., Gifu Univ. Sch. of Med., Gifu, *Dept. of Technol., Osaka City Univ., Osaka, and Dept. of Physiol., Hyoga Coll. of Med., Nishinomiya

The bronchial airway is made up by parent or axial branch which bifurcates to same size branches and by daughter branch or recurrent branch (Horsefield (1968), Ito (1983)) which is smaller and bifurcates to asymmetric branches and fills the empty space between the parent branches. Thus the daughter branch and its subdivision supply lung parenchyma in the inner layer of the lung. The daughter branch in the hilum region has attracted special interest recently. We interested in properties that the daughter branch and its subdivision fill the empty space made by parent branch system and flow dynamic analysis was performed. From the radiogram of hilum region, we reconstructed three dimensional airway model including daughter branch and air flow dynamics was analyzed. Three dimensional Navier-Stokes equation was solved numerically by finite element method. The result had shown the effective deceleration of air flow through daughter branch and this suggests the posible space filling with less branching of airway without excessive air flux.

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THE AIRFLOW-ORIGINATED RESPIRATORY REFLEX FROM THE UPPER AIRWAY AND ITS RECEPTIVE FIELDS. MIYAOKA, Y. AND SHIMADA, K., Department of Oral Physiology, Niigata University School of Dentistry, Niigata 951.

We have previously reported that both inspiratory and expiratory muscle activities are reflexly increased by airflow through the upper airway in lightly-anesthetized rabbits. In the present study, receptive fields for the airflow-originated respiratory reflex were examined. Under tracheostomy breathing, 1.2 L/min steady and 20 ml (in the stroke volume) pulsatory airflows were delivered to the upper airway in the expiratory direction. Although the reflex effect was reduced by applying 2% lidocaine to the laryngeal mucosa, significant increases in respiratory muscle activities were elicited even after the application. Reflex increases were produced by the airflow delivered only to the pharyngeal and nasal regions. Similar increases were also produced by tactile stimulation of the pharynx and by electrical stimulation of the nasal mucosa. The present results suggest that laryngeal, pharyngeal and nasal regions are all responsible for eliciting the airflow-originated respiratory reflex from the upper airway.

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VAGAL REFLEX INDUCED BY HIGH-FREQUENCY INFLATION--COMPARISON OF NORMAL AND ASTHMATIC RABBITS KANAMARU, A., SIBUYA, M., ISOBE, A., IWASE, M., HOMMA, I. Dept. of Physiol. Showa Univ. School of Med., Tokyo 142, JAPAN

It has been reported that triangular-shaped positive pressure pulses, high-frequency inflation (HFI), applied to the airway stimulate pulmonary mechanoreceptors. HFI at higher frequencies, around 50-100 Hz, mainly stimulates slowly adapting receptors (SAR) and decreases the respiratory rate. HFI at lower frequencies, around 10-20 Hz, mainly stimulates rapidly adapting receptors (RAR) and increases the respiratory rate. We report here, the comparison of HFI frequency property of normal rabbits to that of asthmatic rabbits, which were sensitized by Alternaria tenius extract as described by M. P. Shampain et al. (Am. Rev. Respir. Dis. 1982; 126:493). Allergy was proved by the passive cutaneous anaphylaxis method, also described in the above paper. Intravenous antigen challenge with Alternaria extract induced bronchoconstriction. HFI at all frequencies, from 10 to 100 Hz, increased the respiratory rate in asthmatic rabbits. This indicates that, in asthmatic rabbits, the reflex induced by RAR is hyperactive compared to that induced by SAR.

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EFFECTS OF HIGH-FREQUENCY INFLATION AND DEFLATION ON EXPIRATORY ACTIVITY SIBUYA, M., KANAMARU, A., ISOBE, A., IWASE, M., HOMMA, I. Dept. of Physiol. Showa Univ., Tokyo, 142

It has been reported that high frequency triangular-shaped positive pulses, high-frequency inflation (HFI), applied to the airway, stimulate pulmonary stretch receptors and prolong the expiratory phase. In this study, expiratory EMG activity was recorded from the abdominal muscles of rabbits to investigate the effects of HFI. HFI increased the amplitude of the expiratory activity. HFI at higher frequencies (50-100 Hz) was more effective than at lower frequencies (10-30 Hz). The expiratory phase was divided into two substages, E1 and E2, by the onset of the expiratory activity. HFI prolonged the duration of the E2 stage, but that of the E1 stage remained unchanged. The E2 stage was further divided into the active stage of expiration (Ea stage), during which the integrated curve of the activity rose, and the declining stage of expiration (Ed stage), during which the curve declined. In the Ea stage, the rate of rise of the integrated curve was increased by HFI, but the duration of the Ea stage remained unchanged. The duration of the Ed stage was consistently prolonged by HFI. In contrast, high-frequency deflation (HFD) decreased the expiratory activity and shortened the expiratory duration. These results indicate that vagal afferent information can control expiratory activity and duration.

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INHIBITORY SYNAPTIC INPUTS TO RESPIRATORY RHYTHM GENERATOR IN MEDULLA ISOLATED FROM NEWBORN RATS. ONIMARU, H., ARATA, A.* and HOMMA, I. Department of Physiology, Showa University School of Medicine, Shinagawa-ku, Tokyo 142

Pre-I neurons are localized in the rostral ventrolateral medulla (RVL). It is thought that their activity, which precedes cervical root (C4 or C5) inspiratory activity, generates primary respiratory rhythm in brainstem-spinal cord preparations from newborn rats. To determine GABAergic synaptic inhibition involvement in respiratory rhythm generation, we examined the effects of GABA antagonists (picrotoxin, bicuculline), glycine antagonist (strychnine) and reduced perfusate Cl^- concentration on Pre-I neurons and inspiratory neurons. Treatment with these antagonists (2-10 μM) blocked the C4 inspiration-related phasic inhibition of Pre-I activity (IIPI). Burst rate and intraburst firing frequency of Pre-I neurons tended to increase. Inspiratory RVL neurons exhibited remarkable increase in intraburst frequency and decrease in burst duration. These effects were also observed when external Cl^- concentration was reduced to 40% of normal. Present results suggest: 1) IIPI is induced by Cl^- dependent GABAergic inhibitory synaptic inputs to Pre-I neurons, and 2) respiratory neurons in the RVL possess a more or less resting Cl^- conductance which may be due to tonic GABAergic inhibition. Phasic Pre-I inhibitory inputs do not need Pre-I rhythm generation but may be important in modulating this activity.

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RESPONSES OF THE CENTRAL RESPIRATORY OSCILLATOR ELICITED BY VAGAL STIMULATION IN EXPIRATION. KITANO, S., KOMATSU, A., HASHIMOTO, Y., TSUNODA, C.★ AND SUZUKI, H.★ Dept.s of Physiol. and Anesthesiol.★ Tokyo Women's Medical College, 8-1, Kawada-cho, Shinjuku-ku, Tokyo 162

The experiments were performed with anesthetized, paralyzed, artificially ventilated and bilaterally thoracotomized rabbits. Electrical stimulation with various conditions was applied to the central cut ends of bilateral vagal nerves and delivered only in expiration (E). The phrenic activity, as the central respiratory output, was recorded. A change of the stimulated expiratory duration compared to the control. Two distinct results were observed. 1) Stimulation with strong intensity, long duration or increased number of pulses elicited prolongation of the expiratory period, which is regarded as a response of afferent fibers from slowly adapting (stretch) receptors. 2) When short train pulses with intermediate intensity were delivered during late E, shortening of the period, that is, premature termination of E, was evoked. It has been reported that the premature termination of E results from stimulation to afferent fibers from rapidly adapting (irritant) receptors. Therefore, it can be concluded that adequate stimulation can selectively evoke these two different responses.

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POSTSYNAPTIC POTENTIALS OF BULBAR RESPIRATORY NEURONS IN THE VAGUS NERVE-MEDIATED INSPIRATORY RESPONSE.

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Single electrical stimuli (0.2 msec, 1-3 V) to the vagal afferents produced, in a certain condition, an augmenting burst activity in the phrenic nerve (PN). Synaptic mechanisms underlying this response were studied by intracellular recordings from bulbar respiratory neurons in decerebrate paralyzed cats after vagotomy. Inspiratory and postinspiratory neurons were penetrated in the ventral respiratory group. The threshold intensity for this response was 1.05-1.10 times the threshold eliciting an antidromic action potential of the laryngeal motoneuron. This stimulus induced a series of postsynaptic potentials (PSPs) consisting of early EPSPs and late IPSPs in all respiratory neurons examined. This sequential PSP-wave lasted 50-70 msec and was succeeded by typical inspiratory patterns of PSPs characteristic of each type of respiratory neuron in synchrony with the PN activity. These results suggest that synchronized vagal afferent inputs may provoke an excitation-inhibiton sequence of change in the medullary respiratory network of neurons probably via nonspecific, reticular systems which exert diffuse excitatory influences on bulbar respiratory neurons. This may set or reset the inspiratory on-switch mechanism.

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Vagal Influence on Phrenic Responses to Respiratory Phase-locked Muscle Afferent Nerve Electrical Stimulation.

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Respiratory depression usually follows termination of continuous muscle afferent nerve electrical stimulation (MES) at intensities above thin-fiber afferent thresholds. We investigated the effects of MES applied to the different respiratory phases, on phrenic responses before and after vagotomy. Integrated signals were obtained from the phrenic nerve in anesthetized, glomectomized, paralyzed and artificially ventilated cats. Gastrocnemius MES was applied to the early 2/3 portion of the inspiratory phase(TI-locked), or the early expiratory phase (TE-locked). RESULTS: (1) Post-stimulus respiratory depression was also observed in the vagi-intact as well as in the vagotomized state. In the vagi-intact state, neither TI- nor TE-locked MES showed consistent phase-dependency of post-stimulus respiratory depression. In cats vagotomized 5 hours before, TI-locked MES evoked post-stimulus respiratory depression greater than TE-locked effects. (2) An examination of changes in excitability of phrenic responses during phase-locked MES yielded the ff: (a) The increase in rate of rise of inspiration, during phase-locked MES in the vagi-intact state wasattenuated after vagotomy. (b) "Evoked inspiratory discharges" during the early expiratory phase in response to TE-locked MES in the vagi-intact state, were abolished 5 hours after vagotomy. (c) On the other hand, respiratory frequency increased during MES after vagotomy. (d) TI-locked vagal electric stimulation restored "evoked inspiratory discharges" during TE-locked MES. The results show phase-dependent excitability changes of phrenic activity during and after MES which are profoundly influenced by vagal modulating input.

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COMPARISON OF THE RESPIRATORY AND CARDIOVASCULAR RESPONSES INDUCED BY STILULATION OF THIN-FIBER MUSCULAR AFFERENTS.

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In anesthetized, vagotomized, glomectomized, paralyzed and artificially ventilated cats, it has been shown that electrical and chemical stimulation of thin-fiber muscular afferents causes naloxone-reversible respiratory suppression a few muniutes after cessation of stimulation. This study was aimed to reveal the relationship between respiratory and cardiovascular responses induced by noxious stimulation of muscular afferents. During stimulation there were significant increases in respiratory outputs, although blood pressure response patterns were variable, the rate of blood pressure rise was significantly correlated with the increases in respiratory activity. On the contrary, there was no consistent tendency for blood pressure changes when respiratory suppression appeared after stimulation. This result suggests that the endogenous opiate system mediating post-stimulus respiratory suppression may act upon the cardiovascular system in a different manner.

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THE EFFECT OF UNILATERAL PULMONARY VAGOTOMY ON RESPIRATORY CONTROL IN MAN.
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We studied breathing pattern at rest and ventilatory responses to progressive hypoxia and hypercapnia in awake 7 patients who had undergone esophageal resection with sectioning the right pulmonary vagal branch by lymphadenectomy. Two months after operation, Pao_2 decreased (91.4±7.9→82.8±9.3 Torr, $p<0.05$) and clinical grade of dyspnea enhanced. Respiratory frequency, minute ventilation and mouth occlusion pressure ($P._2$) at rest significantly increased after operation compared with the preoperative value. The occlusion pressure response to hypoxia ($\Delta P._2/\Delta Sao_2$) and hypercapnia ($\Delta P._2/\Delta PACO_2$) increased from -0.29±0.19 to -0.88±0.53 ($p<0.05$) and from 1.3±1.2 to 1.9±1.1 ($p<0.1$), respectively. Contrary to the vagotomized patients, non-vagotomized 12 patients with esophageal resection revealed no significant change in all the parameters mentioned avove. We suggest that diminished Hering-Breuer inhibitory inflation reflex to the respiratory centers by unilateral vagotomy may have resulted in augmented ventilatory activities obtained in our study.

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DIFFERENCES IN THE COHERENT RELATIONSHIP OF THE HIGH-FREQUENCY OSCILLATIONS BETWEEN PHRENIC AND VAGUS NERVE ACTIVITY.
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We have previously shown that components locked to "high-frequency oscillation (HFO)" in the phrenic nerve activity (PNA) exist in the discharges of the cranial nerves innervating skeletal muscles associated with respiratory movements. To study functional connectivity of the neural networks responsible for the synchronization of HFOs, coherence analyses were performed for following 4 pairs of nerve activities recorded from anesthetized and paralyzed rabbits under normocapnia: 1) bilateral PNA, 2) PNA and ipsilateral vagus (VNA), 3) PNA and contralateral VNA and 4) bilateral VNA. Coherence function between bilateral PNA gave significantly ($p<0.001$) higher value than that of other 3 pairs throughout the analyzed range (5-200 Hz) with its largest value at the HFO-frequency (0.88±0.17 at 112.8±3.4 Hz; mean±SD, n=14), whereas coherences for other 3 pairs gave almost flat spectra close to zero except for single narrow-banded peak of HFO. Moreover, the phase-difference between bilateral PNA was steadily about zero in the range. It is suggested that two kinds of oscillatory activities of different origin exist in PNA besides the respiratory rhythm: one is shared with cranial motor outputs originated from a common HFO generator, and the other is specific to the synchronization of bilateral phrenic outputs.

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EXCITATORY CONNECTIONS BETWEEN INSPIRATORY NEURONS OF THE VENTRAL RESPIRATORY GROUP.
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In Nembutal-anesthetized, immobilized and artificially ventilated cats, we analyzed how bulbospinal inspiratory neurons of augmenting firing type (I-AUG) projected and connected with respiratory neurons within the medulla. The I-AUG neurons were recorded in or around the nucleus ambiguus, i.e., in the rostral VRG. The antidromic mapping test showed that they projected to the contralateral VRG area of predominantly I neurons as well as to the contralateral spinal cord. Intracellular recordings were made from respiratory neurons of the contralateral VRG about the level of the obex. Then membrane potentials were averaged using extracellular spikes of the bulbospinal I-AUG neuron as trigger (spike-triggered averaging). Depolarizing potentials locked to the triggering spikes were obtained and they were shown to be unitary EPSPs. Latencies of the antidromic activation of the triggering I-AUG neurons indicated that the EPSPs were monosynaptic. These excitatory connections of I-AUG neurons were made with both vagal I motoneurons and I-AUG neurons which projected to the contralateral spinal cord.

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EFFECTS OF STIMULATION OF CEREBROFUGAL FIBERS ON THE SPINAL RESPIRATORY NEURON ACTIVITIES IN THE CAT.

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We investigated the effects of single or train pulse stimulation of the cerebral peduncle (CP) on the activities of cervical respiratory neurons and phrenic motoneurons. Cats were anesthetized with pentobarbital sodium at an initial dosage of 35 mg/kg and immobilized with gallamine triethiodide. CP stimulations were applied at A5.0-8.0 levels using bipolar electrodes. Unit activities of the cervical inspiratory neurons (C_1-C_2 segments) and C_5 phrenic root discharges were simultaneously recorded. Contralateral CP stimulation (single, double and triple pulses, 0.2 msec, 1.0-1.5 mA) during inspiration induced biphasic effects : early excitatory (latency 4-7 ms) and succeeding inhibitory (latency 10-15 ms, duration 20-80 ms) effects on both the cervical inspiratory neuron activities and the phrenic nerve discharges. Sectioning of the pyramidal tract at the mid-medullary level abolished the early excitation, but the late inhibition remained almost unchanged. These results suggest that the CP induced short latency excitation is mediated through a pyramidal tract pathway and the late inhibition is transmitted through a non-pyramidal pathway.

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ELECTROPHYSIOLOGICAL AND HISTOLOGICAL INVESTIGATION OF CEREBROFUGAL INPUTS TO THE MEDULLARY AND SPINAL RESRIRATORY NEURONS IN THE CAT.

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Cats were anesthetized with pentobarbital sodium and immobilized with gallamine triethiodide in physiological experiments. Bipolar stimulating electrodes were placed at the sensorimotor cortex (SM) and the cerebral peduncle (CP). Stimulation of the contralateral SM or CP induced the short-latency (2-3 ms) EPSPs and the succeeding IPSPs in the phrenic motoneurons. At the lower stimulus intensities, CP-EPSPs were often induced without the succeeding IPSPs, and the CP-EPSPs were followed by the IPSPs at the higher stimulus intensities. In contrast, stimulation of the ipsilateral SM or CP produced only IPSPs in the ventral respiratory group (VRG) neurons. To observe projections of cerebrofugal fibers to the respiratory center in the medulla and the spinal cord, Phaseolus vulgaris-leucoagglutinin (PHA-L) was chronically injected into the lateral portion of the left SM in two cats. Immunocytochemically labelled fibers were obsereved in the vicinity of the phrenic motoneurnon pool in the right C6 segment and in the region of lateral border of the intermediate zone of the gray matter of the right C2 segment where the propriospinal respiratory neurons are located. Corticobulbar projections to the VRG, the solitary tract nucleus and the Boetzinger complex were not detected or very scarce.

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RESPIRATORY RESPONSES TO ALVEOLAR PCO_2 AT DIFFERENT PO_2 LEVELS IN CAROTID SINUS NERVE DENERVATED CATS.

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In anesthetized, paralyzed and carotid chemodenervated cats, the respiratory responses to alveolar PCO_2 were determined during air-breathing, hyperoxia (alv.PO_2 > 600 Torr) and hypoxia (alv.PO_2 = 40~50 Torr). The integrated Phrenic nerve activity (PNA) was used as an index of the central inspiratory activity. The PNA was related linearly to alv.PCO_2 during air-breathing and the mean PCO_2 apneic point (threshold PCO_2) was 30.4 ± 3.1 Torr(n=28). Transition from air to hyperoxia led to increase in PNA, while alv.PCO_2 decreased. The steady-state PNA-PCO_2 relationship was linear and shifted to the left without significant change in slope. The mean threshold PCO_2 was 24.3 ± 3.0 Torr(n=25). The reverse from air to hypoxia led to decrease in PNA, while alv.PCO_2 increased. The steady-state PNA-PCO_2 relationship was linear and shifted to the right without significant change in slope. The threshold PCO_2 increased by about 6 Torr during hypoxia. These results show that the sensitivity to central PCO_2 is not impaired by central hypoxaemia. Therefore, a marked increase in the threshold PCO_2 as well as a shift to the right of the PNA-PCO_2 relationship in hypoxia as compared with hyperoxia could not be explained completely in terms of the central hypoxic depression.

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ARTERIAL TO END-TIDAL P_{CO_2} DIFFERENCE IN DIFFERENT VENTILATORY CONDITIONS DURING HYPERCAPNIA IN THE RAT. TOJIMA,H.,KURIYAMA,T., FUKUDA,Y., Dept.Chest Medicine and Physiol.,Chiba Univ.,Chiba 280

Arterial and end-tidal P_{CO_2} (P_{aCO_2},P_{ETCO_2}) of the anesthetized rat were measured under following three conditions;spontaneous breathing with CO_2 inhalation,artificial respiration with gas mixture containig CO_2,and artificial respiration with reduced ventilatory volume (hypo-ventilation). In spontaneous breathing,the P_{aCO_2}-P_{ETCO_2} difference (ΔP_{CO_2}) which was 3.3±1.6(mean±SD,n=13)mmHg in control condition became negative(-3.6±1.5 mmHg,n=9) during CO_2 inhalation at the P_{ETCO_2} range from 72 to 77 mmHg. During artificial respiration with constant ventilation, initial positive ΔP_{CO_2} approached to zero when CO_2 was administered (5.2±2.8→1.1±1.6 mmHg). In both conditions the slope of P_{aCO_2}-P_{ETCO_2} relation line was less than 1.0. In contrast ΔP_{CO_2} remained positive when P_{CO_2} increased with reducing the ventilatory volume. These observations suggest that for a given increase in P_{CO_2} by administration of exogenous CO_2, the extent to which P_{aCO_2} increases is smaller than that of P_{ETCO_2}. This relationship together with changes in breathing pattern likely results in negative ΔP_{CO_2} in spontaneous breathing rat.

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ARE LOCATIONS OF CENTRAL CHEMORECEPTORS RESTRICTED TO THE VENTRAL SURFACE OF THE MEDULLA? ICHIKAWA, K., KUWANA, S., & ARITA, H. Inst. Basic Med. Sci., Univ. of Tsukuba, Tsukuba, Ibaraki 305.

Using liquid membrane pH-sensitive microelectrodes, we made continuous measurements of extracellular fluid (ECF) pH deep in the medulla during a step increase in CO2 of the vertebral artery. We found various intramedullary regions in which ECF pH shifted to the acid side in the time course analogous to respiratory excitation, indicating that those responsive regions are suitable environments for pH-dependent central chemoreceptors: the regions with the acid shift are not necessarily restricted to ventral surface of the medulla, i.e., the chemoceptive areas proposed earlier, but they are located in mamy, isolated, intramedullary areas supplied by perforating branches of the vertebral basilar arterial system. Furthermore, histochemical study of the distributions of carbonic anhydrase revealed that glial cells in those areas were stained in agreement with the physiological works described above.

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CHANGES IN BREATHING PATTERN AND VENTILATORY RESPONSIVENESS TO CO_2 WITH GROWTH AND AGING IN THE RAT. FUKUDA, Y., Dept. Physiol., Sch. Med., Chiba Univ., 1-8-1 Inohana, Chiba 280

Ventilatory parameters and ventilatory responsiveness to CO_2 inhalation were determined in the halothane anesthetized tracheotomized rat at various ages; 1.5, 3, 6, 12 and above 20 months after birth. Ventilation and metabolism (O_2 consumption and CO_2 production) decreased progressively with growth and aging. Both tidal volume corrected for body weight and respiratory frequency decreased. The reduction in respiratory frequency was produced mainly by prolongation of expiratory time. Aged animals showed large physiological dead space and hypoxemia during the breathing of normoxic gas. The slope of CO_2-ventilatory response line declined progressively with aging accompanying significant reduction in respiratory frequency-response. Young animals responded to CO_2 with a high respiratory frequency, whereas aged animals showed a large tidal volume response. Alveolar ventilation and the slope of CO_2-ventilatory response line correlated linearly with metabolism (CO_2 production). However, the ratio of the maximum increase in ventilation during CO_2 inhalation to the control ventilation (without CO_2 inhalation) remained almost constant throughout life. The results suggest that a relative 'reserve' capacity for increasing ventilation may be well maintained even with aging although the pattern of breathing changes.

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DEPENDENCY ON VAGAL PULMONARY AFFERENTS OF CARDIOVASCULAR- AND SYMPATHETIC ACTIVITY-RESPONSES TO ACUTE HYPOXIA IN HALOTHANE ANESTHETIZED SPONTANEOUSLY BREATHING RAT

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In the anesthetized spontaneously breathing rat acute systemic hypoxia produces ventilatory stimulation followed by inhibition with accompanying significant reduction in arterial blood pressure. The present study addresses contribution to changes in blood pressure during hypoxia of sympathetic activity in the halothane anesthetized spontaneously breathing rat. Blood pressure (BP)- and renal sympathetic nerve (RN) activity responses during isocapnic progressive hypoxia test were determined with or without section of the carotid sinus nerve (CSN) and/or the vagus nerve(XN). In the CSN and XN-intact rat, hypoxia initiated reduction in RN activity and BP. After XN section, the RN activity was increased during hypoxia, which attenuated the reduction in BP. When both the CSN and XN were sectioned, the RN activity again decreased. However, an extreme hypoxia initiated 'terminal' increase in RN activity even after CSN section. The results indicate that vagal afferents, presumably from pulmonary stretch receptors, inhibits the increase in sympathetic activity due to carotid chemoreceptor stimulation in hypoxia. Changes in blood pressure are the net results of local vasodilator action of hypoxia and efferent sympathetic vasoconstrictor activity being modified by various afferents.

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EFFECT OF CHLORMADINONE ACETATE, A SYNTHETIC PROGESTERONE, ON URINARY ACID EXCRETION, ARTERIAL BLOOD GAS AND CO_2-VENTILATORY RESPONSE.

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Chlormadinone acetate(CMA), a synthetic progesterone is used for the patients with chronic obstructive pulmonary disease(COPD) so as to prevent accumulation of CO_2 in the blood. In an attempt to secure sufficient augmentation of alveolar ventilation, a dose of 50mg/day is currently administered for routine therapy. In preliminary observation, however, we found a significant P_{aCO_2} depression by administering CMA with one tenth the therapeutic dose, 5mg/day. In this study, we systemically examined the effect of this small dose, on urinary acid excretion as well as arterial blood gas and CO_2-ventilatory response(HCVR). Twelve healthy males were participated to a double-blind, cross-over study. The subjects were given either CMA or a placebo orally at a dose of 2.5mg twice a day for 7 days. In HCVR, both $\Delta P.2/\Delta P_{ACO_2}$ and $\Delta \dot{V}_E/\Delta P_{ACO_2}$ as the slopes of response lines increased significantly by CMA. Significant increase in P_{aO_2} and arterial pH, and decrease in P_{aCO_2} and plasma HCO_3^- were detected. We also found suppression in urinary NH_4^+, titratable acidity, and increased pH. We concluded that respiratory alkalosis, induced by augmentation of alveolar ventilation with administering 5mg CMA, resulted in suppression of urinary acid excretion and no appreciable alteration was suspected to occur in the mechanism of ammonia formation in the renal tubular cells.

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NEUROGENIC DRIVES IN THE EARLY PHASE OF EXERCISE HYPERPNEA IN MAN.

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The ventilatory responses to electrically induced, voluntary and passive leg exercise were studied in 20 normal men and 23 patients with spinal cord transection at the level of T5-T12. In the latter group, instead of voluntary exercising, the patients made an intentional effort to move their legs. The increment of $\dot{V}_E$ at 10 s after the onset of electrically induced and passive exercise was significantly larger in the normal subjects than in the patients. In the paraplegics, $\dot{V}_E$ increased significantly right after the onset of intentional effort. The sum of % change in $\dot{V}_E$ at 10 s after the onset of electrically induced exercise in the healthy subjects and that of intentional effort in the patients was larger than % change in $\dot{V}_E$ of voluntary exercise in the healthy group. We conclude that ventilatory response at the onset of mild exercise is related to drives from both the exercising limbs and higher centers. Negative interaction of ventilatory response was assumed to be derived when the two stimuli were simultaneously induced.

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THE RELATIONSHIP BETWEEN THE MAXIMUM AEROBIC CAPACITY AND THE KINETICS OF VENTILATION AND CARDIAC OUTPUT TO A STEP EXERCISE STUDIED IN HEALTHY MEN. GRUCZA,R.*, MIYAMOTO,Y. AND NAKAZONO,Y. *Dept. Appl. Physiol. Med. Res. Centre,Polish Academy, Sci., Poland and Dept. Infrom. Eng. Fac.Eng. Yamagata Univ., Yonezawa 992.

Twenty young untrained men performed two tests on bicycle ergometer in order to verify whether the kinetics of the cardiorespiratory reaction exhibit any relation to $\dot{V}O_2max$. On the first day, the subjects exercised at work intensities of 50 and 100 W, initiated by a step function, for periods of 10 min each. The next day, they performed exercise at a relative intensity of 50% $\dot{V}O_2max$ for 10 min. Ventilation and cardiac output were measured continuously. Time constants for $\dot{V}_E$ and $\dot{Q}$ determined during unsteady-state from rest to 50 W were 52 and 14 sec while those determined from 50 to 100 W were 86 and 45 sec, respectively. Time constants for $\dot{V}_E$ and $\dot{Q}$ determined from rest to 50% $\dot{V}O_2max$,which corresponds to 94±23 W in average, were 65 and 20 sec, respectively. There was a significant correlation between the time constants of $\dot{Q}$ and $\dot{V}O_2max$ ($r=-0.51, p<0.05$ for "on" response, and $r=-0.69$, $p<0.001$ for "off"). No correlation was observed between $\dot{V}_E$ and $\dot{V}O_2max$. The acceleration and deceleration of $\dot{V}_E$ and $\dot{Q}$ kinetics were highly correlated with $\dot{V}O_2max$, and moreover, there was a significant correlation between the $\dot{Q}$ and $\dot{V}_E$ acceleration and deceleration. It was then concluded that a faster adaptation of $\dot{V}_E$ and $\dot{Q}$ to exercise may be expected in subjects with higher aerobic capacity.

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ENTRAINMENT OF RESPIRATION TO KEY-TAPPING RHYTHM IN MAN. NAKAZONO,Y., KAWAHARA,K., and MIYAMOTO,Y. Dept. of Information Engng., Yamagata Univ., Yonezawa 992

For the purpose of clarifying the mechanism of entrainment between two biological rhythms, following experiments were studied. Subjects were instructed to follow buzzer sounds by tapping a key as quickly as possible. When they could not follow within a predetermined delay, they were penalized (a brief electrical stimulation on their hand). After enough conditioning was attained, following experiment tasks were given. 1)The subject listened to a train of regular buzzer sounds (1.0s interval) in a period of 4 min during which he tapped the key. 2)After listening to regular sounds for 1 min, he continued tapping without sounds for 3 min. 3)Tapping for 4 min following to random interval sounds. Breathing intervals were measured from respiration curves monitored by a thorax displacement pick-up.

Time delay of tapping in task 1 and 2 showed a negative value. This means that the tasks were regarded as a predicted motion. On the other hand in task 3, the time delay was more than 100 msec. Not only in task 1 but also in task 2 was it observed that the breathing rhythms were entrained to the tapping rhythm ($p < 0.0002$). These results suggest that the prediction to the key tapping was not mediated by any sensory stimulus. The entrainment between the tapping and respiratory rhythms seem to originate in some central mechanism.

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INTERRELATION OF WORK LOAD, PEDAL RATE AND METABOLIC RATE TO VENTILATORY RESPONSES DURING STEADY-STATE CYCLE EXERCISE. TAKANO, N. Dept. of School Health, Fac. of Education, Kanazawa Univ., Kanazawa 920

Ventilatory responses during the steady state of light to moderate cycle exercise were measured in 13 untrained female subjects under nine exercise conditions: at three work loads (0, 1, 0.5 kp in this order) each at three different pedal rates (30, 50, 76 rpm in this order), each for 3 min. A linear multiple regression analysis showed that on the average, relative contribution of three stimuli of work load (F), pedal rate (P) and $\dot{V}co_2$, to increasing (shown in + sign) respiratory quantities during exercise are as follows. $\dot{V}_E$: $0.06F+0.12P+0.87\dot{V}co_2$, V_T: $0.14F+0.03P+0.87\dot{V}co_2$, and f: $0.18F+0.55P+0.34\dot{V}co_2$. Relative contribution of F and P to exercise hyperpnea, considered as a neural component, was shown to decrease with work rates. The magnitude of neural component varied greatly from subject to subject, in five subjects exercise hyperpnea being accounted for solely by a humoral component which was mediated by changes in $\dot{V}co_2$.

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OCCLUSION PRESSURE IN THE UNTRAINED SUBJECTS AND ENDURANCE ATHLETES.
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Oxygen uptake, pulmonary ventilation and heart rate were determined during maximal treadmill exercise in the 13 untrained subjects and 8 endurance athletes. In addition, occlusion pressure (P0.2), tidal volume (VT) and inspiratory duration (VI) for each subject were measured at rest and during submaximal bicycle ergometer exercise.
It was found that maximum oxygen uptake per kilogram of body weight and maximal pulmonary ventilation were significantly higher in the athletes than that in the untrained subjects. The regression coefficient of VT/VI and P0.2 tends to high in the trained group as compared with untrained one, while there are no significant difference in the P0.2 between untrained and trained groups.
From these results, it was suggested that impedance at rest and during submaximal exercise may reduced by endurance training for long periods.

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A MODEL ANALYSIS OF DIFFUSION PATHWAY OF OXYGEN IN OX LUNG
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The main purpose of the present study is the estimation of the possible effect of phospholipid layers on the oxygenation of erythrocytes in the pulmonary capillary vessel. The oxygenation process of erythrocytes in the lung was calculated with a model in which diffusion pathway for oxygen was separated into several micro-steps. The diffusion coefficients of cell membranes of pneumocytes plus endothelial cells, cytosol plus blood plasma, erythrocyte membranes, and hemoglobin solution in erythrocytes were estimated from the viscosity values measured with a time resolved fluorometer and a rotating disk viscosimeter. The fluorometrically measured membrane viscosity was assumed to represent the viscous friction which the oxygen moleclues encounter in the phospholipid bilayers. The solubility of oxygen in the phospholipid bilayers was assumed to be 5 times of that in the blood plasma. The time course of oxygen partial pressure distribution was numerically calculated with the approcimation method of the possitive differentiation for the one-dimensional diffusion. The high viscosity of the phospholipid bilayers seems to cause a reduction in the rate of oxygenation of the hemoglobin solution in the red cell in the lung capillary by 11 % compared with a uniform pathway filled with cytosol and plasma.

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POSSIBLE CORRELATION OF MYOGLOBIN (Mb) CONTENTS TO OXYGEN REQUIREMENTS IN AVIAN GIZZARD MUSCLES.
ENOKI, Y., SAKATA, S., OHGA, Y., KOHZUKI, H., SHIMIZU, S. AND NAKATANI, A. Dept. Physiol., Nara Medical Univ., Shijō-chō, Kashihara, Nara 634

Mb has been generally considered to exist in skeletal and cardiac muscles, but not in smooth muscles. We showed previously the only exception to this rule in smooth muscle of chicken gizzard and reported structural and functional characterizations of the Mb isolated therefrom. In an attempt to assess physiological significance of the protein in muscles we determined the gizzard Mb contents in 78 avian species with special reference to their feeding habits. These species of bird could be divided into two groups, the one with Mb-rich gizzards and the other with Mb-poor; the average content (mg/g wet muscle weight) was found to be 8.71 ± 2.98 in the former (n=37) and 1.91 ± 0.83 in the latter (n=41). No correlation was found between Mb contents of the gizzards and of the breast muscles. Feeding habits were mostly herbivorous in the former and carnivorous or omnivorous in the latter, thus suggesting that the Mb contents may be a reflection of the mechanical tasks, and possibly the oxygen requirements, of the gizzard muscles.

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INCREASED BLOOD-OXYGEN AFFINITY DECREASES OXYGEN UPTAKE IN EXERCISING GRACILIS MUSCLE. KOHZUKI, H., ENOKI, Y., OHGA, Y., SAKATA, S., SHIMIZU, S. AND MATSUDA, M. SECOND DEPT. PHYSIOL., Nara Med. Univ., Kashihara, Nara 634.

Influence of high O_2 affinity of blood on O_2 supply-demand relationship was studied in isolated dog gracilis muscle stimulated to produce one twitch/s isometric contractions. The steady state $\dot{V}_{O_2}$ at this twitch rate corresponded to roughly 20 % of the $\dot{V}_{O_2}max$. The contracting muscle was alternately perfused with normal and high O_2 affinity blood of constant C_{aO_2} at varying perfusion rates with an interval of 100 s. Average P_{50} for normal blood was 33.7 Torr as contrasted to 15.5 Torr in high O_2 affinity blood which was prepared by incubation for 24 h with cyanate. In a range of O_2 delivery from 5 to 10 ml/min·100g, $\dot{V}_{O_2}$ with high O_2 affinity blood (3.37±0.31 ml/min·100g) was significantly reduced as compared with that with normal blood (4.14±0.27). A reduced O_2 extraction was noted in the high affinity perfusions. All through the present O_2 delivery range, P_{vO_2} for the high affinity perfusion was significantly lower than that for normal blood. We conclude that the reduced $\dot{V}_{O_2}$ with low P_{50} blood perfusion was due to a decrease in O_2 extraction.

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NASAL 'FLOW' RECEPTORS IN THE RAT. TSUBONE, H. Bas. Med. Sci. Div., Natl. Inst. Environ. Stud., Tsukuba, Ibaraki 305

This study was performed to identify nasal 'flow' receptors and to investigate their firing characteristics related to nasal airflow. For this purpose, single or a few fiber afferent activity was recorded from the anterior ethmoidal nerve in the anesthetized rat breathing through the nose or tracheostomy. With nasal breathings, 40 receptors in 14 rats were identified as 'flow' receptors which were strongly stimulated by exposure to cold air(0-15°C) and inhibited by warm air(30-45°C). Their spontaneous activity, shown as an inspiratory modulation, disappeared in the absence of nasal airflow during nasal occlusions. With tracheostomy breathings, 85 flow receptors in 11 rats were markedly stimulated by the constant unidirectional airflow with room air or cold air through an upper airway cannula, where the discharge frequency depended on the flow rates(100-300 ml/min). Some receptors(Type R1, R2) exhibited a dynamic response to the constant flow, while another receptor(Type S) a static response. In all flow receptors, a decrease in temperature was a primary factor to excite them. These evidences suggest that the trigeminal nerve has a number of nasal flow receptors which operate as one of thermoreceptors.

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VENTILATORY AND CIRCULATORY RESPONSES TO CAROTID BARORECEPTOR STIMULATION IN MEN. SAKAKIBARA, Y., HONDA, Y., PETERSEN, E.S.*, ROBINS, P.*, KHAMNEI, S.* Dept. of Physiol., Chiba Univ., Sch. of Med., Chiba 280, *Oxford Univ., Univ. Lab. of Physiol., Oxford, United Kingdom

We stimulated the carotid baroreceptors by a neck suction(N.S.) using a neck colour in 16 healthy men. The test was conducted under four steady state different blood gas conditions as well as during Read's CO2 rebreathing test. Heart rate dropped 15 % at the 2nd breath during N.S. with -60 mmHg, almost independently of blood gas conditions. The ventilatory response to N.S. was strongly influenced by blood CO_2 concentration, but not by O_2 level. In eucapnic condition, N.S. induced hyperpnea. Ventilation was depressed 12 % by N.S. at PAco2 60 mmHg during CO_2 rebreathing test. We considered that the bradycardic response is fairly independent of blood gas state, and that N.S. elicited two opposite ventilatory effects; nonspecific stimulation and inhibition probably due to baroreceptor stimulation, the former being suppressed by an increased CO_2 concentration.

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DISTRIBUTION PATTERN OF COLLATERAL BRANCHES OF UPPER CERVICAL INSPIRATORY NEURONS IN THE CAT LOWER SPINAL CORD. SASAKI, S.-I., EDAMURA, M. YOKOGUSHI, K. AND AOKI, M. Department of Physiology, Sapporo Medical College, S.1, W.17, Chuo-ku, Sapporo 060 Japan.

The present study was performed to investigate branching patterns of cervical inspiratory neurons in cervical, thoracic and lumbar spinal cords. Extracellular spike activities of inspiratory neurons were recorded in the lateral border of the gray matter of C1, C2 spinal segments on anesthetized cats. Effective stimulating sites for antidromic activations of cervical neurons were mapped in cervical, thoracic and lumbar spinal segments systematically. Thirty five of 41 cervical neurons had descending axons to the lumbar spinal cord. Five of 30 cervical neurons had axon collaterals in C5, C6. The sites of collaterals were not within the phrenic nucleus but more medial and dorsal to the nucleus. In contrast to the cervical cord, all cervical neurons examined had many collaterals in thoracic and lumbar segments. These collaterals were distributed in more than one segment. To investigate the synaptic connections between cervical neurons and respiratory motoneurons (phrenic, internal and external intercostal and lumbar abdominal motoneurons), the spike-triggered averaging method was employed. However, no evidence for monosynaptic connections has been obtained. It is suggested that cervical neurons may exert synaptic effects to respiratory motoneurons via interneurons.

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LOCALIZATION AND FUNCTION OF PHASE-SPANNING RESPIRATORY NEURONS IN THE PONS AND MEDULLA OF CAT. KOBAYASHI,N., FUJITO,Y., and AOKI,M. Department of Physiology, Sapporo Medical College, S.1, W.17, Chuo-ku, Sapporo 060 Japan.

Phase-spanning (P-S) neurons which start firing just before the end of inspiration are suggested to be involved in the off-switch mechanism of respiration. This study aimed to investigate the localization and function of P-S neurons in the rostral pons and medulla. Extracellular unit activities of respiratory neurons and the phrenic root discharges were recorded in cats anesthetized with pentobarbital sodium. Bilateral vagotomy was performed to prevent the pulmonary feedback. There were only phasic type respiratory neurons in the medulla. Both phasic and frequency modulation type neurons were located in the rostral pons. P-S neurons close to the Boetzinger complex started firing just before the end of inspiratory phases. P-S neurons of the rostral pons had a tendency to be located more medial and ventral to the nucleus parabrachialis medialis (Pbm) and the firing frequency of these neurons gradually increased toward the end of inspiratory phases. Electrical stimulations of the lateral side of Pbm had "off-switch" effects on inspiration. In contrast, electrical stimulations of the medio-ventral side of Pbm where P-S neuron activities were recorded had little effects on inspiration. It is suggested that the P-S neurons of the rostral pons may not be directly involved in the off-switch mechanism of respiration.

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EFFECTS OF SOME FOODS ON THE pH OF HUMAN SALIVA. NANBA,R. Faculty of Education, Okayama Univ., Okayama 700

Effects of some foods on the pH ofhuman saliva in the oral cavity were studied from each of four healthy young adult female subjects. Therefore, the pH of mixed saliva(submandibular and sublingual saliva) was measured by means of a glass micro-combination pH electrode. The results are summerrized as follows :

1. The pH of saliva was increased remarkably just after meal. The value of pH was decreased, however, gradually after that. And the recovery time to the value of pH before meal was required about 45 minutes.
2. The condiment and lemon juice increased the value of pH of mixed saliva.
3. Milk,water and green tea were no change on the salivary pH.
4. Japanese noodle; so called the UDON or SOHMEN was no change on the salivary pH. When the condiment or pepper was added into the noodle-soup, the pH of saliva in the oral cavity was increased remarkably.

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TIME COURSE OF BICARBONATE CONCENTRATION IN PAROTID SALIVA AFTER SINGLE TONGUE STIMULATION. INOMATA, K., TAKAKUWA, M., SAITO, S., HOSHI, M. AND KURAHASHI, M., Dept. of Oral Physiol., School of Dent., Higashi-Nippon-Gakuen Univ., Ishikari-Tobetsu, Hokkaido 061-02

Flow rate, pH and Pco_2 of parotid saliva obtained after single acid stimulation to tongue were measured simultaneously in five subjects. Bicarbonate concentration of saliva was estimated from pH and Pco_2. Pco_2 and pH of saliva were measured by IL system which is used for the measurement of blood samples, or by Kurary pH monitor. Maximum salivary flow rate and Pco_2 appeared at 7 to 18 sec after stimulation, and they were 0.5 to 4.1 ml/min and 76 to 114 mmHg respectively. Time course of Pco_2 is closely consistent with that of flow rate. On the other hand, maximum pH appeared at 2 to 4.3 min after stimulation, the change in pH was slower than that of Pco_2. Maximum bicarbonate concentration appeared at 1 to 6 min after stimulation. Time course of bicarbonate concentration was similar to that of pH. When tongue was restimulated 30 min after first stimulation, parotid gland was able to recover the secretory response. When pH and Pco_2 of saliva were directly measured by micro pH and Pco_2 sensors set in suction capusula, maximum Pco_2 appeared at 1 to 5 min after stimulation. Time course of bicarbonate concentration measured by this direct method was not different from that by IL system.

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STARCH DIGESTION IN THE GASTROINTESTINAL TRACT OF NORMAL AND PAROTID DUCT-LIGATED RATS. KURAHASHI, M. AND INOMATA, K., Dept. of Oral Physiol., School of Dent., Higashi-Nippon-Gakuen Univ., Ishikari-Tobetsu, Hokkaido 061-02

Both amylase activity and starch digestion in gastrointestinal tract after feeding were investigated in normal and parotid duct-ligated rats. In normal rats, both parotid and pancreatic amylase activity decreased after feeding, while the amylase activity appears in gastric and intestinal chyme. Amylase activity in gastric chyme was markedly lower in parotid duct-ligated rats than in normal rats. Thirty seven and 9.4 % of starch in gastric chyme were digested to reduced sugar in normal and parotid duct-ligated rats respectively. Gastric emptying of carbohydrate was significantly faster in parotid duct-ligated rats than in normal rats. Both increased water intake and decreased production of reduced sugar in stomach seem to accelerate the gastric emptying of cabohydrate in parotid duct-ligated rats. Although total amylase activity in intestinal chyme was significantly lower in parotid duct-ligated rats than in normal rats, the starch digestion in small intestine was not different between normal and parotid duct-ligated rats. These results suggested that parotid amylase plays an important role in starch digestion in mouth and stomach of normal rats, and increased rate of gastric emptying compensates the delay of starch digestion in stomach of parotid duct-ligated rats.

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STUDIES ON SELF-DEFENCE MECHANISM IN GASTRIC MUCOSA (2) THE ROLE OF THE ADRENAL GLAND.
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This study involving adrenalectomized (Adrex) and enucleated (Enu) rats was attempted to evaluate the role of the adrenal gland in the pathogenesis of stress ulcer induced by the application of restraint and water immersion stress and revealed that 1) the gastric blood flow in the non-operated (Intact) rats was 68ml/min/100g. It fell to 33ml/min/100g at 2hrs after the stress. In the Adrex rats, the highest value was before the stress. However, at 2hrs, it decreased and became comparable with that of the Intact and Enu rats. 2) the histamine concentration in the gastric mucosa before the stress was significant lower in the Adrex (0.14μM/g) and Enu (0.29μM/g) rats than in the Intact rats(0.53 μM/g). During the stress, there were no changes in the Intact, Adrex and Enu rats. 3)the norepinephrine concentration in the gastric mucosa before the stress was 0.81nM/g in the Intact rats. This level rose to value of 1.37nM/g at 2hrs after the stress. In the Adrex and Enu rats, the values were significantly lower than those in the Intact rats and were unaffected by the stress. 4) the epinephrine concentration in the gastric mucosa before the stress was 0.23nM/g in the Intact rats. This level dropped to value of 0.16nM/g at 2hrs after the stress. In the Adrex and Enu rats, the values were significant lower than those in the Intactrats and were unaffected by the stress. These results suggest that the adrenal gland may play an important role in the development of stress ulceration.

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STUDIES OF PENETRATION THROUGH INTESTINAL MEMBRANE ON THE VENTROMEDIAL HYPOTHALAMIC OBESE RAT.
Terao, T., T. Fujise, T. Yoshioka, S. Nakano and *T. Shiraishi Dept. of Physiol. 3, and *Dept. of Physiol. 1, Tokai Univ. Sch. of Med., Isehara, 259-11

We have been investigating penetration of the metabolites, glucose, amino acids, and insulin as an active polypeptide, through everted rat intestine by our own circulation apparatus, which is automatically computer analyzed. We report here, the intestinal penetration of L-phenylalanine, L-tryptophan and insulin by ventromedial hypothalamic lesioned (VMH) obese rats and sham lesioned controls. One group had 6 weeks of walking exercise (WE) and the other was sedentary. Penetration of L-tryptophan through intestinal membrane of WE and sedentary VMH rats was higher, but not significantly than that of sham rats. Penetration of L-phenylalanine by VMH WE rats was significantly ($p<0.05$) greater than that of VMH sedentary or sham controls. The meaning of this is not yet clear. Penetration of insulin by WE and sedentary VMH rats was significantly higher than that of sham sedentary rats. There was no difference between WE and sedentary VMH rats. This data support previous results of abnormal intermediate metabolism in obese VMH rats. VMH lesions also disrupt the light-dark cycle of meal patterns which persists even when rats become obese. The present results suggest that one cause of VMH obesity may be increased insulin penetration through the intestinal membrane.

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ROLE OF CCK IN LUMINAL FEEDBACK REGULATION IN THE CONSCIOUS RAT.
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Pancreatic exocrine secretion in the conscious rat is mainly regulated by intestinal proteases secreted by the pancreas, and an exclusion of bile and pancreatic juice (BPJ) from the intestine stimulates pancreatic secretion (luminal feedback). In the present study, effects of BPJ diversion on plasma CCK, pancreatic polypeptide (PP), insulin, glucose and gastrin concentrations were examined in the conscious rat. Plasma CCK concentration measured by a bioassay using dispersed acini was significantly increased by BPJ diversion (from 0.45 to 18 pM), changing in parallel with protein output. However, an additional CCK infusion (100 pmol/kg/h) during BPJ diversion could not further increase pancreatic secretion. The magnitude of pancreatic stimulation induced by infusion of 300 pmol/kg/h of CCK-8 during BPJ returning was comparable to that induced by BPJ diversion. BPJ diversion increased PP concentration but the increase was abolished by atropine. BPJ diversion did not affect other endocrine functions. The present study has demonstrated for the first time that BPJ diversion is the strongest endogenous stimulant of CCK release in rats. Furthermore the results also more directly confirmed the previous suggestion that CCK is a main regulator in luminal feedback regulation in this species.

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HORMONAL CONTROL OF MACROMOLECULAR UPTAKE BY INTESTINE OF SUCKLING RATS

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An uptake of intact proteins from the intestinal lumen into the systemic circulation is increased in neonates. The hormonal control of macromolecular uptake was investigated in the suckling rats. The intestinal uptake of bovine IgG was inhibited by subcutaneous injection of hydrocortisone (H), thyroxine (T), insulin (I), EGF (E), and CCK-8 (O), but was not affected by caerulein and pentagastrin. Induction of sucrase activity corresponded to the inhibition of uptake. Morphological changes of epitherial cells were observed by H, T, and I injections. These results suggest a possibility that precocious maturation of enzyme activity and macromorecular uptake in the intestine is complementally induced by not only H and T, but I, E, and O.

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BILE EVACUATION FOLLOWING FOOD INGESTION: RELATIONSHIP BETWEEN GALLBLADDER AND SPHINCTER OF ODDI ACTIVITY IN CONSCIOUS DOGS.

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The relationship between gallbladder pressure and activity of the sphincter of Oddi following ingestion of food was studied in conscious dogs. Each of four beagle dogs was provided with a gastric fistula, a gallbladder fistula, and a duodenal fistula opposite to the papilla of the common bile duct under ether anesthesia. The activity of the sphincter of Oddi was measured by canulating the papilla with a catheter pressure transducer (1 mm diameter). During the quiescent period of the stomach and duodenum, gallbladder pressure was about 2 mmHg and basal pressure of the sphincter was about 12 mmHg, over which phasic contractions (about 30 mmHg) were superimposed. Following ingestion of 300 ml of milk or 300g of meat, gallbladder pressure increased but the frequency and amplitude of sphincter of Oddi activity were reduced. Basal sphincter pressure decreased to the levels of gallbladder pressure (4-5 mmHg) and bile was evacuated in 3-6 min. An entry of food into the duodenum was observed 10-16 min after food ingestion. Gallbladder contraction and sphincter relaxation by food were inhibited by hexamethonium (5mg/kg-h). It is concluded that gallbladder contraction, sphincter relaxation and bile evacuation occur before the entry of food into the duodenum by a mechanism sensitive to ganglionic blockade.

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THE PANCREATIC EXOCRINE SECRETION RESPONSE INDUCED BY STIMULATION OF CANINE SEPTAL AREAS.

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In chloralose anesthetized and hemispherectomized dogs whose pyloric sphincter was submucosally ligated, the pancreatic secretory response to electrical (ES) and chemical (CS) stimulations of the septal area and paraterminal gyrus was studied. ES (20 Hz, 0.2 mA, 3 msec) and CS (microinjection of 0.1 M dl-homocysteic acid, 1.0-2.5 µl) were applied through a double barrel glass electrode.

The increased pancreatic outflow was induced by ES and CS mainly on the lateral septal nucleus, the bed nucleus of the stria terminalis and the paraterminal gyrus, and partly on some points of the medial septal nucleus and dorsal septal nucleus. The pancreatic outflow was increased from the control value 57±8.3 µl/5 min (M±SE, N=24 dogs) to 231±34.5 µl/5 min by ES. The increased response was usually accompanied with an increase of the tone, amplitude and rate of the gastric antral motility. Both responses were abolished by a mid-hypothalamic transection, cervical vagotomy or atropine injection. In a few cases the slightly reduced response was induced by ES and CS.

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DOSE-DEPENDENT LOWERING ACTION OF CATTLE BILE TO PLASMA ETHANOL LEVELS IN THE RATS.
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Effects of cattle bile on metabolism, elimination and absorption of ethanol(EtOH) were studied in eight weeks male Sprague Dawley rats, fasted for 16 hrs. Various dosage (0-400mg/kg B.W.) of cattle bile 30 min before oral administration of EtOH(1g/kg B.W., as 20% soln.) were received to the rats by intragastric intubation. Concentrations of EtOH([EtOH]) in plasma and stomach, gastric contents and the specific activities of cytosolic alcohol dehydrogenase(ADH) and mitochondrial acetaldehyde dehydrogenase(ALDH) in the liver were determined at constant intervals. The maximum plasma [EtOH](C_{max}) and the time required to reach C_{max} decreased and increased according to the dose-response with the increase of the cattle bile, respectively. The disappearance time of plasma [EtOH] was insensitive to the bile. No liver ADH and ALDH activities were induced by cattle bile. No gastric contents, EtOH and cattle bile in stomach were observed at 270 min after administrations of EtOH. Apparent decay rate constants of plasma [EtOH] were not influenced by bile dosage. These results suggest that dose-dependent lowering action of cattle bile to plasma EtOH level is ascribed to the changes of the absorption process of EtOH, and independent of the changes of liver ADH and ALDH activities.

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CHANGES IN SUBSTANCE P AND SOMATOSTATIN CONTENT IN GASTROINTESTINAL TRACT OF STREPTOZOTOCIN DIABETIC RATS.
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It is reported in experimental diabetic rats that somatostatin(SOM) is increased in stomach and vasoactive intestinal polypeptide is increased in ielum. We found the decreased spontaneous motile activity and the decreased contractility induced by substance P(SP) and acetylcholine in isolated intestinal segments of streptozotocin(STZ) diabetic rats in vitro. Therefore, we examined the SP and SOM content in gastrointestinal tract of STZ diabetic rats(1 month after STZ injection), extracting with 80% acetone and using radioimmunoassay. SOM content was significantly increased about two times in corpus of stomach when expressed in ng/corpus and ng/wet weight(ww), in duodenum and jejunum (ng/unit length, cm) but not in ileum and colon(ng/cm), when compared with normal controls. In contrast, SOM in caecum was significantly decreased(ng/organ and ng/ww). However, SOM was not significantly increased in duodenum, jejunum, ileum, colon and pancreas when expressed in ng/ww. SP content was also significantly increased in corpus(ng/ww and ng/organ), duodenum(ng/ww and ng/cm) and in caecum(ng/ww). SP content of intestinal tract was difficult to simply correlate to disordered contractility induced by SP.

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DECREASED INTESTINAL RESPONSES TO ACETYLCHOLINE AND SUBSTANCE P IN STREPTOZOTOCIN DIABETIC RATS IN VITRO.
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We reported previously that in in vitro tube form-preparations of isolated segments of intestine of streptozotocin(STZ) diabetic rats, frequency of spontaneous intraluminal pressure waves was significantly decreased in duodenum, when compared with normal controls. Isolated tube form intestinal segments were split half and the split-half was called longitudinal muscle preparations. Transverse slit of 5 mm were made alternately from right and left edge of slit-opened segments at 5 mm intervals and this was called circular muscle preparations. We could confirm the decreased frequency of spontaneous length changes in isolated longitudinal and circular muscle preparations of diabetic duodenum in vitro, 1 month after STZ injection. Furthermore, amplitude of spontaneous length changes was significantly decreased in circular muscle preparations of duodenum, jejunum and ileum but not in colon and not in longitudinal muscle preparations. In addition, we examined the contractility induced by acetylcholine(Ach) and substance P(SP), of longitudinal and circular muscle preparations. Dose-response curve revealed that both Ach and SP responses were significantly decreased in longitudinal and circular muscle preparations of diabetic duodenum, jejunum and ileum but not of colon.

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THE EFFECTS OF A CARBONIC ANHYDRASE INHIBITOR ON PANCREATIC B-CELL. SUGIMOTO, Y. and KITASATO, H. Dept. Physiol., Shiga Univ. Med. Sci., Ohtsu, 520-21.

Lowering pH_i in pancreatic B-cell was reported to decrease the potassium conductance resulting in the depolarization observed as the glucose-induced electrical activity. We assume that proton may be derived from the hydration of carbon dioxide by carbonic anhydrase. The rate of depolarization at the introduction of glucose in the presence of acetazolamide is slower than that in the absence of acetazolamide. The withdrawal of external sodium in the presence of acetazolamide led to a initial hyperpolarization and a subsequent depolarization whose rate was much slower than that observed in the absence of acetazolamide. In the present study carbon dioxide arisen from glucose metabolism is proved to be a major supplier of proton in pancreatic B-cell. However, in the presence of glucose 0.1mM acetazolamide enhanced the potential of the silent phase. Although acetazolamide reduces the proton production, it also has some effects on the membrane which lead to the depolarization.

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INHIBITORY ACTION OF CARBACHOL ON THE D-GLUCOSE-INDUCED ELECTRICAL ACTIVITIES OF PANCREATIC B CELLS. SAKAMOTO, Y. AND IMANAGA, I. Dept. of Physiol., School of Medicine, Fukuoka University 7-45-1, Nanakuma, Johnan-ku, Fukuoka 814-01

We examined the effects of Carbachol on the burst-type activities induced by 11.2 mM D-glucose in the pancreatic B cells of the mouse.

Carbachol(10^{-6}M) generally induced a further depolarization and increased a frequency of the slow wave induced by D-glucose(11.2mM).

The B cell was classified into two types according to degree of membrane depolarization(type a,6.0±0.6mV ;type b,14.0±0.4mV). In type b cells, spike potentials were disappeared, but small amplitude of potential fluctuation was observed on the plateau level. In type a cells, the frequencies of the slow waves increased to 153.0±0.4% ,and the duration of active plateau phase and silent phase inversely decreased to 66.3±4.8% and 34.0±2.8% respectively. In the Carbachol-pretreated cells, D-glucose did not induce the electrical activities in early periods, but depolarized the membrane. The further depolarization of the drug was not affected by Na and Cl ions, but reduced by high Ca.

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EFFECTS OF PROSTAGLANDIN E_1 ON PANCREATIC HORMONES OF PLASMA IN HEALTHY MEN AND PATIENTS WITH ARTERIOSCLEROTIC OBLITERANS. KAKU, M., SUZUKI, H. * AND HORI, S. 1st Dept. of Physiol., *4th Int. Med. Hyogo Coll. of Med. Nishinomiya

The effects of intravenous infusion of PGE_1 (7.5ng/min/Kg body weight) during 30min on plasma insulin, C-peptide, glucagon, somatostatin levels and some other plasma components as well as blood pressure were studied in healthy men (n=5) and in patients (n=5) with arteriosclerotic obliterans (ASO).

Insulin and C-peptide levels decreased within 1 min after PGE_1 infusion (acute insulin and C-peptide falls) and recovered to the basal levels within 5min, followed by the gradual decreases (delayed decreases) of both pancreatic peptides during period from 5 to 30min. The maximum decrements of acute insulin falls were 2.6 $\mu U/m\ell$ (41%) and 0.9$\mu U/m\ell$ (11%) in healthy group and in ASO group, respectively. On the contrary, plasma glucagon increased within 1 min after PGE_1 infusion (acute glucagon rise). The maximum increments of actute glucagon rise were 44.2 pg/ $m\ell$ (61%) and 8 pg/$m\ell$ (8%) in healthy group and in ASO group respectively. These acute responses in healthy group were 1.7 ~ 7.6 times stronger than those in ASO group. Other plasma components, plasma glucose, free fatty acid, phospholipids, β-lipoprotein etc, changed slightly. Blood pressure was lowered gradually and slightly, too. These results show that acute insulin and C-peptide falls and acute glucagon rises occured due to direct inhibitory effect on pancreatic β-cell or insulin degrading effect and releasing effect on pancreatic α-cell by PGE_1 respectively.

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MOVEMENT AND FUSION OF SECRETORY GRANULES IN CHROMAFFIN CELLS.

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To examine the intracellular mechanism for secretory processes in living adrenal chromaffin cells, we employed a Nomarski microscope and a digital image processor combined with a video camera. Chromaffin cells could be divided in three types: 1) cells with motionless granules, 2) cells with slowly moving granules, and 3) cells with granules showing a rapid Brownian motion. A digital subtraction process revealed that K-depolarization induced an exocytotic response in type 1) cell. Small spots representing secretory granules appeared or disappeared suddenly at a rough rate of 1 event per cell per sec. A contrast enhancement revealed that the same stimulation induced a reversible increase in granular movement in type 2) cell, and an adhesion of granules and emergence of granules of a large diameter (1 μm) in type 3) cell. A Ba containing solution and a hypotonic solution induced similar responses in type 3) cell. The secretory activation is, in part, mediated by alteration in physical properties of granules and cytoskeletons.

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COMPARISONS OF THE BIOLOGICAL ACTIVITIES OF NATIVE AND SYNTHETIC CORTICOTROPHIN--RELEASING FACTOR (CRF) IN CULTURED RAT ADENOHYPOPHYSEAL CELLS. YASUDA, N., YASUDA, Y. Dept. Physiol., Iwate Medical University, Morioka, Iwate and Div. Endocrinol., Oregon Health Sciences University, Portland, Oregon

The dose-response characteristics of partially purified bovine hypothalamic CRF frac--tions were compared to those of synthetic 41-residue CRF, sauvagine, or dibutyryl- or 8-bromo cyclic adenosine monophosphate in cultured rat adenohypophyseal cells prepared by two different methods. Cells were dispersed using either a combination of trypsin and pancreatin, or collagenase and deoxyribonuclease. All of the tested substances induced significant ACTH and/or β-endorphin secretion from cultured cells. The dose--response slopes and the maximum ACTH and/or β-endorphin secretion for the synthetic 41-residue CRF, sauvagine, or two forms of cyclic adenosine monophosphate were quite comparable. In contrast the dose-response slopes for partially purified bovine CRF were much steeper and the maximum ACTH and/or β-endorphin secretion much grater than those for other CRF substances tested. Addition of arginine vasopressin and/or ascorbic acid to synthetic CRF did not reproduce the dose-response patterns of partially purified bovine CRF suggesting that the hypothalamus might contain some CRF component(s) different from the 41-residue CRF or vasopressin.

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MODULATORY EFFECT OF PAF-DERIVATIVES ON PAF-INDUCED GLUCOCORTICOID SECRETION BY THE PERFUSED GUINEA PIG ADRENAL. SHIMADA,T., MINE,Y., HIROSE,T., MATSUMOTO,I. AND AIKAWA,T. Dep. Physiol. Nagasaki Univ., Sch. Med., Nagasaki 852

PAF(1-o-hexadecyl/octadecyl-2-acetyl-sn-glycero-3-phosphocholine) is a chemical mediator of anaphylaxis and inflammation. We previously reported that PAF increases the secretion of cortisol(F) and cortico=sterone from the perfused guinea pig adrenal gland. In the present study, the effect of CV-3988, a synthetic PAF receptor antagonist, and 1-o-hexadecyl/octadecyl lyso PAF, a precursor of PAF, on PAF-induced F secretion was investigated. CV-3988 significantly inhibited the secretory response to 10 nM 1-0-hexadecyl PAF at 10 μM. The continuous infusion of 0.01 to 10 nM 1-o-hexadecyl lyso PAF dose-dependently inhibited the secre=tory response of F to 10 nM 1-o-hexadecyl PAF.Maximum inhibitory effect of 1-o-hexadecyl lyso PAF was observed at 1 nM and the secretory response was about one third the response without lyso PAF. The secretory response to ACTH was entirely free from the inhibitory effects of CV-3988 and lyso PAF. These results suggest that lyso PAF may modulate the action of PAF on the adrenal cortex at subnanomolar concentration in guinea pigs.

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EFFECT OF H1- AND H2-RECEPTOR ANTAGONISTS ON THE RESPONSE OF EPINEPHRINE, CORTISOL AND PLASMA RENIN ACTIVITY INDUCED BY BRAIN MAST CELL STIMULATION IN DOGS. MATSUMOTO, I., HIROSE, T., MINE, Y., SHIMADA, T. AND AIKAWA, T. Dept. Physiol., Nagasaki Univ. Sch. of Med., Nagasaki 852.

We previously reported that the adrenal secretion of epinephrine (Epi) & cortisol (F) and plasma renin activity (PRA) significantly increased after intracerebroventricular (i.c.v., V_{III}) infusion of comp.48/80, a histamine releaser from mast cells, and that the increase in Epi, F and PRA is fairly abolished by oral administration of ketotifen for 1 week in dogs. In the present study, the effect of H_1- and H_2-histamine receptor antagonists on the response of Epi, F and PRA to brain mast cell stimulation was examined. The increase in Epi, F and PRA in response to i.c.v. infusion of comp.48/80 was significantly reduced by simultaneous i.c.v. administration of pyrilamine, a H_1-histamine receptor antagonist. Simultaneous i.c.v. administration of metiamide, a H_2-histamine receptor antagonist, augmented the increase in F but did not change that in Epi and PRA. These results suggest that endogenous histamine liberated from brain mast cells may activate Epi & F secretion and PRA via central H_1-histamine receptor.

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DEVELOPMENTAL PLASTICITY IN ACTH RESPONSIVENESS TO STRESS STIMULI IN RATS. Hamamura, M. AND Onaka, T., Dept. Physiol., Jichi Med. Sch., Minamikawachi-machi, Tochigi 329-04

Effects of preweanlingly given stress stimuli were studied on plasma ACTH after stress stimuli given during adulthood in male rats. Pups were removed from their mothers and placed in an individual plastic beaker for 10 min every day during period between 3 and 20 days of age. At 45 days of age plasma ACTH level in these rats after light and sound given for 5 min in a white chamber was significantly lower than in the control rats without preweanling manipulation, while basal ACTH levels were not significantly different between these groups. Similar results were obtained between experimental and control rats of littermates. In the rats that were given electric shocks (5-ms pulses of 50 Hz, 0.2-mA intensity, 3-min duration) during preweanling period and tested by footshocks (50 Hz, 0.4-, 0.8-, 1.6-mA intensity, 1-min duration) in adulthood, ACTH responsiveness was also significantly lower than in control rats given preweanlingly 0-mA shocks. These data support the view that stress stimuli exposed during preweanling period suppresses ACTH responsiveness in adult rats.

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DEXAMETHASONE POTENTIATES cGMP FORMATION STIMULATED BY ANP IN CULTURED RAT RENAL CELLS. K. KANDA, Y. NIWA, H. MIYAMOTO, H. SEO and N. MATSUI Dept. Endocrinol. & Metab. The Res. Inst. Environ. Med., Nagoya Univ., Nagoya, 464-01 Japan

The renal action of atrial natriuretic peptide(ANP) is mediated by the change in c-GMP. We reported that ovarian steroid hormones, but not glucocorticoids(GC), suppress cAMP response to vasopressin in renal cells. In this study, modification of renal action of ANP by various hormones was examined.

Rat renal cells were dispersed, cultured and preincubated with various hormones for 48 hours. Thereafter, cells were incubated with ANP(h-ANP or r-ANP) for 10 minutes and intracellular cyclic nucleotides were determined by radioimmunoassay.

1. Dexamethasone(Dex) at 10^{-8} M increased h-ANP-stimulated cGMP formation without affecting cAMP and basal cGMP levels. 2. Dex increased cGMP formation stimulated by r-ANP in the same fashion as h-ANP. 3. Dex did not affect cGMP formation stimulated by sodium nitroprusside which activates soluble guanylate cyclase in the cytosol. 4. Effect of cortisol on ANP-stimulated cGMP was similar but weaker than Dex. Other hormones such as corticosterone, aldosterone, triiodothyronine, estradiol and testosterone did not influence it.

It is suggested that potentiation of ANP action may be involved in the diuretic action of GC.

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RELATIONSHIP BETWEEN THYROID FUNCTION AND GH SYNTHESIS. T.Kamijyo*, H.Seo and N.Matsui, Dept. Pediat. School of Med., Nagoya Univ. and The Res. Inst. Environ. Med., Nagoya Univ., Nagoya 464 Japan

To evaluate the relationship between thyroid function and GH synthesis and secretion, the effect of GRF on GH secretion, pituitary GH content and its mRNA were studied in rats with various thyroid status.

Rats were rendered hypothyroid by thyroidectomy (Tx). Four weeks after Tx, T4 was administered by i.p. injection. After 7 days, GRF (8ug/day) was given s.c. intermittently for another 7 days by osmotic pump while T4 administration was continued. Twelve hours after the last GRF delivery, bolus GRF(1ug) was given i.v..

Hypothyroid rats treated with or without GRF for 7 days showed a significant reduction in GH response to GRF. By T4 treatment, GH response to GRF became comparable to the level observed in control euthyroid rats. In hypothyroid rats, GH content and GH mRNA in the pituitary were not increased by GRF treatment by osmotic pump. However, in euthyroid rats, GRF significantly increased GH mRNA. It was noted that GRF treatment by osmotic pump resulted in the reduction of serum T4 and T3 in Tx rats treated with T4. These data indicate that thyroid hormone is required for the action of GRF on somatotrophs. Increased GH secretion by intermittent GRF administration in the rat may cause altered thyroid hormone metabolism.

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THYROID FUNCTION AND TRH CONCENTRATION OF PLASMA, HYPOTHALAMUS, EXTRAHYPOTHALAMIC BRAIN AND GASTROINTESTINAL ORGANS IN STREPTOZOTOCIN DIABETIC RATS.
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We examined the effects of streptozotocin(STZ)-induced diabetes mellitus on the thyroid function and the thyrotropin releasing hormone(TRH) concentration of plasma, hypothalamus, extrahypothalamic brain and gastrointestinal organs in adult male Wistar rats. Rats were decapitated at 10 and 90 days after STZ treatment(60 mg/kg body weight, i.v.). Free thyroxine(T_4), triiodothyronine(T_3) and TRH were measured by specific radioimmunoassay. TRH was extracted with acetone and petroleum ether. The plasma free T_4 level in diabetic rats was significantly lower than that in controls(3.0+1.0 vs 9.2+1.4 ng/dl at 90 days). The plasma T_3 level in diabetic rats was also lower than that in controls (0.26+0.03 vs 0.48+0.09 ng/ml at 90 days). TRH content of pancreas in diabetic rats was significantly decreased to about 10% of controls. There was no significant changes in TRH content in other gastrointestinal organs(fundus, antrum, duodenum, ileum, jejunum, colon and caecum). TRH concentration of hypothalamus, extrahypothalamic brain and plasma did not change throughout experiment. These findings seem to suggest that in diabetic rats, primary cause of pituitary thyroid axis alterations may not be the reduction in hypothalamic TRH concentration.

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DISAPPEARANCE OF ATRIAL NATRIURETIC PEPTIDE IN THE CANINE
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To clarify the disappearance of atrial natriuretic peptide(ANP) in the body of canine, blood samples were simultaneously collected from the arteries and veins of various organs, and plasma ANP concentrations were measured. Fine catheters were fixed in both arteries and veins of the lung, liver, kidney, spleen and cervix, and the coronary sinus, the supramesenteric artery and the portal vein in canines infused with exogenous ANP (28 ng/kg/min, n=7) and not infused with exogenous ANP (n=6). The plasma ANP degradation did not occur after a 60 min incubation at 37=c of the blood samples obtained simultaneously from the catheters.

The present study suggests that the arteriole wall degrade plasma ANP or consume it in the binding sites, since the plasma ANP concentrations in the veins were lower than those in the arteries in every organ examined by almost the same ratio. No specific organ for ANP degradation could be estimated. The plasma from the coronary sinus and forearm vein contained essentially the same ANP molecular forms, as obtained by gel permeation chromatography. Thus, the circulation of blood through various organs dose not cause high molecular weight ANP to be changed to other forms.

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INVOLVEMENT OF BRAIN DOPAMINERGIC SYSTEM IN VASOPRESSIN RELEASE CAUSED BY ANGIOTENSIN II. YAMAGUCHI, K. AND KARAKIDA, T. Dept. Physiol., Niigata Univ. Sch. Med., Asahimachi, Niigata 951

To evaluate the roles for brain catecholamines in angiotensin II (AII)-induced vasopressin (AVP) release, the effects of intraventricular (ivt) injections of catecholamine antagonists (0.15 μmol) were examined on plasma AVP responses to ivt administrations of its agonists (0.15 μmol) and AII (48.2 pmol) in conscious rats. Blood samples were collected by decapitation, and plasma AVP was determined by radioimmunoassay. Dopamine, phenylephrine (an alpha-adrenergic agonist) or ANG II increased plasma AVP 90 sec after the injection. Blood pressure was not appreciably changed by dopamine or phenylephrine, whereas it was significantly elevated by AII. Isoproterenol (a beta-adrenergic agonist) did not change plasma AVP. The AVP responses to both dopamine and AII were significantly ($P < 0.01$) diminished by haloperidol (a dopamine blocker) given 10 min before the injections of these agents. Pre-administration of phenoxybenzamine (an alpha antagonist) which abolished the AVP releasing effect of phenylephrine, or propranolol (a beta antagonist) did not inhibit the AVP response to AII. Administration of haloperidol, phenoxybenzamine, or propranolol alone did not affect basal plasma AVP level. These results suggest that the periventricular dopaminergic system may participate in AII-induced AVP secretion.

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VASOPRESSIN SECRETION: BIMODAL EFFECTS OF NOXIOUS STIMULI IN RATS. ONAKA, T. AND YAGI, K., Dept. Physiol., Jichi Med. Sch., Tochigi 329-04

Effects of footshocks (FS) on plasma immunoreactive vasopressin (ir-VP) and adrenocorticotropic hormone (ir-ACTH) were studied in rats under a hypertonic condition (0.5 M NaCl 20 ml/kg b.w. injected s.c. 35 min before blood collection). Plasma ir-VP level was significantly lower after low-frequency (0.05-0.2 Hz) but higher after high-frequency (5 Hz) FS (3 mA) than the unshocked control level. Plasma ir-ACTH level was consistently higher in rats after FS at any frequency (0.05-5 Hz) than in the control. A significant decrease in plasma ir-VP was observed after 0.2-Hz FS (1.5, 3.0 or 4.0 mA) but the magnitude was not significantly different among these FS intensities, whereas plasma ir-ACTH was increased in an intensity-related manner. Plasma ir-VP was transiently decreased and returned to the control level within 20 min after FS initiation (3 mA, 0.2 Hz, 5 min). In rats anesthetized with α-chloralose and urethane (60 and 600 mg/kg b.w., i.p.) a significant increase in plasma ir-VP occurred after 0.2- as well as 50-Hz FS. These data support the hypothesis that noxious stimuli activate two distinct neural mechanisms; one potentiates and the other suppresses VP secretion.

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CALCIUM FLUX ANALYSIS IN THE RAT NEUROHYPOPHYSIS WITH CALCIUM MICROELECTRODES. SHIBUKI, K. Department of Physiology, Jichi Medical School, Minamikawachi-machi, Kawachi-gun, Tochigi-ken 329-04.

Extracellular Ca^{2+} changes were measured in the rat neurohypophysis in vitro by Ca^{2+}-sensitive microelectrodes. Electrical stimulation (20 Hz, 10 s) evoked $[Ca^{2+}]_o$ decreases by 27.5 ± 0.5 % (mean ± S.E., n=7) which were blocked by tetrodotoxin (1 μM) and Cd^{2+} (1 mM). Changes in $[Ca^{2+}]_o$ at the electrode tip were unlikely to be modified by diffusion between the tissue and the perifusing media within 20-40 s of the estimated diffusion time. Assuming that $[Ca^{2+}]_o$ during stimulation were determined by Ca^{2+} influx and efflux while $[Ca^{2+}]_o$ after the cessation of stimulation was largely determined only by Ca^{2+} efflux, Ca^{2+} fluxes were estimated from the rates of $[Ca^{2+}]_o$ changes. The estimated Ca^{2+} influx was 13.44 ± 1.48 %/s (1 %/s corresponds to about 3 nmole/s/g tissue) at 1 s after the initiation of 20 Hz stimulation, and was followed by sharp reduction in the amplitude within 2-3 s during the stimulation. The estimated efflux reached the peak of 4.77 ± 1.01 %/s at 2 s after the initiation. Extracellular Na^+ and Ca^{2+} influx facilitated the Ca^{2+} efflux.

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ROLE OF CORTICOTROPIN RELEASING FACTOR IN STRESS-INDUCED OXYTOCIN RELEASE IN THE RAT. HIGUCHI, T., TAKANO, S and NEGORO, H. Dept. Physiol., Fukui Medical School, Matsuoka, Fukui 910-11

To test whether corticotropin releasing factor (CRF) neurons in the paraventricular nucleus (PVN) are involved in stress-induced oxytocin (OT) release, we examined OT release in response to intracerebroventricular injection of CRF and an effect of PVN lesion on OT release observed during immobilization stress in the female rats. Injection of CRF into the 3rd ventricle in conscious rats evoked a dose dependent OT release determined by radioimmunoassay. OT response to CRF (2 nmol) occurred without a change in arterial blood pressure and was not altered by dexamethasone pretreatment to block ACTH secretion. Lesion of the PVN significantly reduced OT secretion during immobilization, but had no effect on OT release induced by i.p. administration of hyperosmotic saline (1.5 M, 5 ml/kg). Lesion of the supraoptic neucleus (SON) which damaged OT fibers from PVN as well reduced OT release evoked by either immobilization or osmotic stimulation. From these results it is indicated that CRF locally released in the PVN may mediate OT release during immobilization stress in the rat.

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CORTICOTROPIN RELEASING FACTOR FACILITATES BACKGROUND ACTIVITY OF OXYTOCIN NEURONS IN RATS. TAKANO,S.,NEGORO,H. AND HIGUCHI,T. Dept. Physiol., Fukui Medical School, Fukui 910-11

Stress-loading and intracerebroventricular(ivt) injection of corticotropin releasing factor(CRF) increase oxytocine(OT) release. This study was designed to investigate the effect of CRF to basal activities of OT neurons in vivo. Extracellular recording from the paraventricular nucleus and ivt injection of CRF(1.5 nmole) were made in urethane-anesthetized(1.1g/kg) lactating rats. Neurosecretory neurons in the paraventricular nucleus were classified as OT neurons and vasopressin neurons by their characteristic high-frequncy burst of spikes preceding the reflex milk ejection and phasic firing respectively. Basal activities of OT neurons(n=17) were elevated significantly ($p<0.01$) from 24.5 ± 4.2(spikes/10s,means$\pm$SE) to 35.2 ± 5.8 by the injection and returned to the original level after 40 min while responses of vasopressin neurons were inconsistent(excited:n=4, inhibited:n=3, unresponsive:n=2). These results indicate that CRF increases the excitability of OT neurons and that stress-induced OT release is mediated by CRF.

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LATERAL HYPOTHALAMIC AREA AND PARAVENTRICULAR NUCLEUS CONNECTIONS WITH SUBFORNICAL ORGAN NEURONS. TANAKA, J. and SETO, K., Dept. Physiol., Kochi Med. Sch., Nankoku, Kochi 781-51

The role of pathways from the lateral hypothalamic area (LHA) to the hypothalamic paraventricular nucleus (PVN), through the subfornical organ (SFO) in regulating the activity of vasopressin (VP)-secreting neurons in the PVN was examined in urethane-anesthetized male rats. Since we had found that the majority of LHA neurons projecting to the SFO have the sensitivity to angiotensin II (A II), these LHA neurons were activated by microinjection of A II into the LHA. Activation of A II-sensitive LHA neurons facilitated the activity of nearly half (8/18) of SFO neurons antidromically identified as projecting to the PVN as well as the excitability of approximately one-quarter (11 / 45) of putative VP-secreting neurons in the PVN. The excitatory responses (8/8) of the putative VP-secreting neurons were prevented or attenuated by pretreatment with the A II antagonist, saralasin (Sar), in the SFO. Electrical stimulation of the SFO, on the other hand, produced excitation (17/52) or inhibition (14/52) of the putative VP-secreting neurons in the PVN. A half (7/14) of the excitatory responses to LHA stimulation were blocked or attenuated by pretreatment of Sar in the SFO, whereas the inhibitory responses (0/11) were not affected. These results suggest that A II-sensitive LHA neurons projecting to the SFO may act to enhance the excitability of putative VP-secreting neurons in the PVN via an excitatory influence on the A II-sensitive SFO neurons.

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CHEMORECEPTOR STIMULATION INFLUENCES ACTIVITIES OF MAGNOCELLULAR NEUROSECRETORY CELLS IN PARAVENTRICULAR NUCLEUS OF FEMALE RATS. AKAISHI, T.[1], SATO, A.[2], SATO, Y.[2] and SUZUKI, A.*[2] 1; Dept. Physiol., Niigata Univ. Sch. Med., Niigata 951 and 2; Dept. Physiol., Tokyo Metropol. Inst. of Gerontol., Tokyo 173.

The effects of stimulation of chemoreceptors either by hypoxia or by hypercapnia on the antidromically identified, tonically firing magnocellular neurosecretory neurons in the hypothalamic paraventricular nucleus were studied using ovariectomized and estrogen treated rats under urethane anesthesia. The animals were immobilized by gallamine triethiodide and were artificially ventilated. Either the hypoxia between $F_{ET}O_2$ 6 and 14% under the constant $F_{ET}CO_2$ at 5.0% or the hypercapnia between $F_{ET}CO_2$ 6 and 10% under the constant $F_{ET}O_2$ at 16% produced excitation of these neurons stimulus-dependently. The increased responses of these neurons remained even after denervation of bilateral carotid sinus nerves and aortic nerves, indicating that afferent informations from peripheral chemoreceptors are not absolutely necessary for producing the activation of these neurons to either hypoxic or hypercapnic stimulation.

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RAT GH RELEASE RESPONSE TO HUMAN GH RELEASING FACTOR (hGRF) IN VITRO IS ATTENUATED BY LESIONS OF THE PERIVENTRICULAR NUCLEUS. SOYA, H. AND SUZUKI, M., Department of Physiology, Institute of Endocrinology, Gunma University, Maebashi 371

We have reported that GH release response to hGRF in an in vitro perifusion system was blunted within 1 day after anterolateral hypothalamic deafferentation (AHD), accompanying a marked decrease in somatostatin (SRIF) content in the stalk median eminence (SME). To examine a role of tuberoinfundibular SRIF neurons to maintain the response of the pituitary to hGRF, the effect of electrolytic lesions of the periventricular nucleus (Pe) on the pituitary GH response to hGRF was studied. Pe-lesions caused a significant decrease both in the GH release response to hGRF and SME-SRIF content after 1 and 10 days as the effect of the AHD. However there were no significant changes in GH content and pituitary weight, although those changes were observed in 3 and 10 days after the AHD. In addition, Pe-lesions caused no significant change in rGRF content of the SME as the effect of the AHD.

These results suggest that the anterior hypothalamic area, particularly the Pe is required to maintain pituitary response to hGRF.

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REDUCED VIP IMMUNOREACTIVITY IN THE PITUITARIES OF HORMONE-DEFICIENT MUTANT MICE. NOGUCHI, T., SUGISAKI, T., AND KANAMATSU, T. Dept. Physiol., Toho Univ. Sch. Med., Ohmori-nishi, Tokyo-143.

The prolactin-producing cells of the bovine anterior pituitary were found to contain a vasoactive intestinal polypeptide (VIP) immunoreactive substance, thus suggesting a role for VIP in the regulation of prolactin release.

The pituitaries of the dw and lit strains of mutant mice, congenitally deficient in prolactin-producing cells, and hyt mice, which was found to have reduced numbers of prolactin-producing cells, showed a markedly reduced VIP immunoreactivity. Hypothalamic VIP immunoreactivity, however, was found to be unchanged in the three strains of mutant mice, indicating that the high concentration of VIP in the hypothalamus does not derive from the adenohypophysis through retrograde flow. The deficiency in the mutant mice seems to be due to the lack of prolactin target cells in the pituitary.

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THE PROTEIN KINASE C INHIBITOR POLYMYXIN B INFUSED INTO THE ACCESSORY OLFACTORY BULB PREVENTS THE FORMATION OF AN OLFACTORY MEMORY.
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On mating with a stud male, female mice form an olfactory memory to this male. The memory is formed during a critical period of 4 h immediately after mating, and is dependent on the noradrenergic innervation of the accessory olfactory bulb (AOB). However, removal of the noradrenergic innervation after memory formation has no effect on memory recall, suggesting that synaptic processes responsible for memory storage may occur at the AOB. The purpose of this study was to evaluate the effect of microinfusions of the protein kinase C inhibitor polymyxin B into the AOB. Polymyxin B infused immediately and 1.5 h after mating blocked the memory formation. Further study was undertaken to examine if polymyxin B or the local anaesthetic lignocaine infused into the AOB interferes with the neural transmission resulting in pregnancy block. Infusions were carried out immediately before each of two 4-h exposures to the pheromones of a strange male, coinciding with the nocturnal and diurnal prolactin surges on day 1 of pregnancy. Lignocaine blocked the transmission, while polymyxin B was without effect. These studies suggest that activation of protein kinase C within the AOB is important for the formation of an olfactory memory.

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EFFECTS OF PARASYMPATHETIC DENERVATION ON ANDROGEN RESPONSIVENESS OF THE RAT SUBMANDIBULAR GLAND.,
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Androgen responses of esteropeptidase and 5α-reductase activity were investigated in the submandibular glands of the rat(female Wister,8 weeks of age)with section of the chorda tympani to determine whether or not the parasympathetic nerve plays any role in androgen action. The right chorda tympani was cut within the ear. Rats were divided into two groups: 1) animals with denervation and 2) animals with denervation and administration of testosterone propionate(TP,30 mg/Kg BW) for five days from the 16th day afer the operation. On the 21th day after the operation, the weight of the right gland decreased markedly compared with that of left gland(non operated gland). The atrophy of the right gland was slight when TP was given , indicating that androgen produced greater increases in weight in the right gland than in the left gland. Specific activities of esteropeptidase and 5α-reductase in the right gland were increased by denervation alone while those in the left gland did not change. In rats with denervation and TP treatment, specific actities of both enzymes were high in the right gland compared with the left gland. These findings suggest that parasympathetic denervation result in increased androgen responsiveness of the submandibular gland in the rat.

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EFFECTS OF ESTROGEN ON THE POPULATION OF GERM CELLS IN THE GONAD OF DEVELOPING MALE QUAIL.
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Estradiol benzoate(E)(0.02 mg) was injected into yolk sac of fertilized egg of genetic males quail on the zero daystage. The numbers of germ cells were estimated in the cortex and medulla of embryo testes from fourth to fifteenth days of incubation. Moreover the proportion of germ cell numbers to area of gonad($10^{-2}mm^2$) was estimated and compared with that of treated and control male. That of the left cortex in the treated male was 24 cells on the fourth day, 44 cells on the eleventh day and 59 cells on the fifteenth day, and similar to that of the control (23 cells on the fourth day, 84 cells on the eleventh day and 52 cells on the fifteenth day). On the other hand, that of the left or right medulla in the treated male was 5 cells on the fourth day, 17 cells on the eleventh day and 15 cells on the fifteenth day and showed a decrease against that in the control (7 cells on the fourth day, about 22 cells on the eleventh day and 34 cells on the fifteenth day). These results indicate that E is able to act on cortical proliferation and regression of medulla and male gonad developes into ovary-like structure.

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ANTIBODY AGAINST NERVE GROWTH FACTOR BLOCKS TESTOSTERONE-DEPENDENT MASCULINE ORGANIZATION OF THE NEONATAL RAT BRAIN. YANASE, M., [1]HONMURA, A., [2]AKAISHI, T. AND [2,3]SAKUMA, Y. Dept. Laboratory Med., St.Marianna Univ. Sch. Med., Kawasaki 213, [1]Res. Div., Kanagawa Pref. Rehabil. Ctr, Atsugi 24301, and [2]Dept. Physiol. II, Niigata Univ. Sch. Med., Niigata 951. [3]Present address: Dept. Physiol. I, Hirosaki Univ. Sch. Med., Hirosaki 036.

Injection of antibody against nerve growth factor into the cerebral lateral ventricle blocked testosterone-induced behavioral defeminization of neonatal female rats. When tested in adulthood, the injected animals showed a significantly higher lordosis quotient than the testosterone-teated, normal rabbit serum infused controls. Failure of vaginal opening and clitoral enlargement manifested the masculinizing effect of testosterone on the genitalia in the experimental as well as the control animals. Estrogen-sensitivity of hypothalamic neurons which are responsible for the induction of lordosis was retained in the experimental animals. Recordings of the antidromic action potentials from neurons in the ventromedial nucleus of the hypothalamus following stimulation of the midbrain central gray revealed that estrogen decreased the antidromic activation threshold and shortened the absolute refractory period of the hypothalamic efferents along with the estrogen-induced behavioral activation in the experimental animals. In the control group, the estrogen-induced neuronal activation was lost altogether with the behavioral activation.

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CHANGE OF PLASMA CALCIUM LEVEL IN THE OVIPAROUS SNAKE, Elaphe quadrivirgata, DURING REPRODUCTIVE PERIOD. YOSHIHARA, M., UCHIYAMA, M. AND MURAKAMI, T. Dept. of Oral Physiol., School of Dentistry at Niigata, The Nippon Dental Univ., Niigata 951

In the oviparous snake, Elaphe quadrivirgata, plasma calcium level during reproductive period were studied. Plasma calcium level in female snakes before ovulation (May) was higher than that in male snakes (15-30 vs. 13-15 mg/100 ml). At the begining of ovulation (early and mid June), plasma calcium level in female snakes showed a remarkable increase (30-200 mg/100 ml) and it decreased after ovulation (12-14 mg/100 ml). This level was maintained till 1-2 weeks before oviposition. However, plasma calcium level began to increase again and the level at oviposition (late June and early August) was higher (20-40%) than that in pre-oviposition. These results indicate that the pattern of change of plasma calcium level in reproductive female snakes is similar with laying hen. However, the change is more drastic in snakes than the laying hen.

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ACID STABLE TRYPSIN INHIBITOR (ASTI) IN SEMINAL PLASMA AND ITS EFFECT ON FERTILIZATION. MATSUOKA, Y., SUMI, H., YOSHIDA, E., TSUSHIMA, H., MARUYAMA, M., IKEDA, R., MORIMOTO, N., SUGIKI, M., ETOH, Y., HAMAI, K., HAYASHI, M., HAMASUNA, S., MIHARA, H. Dept. Physiol., Miyazaki Medical College, 5200 Kihara, Kiyotake-cho, Miyazaki 889-16, Japan

ASTI having the same antigenicity as urinary trypsin inhibitor (UTI) was first detected in seminal plasma by ELISA. The level in seminal plasma taken from healthy individuals was 1.5 ± 0.3 (mean ± SD) μg/ml and that of acid-treated seminal plasma was 0.37 ± 0.11 μg/ml (n=8). Two molecular forms of the inhibitor were observed. The main form had a molecular weight of about 30,000 and the minor one, a molecular weight of about 140,000 as determined by gel filtration on Sephacryl S 300. ASTI had a broad spectrum for serine proteases such as trypsin, chymotrypsin and plasmin. It also strongly inhibited acrosin. In view of these data, we further investigated whether or not UTI and TLCK were effective as vaginal contraceptives in ICR mice. UTI and TLCK (in Krebs Ringer phosphate buffer) were thoroughly mixed with an equal volume of a sterile lubricant. 0.1 ml of the mixure was deposited into the vagina. The final concentration of the inhibitors was 0.5 mg/ml and 1.5 mg/ml, respectively. The mice were bred as soon as possible, and they were killed later to count the fetus numbers. TLCK was not effective for antifertility at each level. UTI was slightly effective at a level of 0.5 mg/ml, rather than at a level of 1.5 mg/ml.

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STIMULATION OF THE ACCESSORY OLFACTORY BULB EXCITES TUBEROINFUNDIBULAR ARCUATE NEURONES.
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The role of the accessory olfactory bulb (AOB) in conveying pheromonal information to tuberoinfundibular (TI) arcuate neurones was examined electrophysiologically in chloral hydrate-anaesthetized, oestrogen (0.5 μg in silastic capsules)-treated and untreated ovariectomised Balb/c female mice. Electrical stimulation of the AOB orthodromically excited part of TI neurones antidromically stimulated from the median eminence and histologically verified as being located within the arcuate nucleus. No inhibitions were following AOB stimulation. The excitatory response to AOB stimulation was reversibly blocked by the local anaesthetic, lignocaine infused into the amygdala. The percentage of TI arcuate neurones responding to AOB stimulation was significantly higher in oestrogen-treated than in untreated animals. In oestrogen-treated preparations, TI arcuate neurones responsive and unresponsive to AOB stimulation could be distinguished by the frequency of successful antidromic propagation into the soma.

These studies demonstrate that relay neurones in the AOB act to enhance the activity of a subpopulation of TI arcuate neurones via the amygdala and this neural transmission is modulated by oestrogen.

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WEIGHT INCREASE IN HUMAN PINEAL GLAND IN CASES OF NEOPLASTIC DISEASES, AMYOTROPHIC LATERAL SCLEROSIS AND CEREBELLAR ATAXIA.
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We aimed to obtain some clues or suggestions as to the functional and medical significance of the human pineal gland from postmortem gross-anatomical observations in pathological and medico-legal autopsy cases.

Pineal weights were measured in 88 disease cases and the controls were obtained from 37 medico-legal autopsy cases. The subjects were male and female, over 20-year-old Japanese. The pineal weights of the controls were usually under 210mg ($\bar{X}$±SD, 137.9±36.3; maximum value, 205mg). Some, but not all, benign — teratoma of ovary (1/1) — and malignant neoplastic disease cases (5/41), systemic neurodegenerative disease cases (2/4) like amyotrophic lateral sclerosis and spinocerebellar degeneration including cerebellar ataxia, diabetes mellitus cases (2/3) and a hypotension case showed high values of over 220mg. None of the 37 other disease cases showed such high values.

Thus, in addition to neoplastic diseases and diabetes mellitus which have already been examined, the functional relation of the pineal gland to the systemic degenerative diseases in the nervous system is an interesting problem that needs to be examined.

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EFFECTS OF THYROID HORMONE ON THE LATENCY OF THE EVOKED POTENTIALS BY PHOTIC AND ELECTRICAL STIMULATION OBSERVED IN THE LATERAL GENICULATE NUCLEUS AND THE VISUAL CORTEX
TAKEDA, M., SUZUKI, M., KATO, M., Dep. Physiol, Institute of Endocrinology, Gunma Univ, Maebashi 371, Japan.

To analyze the functional change in the visual system, we measured the evoked potentials in the visual cortex (VC), the lateral geniculate nucleus (LGN), and the optic chiasm (OC) of normal, thyroidectomized (Tx), the Tx-T3 or Tx-T4 supplemented rats under pentbarbital anesthesia. After thyroidectomy, the latencies of photic evoked potentials in the VC and the LGN were gradually prolonged for 8 or 14 days. T3 supplement to Tx rat rapidly restored the prolonged latency in the VC to the normal level by 12 hr, while those in the LGN and the OC were gradually restored to the normal levels after 4 or 8 days. Futhermore, when the evoked potentials in the VC, the LGN and the VC were recorded after electrical stimulation of the OC, the OC and the LGN, respectively. These latency were also prolonged after thyroidectomy. T3 supplement to Tx rats rapidly restored the prolonged latencies of evoked potentials in the VC by electrical stimulation of the LGN and the OC within 24 hr, while that in the LGN by the electrical stimulation of the OC was not restored. These results indicate that 1)thyroid hormone is required to maintain the normal function of the visual system. 2)the hormone acts on the each component of the visual system in different manners.

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IN VITRO ACTIONS OF PROLACTIN, SEROTONIN AND ENKEPHALIN ON TUBEROINFUNDIBULAR DOPAMINERGIC NEURONS. ARITA, J., KIMURA, F. Dept. Physiol., Yokohama City University School of Medicine, 3-9 Fukuura, Kanazawa-ku, Yokohama 236

It has been shown by in vivo studies that prolactin stimulates and serotonin and enkephalin inhibit dopamine release from tuberoinfundibular dopaminergic (TIDA) neurons. The present study determined in vitro actions of prolactin, serotonin and enkephalin on dopamine synthesis in TIDA neurons. In vitro dopamine synthesis in TIDA neurons was estimated by DOPA accumulation in the median eminence after incubation of hypothalamic slices with a DOPA decarboxylase inhibitor. Neither rat prolactin (10 ug/ml) nor the serotonin agonist quipazine (10-50 uM) had effects on basal, Ca^{2+}-dependent and cAMP-dependent dopamine synthesis in the median eminence. The enkephalin agonist [D-Ala^2]-Met-enkephalinamide (5 uM) significantly decreased basal dopamine synthesis without changing Ca^{2+}-dependent and cAMP-dependent synthesis.

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INHIBITION OF LH AND STIMULATION OF PROLACTIN SECRETION BY PREOPTIC INJECTION OF VIP IN OVARIECTOMIZED RATS. AKEMA, T., KIMURA, F. Dept. Physiol., St. Marianna Univ. Sch. Med., 2-16-1 Sugao, Miyamae-Ku, Kawasaki 213., Dept. Physiol., Yokohama City Univ. Sch. Med., 3-9 Fukuura, Kanazawa-Ku, Yokohama 237.

Serum LH concentrations showed pulsatile change at the frequency of 2-3 pulses/h and prolactin levels fluctuated irregularly in unanesthetized ovariectomized rats. Microinjection of 1μg VIP into the medial preoptic area reduced the frequency of LH pulses and stimulated prolactin secretion. Preoptic injection of saline or the same dose of secretin or PHI did not have such effects, indicating the specific action of VIP on the preoptic neuroendocrine apparatus regulating LH and prolaction secretion. Pretreatment of the rat with -methyl-p-tyrosine, a dopamine synthesis inhibitor, or with pimozide, a dopamine receptor blocker, did not affect basal pulsatile LH secretion, but almost completely abolished the inhibitory VIP action on the LH pulse frequency. These results suggest that the inhibitory VIP action on LH pulse generator requires intact dopaminergic transmission.

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SOMATIC SENSORY REGULATION OF A HYPOTHALAMIC SECRETION OF CORTICOTROPIN-RELEASING HORMONE. HOTTA,H.[1], KUROSAWA,M.[1], SATO,A.[1] and SUMITOMO,T.[*2] 1; Dept. of Physiol., Tokyo Metropol. Inst. of Gerontol., Tokyo 173, 2; Dept. of Medicine, Tokyo Women's Medical College, Tokyo 162.

The purpose of the present study was to examine responses of a hypothalamic secretion of corticotropin-releasing hormone (CRH) to either noxious or innocuous mechanical stimulation of skin. Male Wister rats were anesthetized with halothane (1.0%) and their respiration was maintained artificially by a respirator. Hypothalamo-hypophysial-portal blood was collected continuously to calculate a secretion rate of CRH by measuring CRH concentration in plasma using radioimmunoassay method and by measuring that plasma flow, before, during and after the cutaneous stimulation. It was found that noxious stimulation of hindpaws for 20 min by pinching with a surgical clamps produced an increase (about 50% increase) in secretion of CRH whereas innocuous stimulation of abdomen by brushing with a tooth brush did not influence that secretion.

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EFFECT OF HORMONES AND NUTRITION ON THE GROWTH AND DEVELOPMENT OF SNELL'S DWARF MOUSE.

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The intraperitoneal administration for 3 weeks of PBS(phosphate buffered saline, 10 µl/g/day, 5 days/week) or PBS containing thyroid hormone(T_3;20 to 100 µg/ml) or growth hormone(hGH;0.1 to 0.4 U/ml) resulted in body weight gain of 1.8±1.2 g(mean± S.D.)(Exp. No., initial age and body weight;10, 75±35 days, 8.8±2.8 g), 3.5±1.2 g(9, 62 ±34 days, 8.8±3.4 g) and 3.0±1.5 g(10, 59±44 days, 7.0±2.7 g) in Snell's dwarf(dw) mouse, respectively. The analysis of SDS-PAGE of urine demonstrated that the treatment with T_3 or hGH induced the secretion of MUP(major urinary protein) in dw mice of both sexes. These hormone-induced secretion of MUP ceased after the termination of hormone administration and reappeared by the resumption of hormone administration. In the course of these experiments, a group of mouse characterized by a unique profile of growth was found in our dw mouse colony. These mice followed such a growth curve as suspected of dwarfism during the first 4 weeks of life. Thereafter, however, they grew markedly to have body weight, length and fertility comparable to those of normal littermates. The initiation of MUP secretion in these "growth retardated" mice occured 2 or more weeks later than in normal littermates.

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MECHANICALLY INDUCED ELECTRICAL RESPONSES IN MURINE MAMMARY EPITHELIAL CELLS IN PRIMARY CULTURE.

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In mouse mammary epithelial cells in primary culture, mechanical stimulation of a cell induced in other cells within the same colony a short depolarization of less than 15 mV with a duration of 1-8 s and a subsequent, prominent hyperpolarization of 6 mV lasting 10-40 s. Epidermal growth factor induces a spontaneous hyperpolarizing response in cultured mammary cells, and in cells treated with EGF mechanical stimulation produced a greater hyperpolarization, while the amplitude of the depolarizing response was not affected. The amplitude of the mechanically induced hyperpolarization was markedly reduced by quinine and tetraethylammonium, blockers of the Ca^{2+}-dependent K^+ channel. The results suggest that the Ca^{2+}-dependent K^+ channel was involved in the hyperpolarization.

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CORRELATION IN HORMONAL SECRETIONS IN NONSHIVERING THEMOGENESIS (NST). KUROSHIMA,A., YAHATA,T., OHNO,T., Dept. Physiol., Asahikawa Medical College, Asahikawa 078 and Lab. Nutrition Physiol., Hokkaido Univ. of Education, Hokumoncho 9, Asahikawa 070

In order to evaluate significant roles of other humoral factors than noradrenaline (NA) in cold-induced NST, the changes in plasma levels of glucagon and glucocorticoids and in glucagon level of thermogenic tissue, brown adipose tissue (BAT) were studied when NST was maximally stimulated by single ip injection of NA (40μg/100g) in cold-acclimated rats (5℃, 4wk) and warm controls (WC). Plasma glucagon level increased 10 to 40 min after NA, but not saline, injection in both WC and CA. However, the magnitude of elevation was significantly greater in CA. Plasma corticosterone and its immediate precursor, deoxycorticosterone, levels increased by saline injection, but NA caused more significant elevations of these steroid hormones. The magnitudes of their increases were also greater in CA. In contrast to the changes of these hormones, the changes in plasma energy substrates such as glucose and free fatty acids were smaller in CA. There were observed significant increase in glucagon levels of BAT after NA injection in either WC or CA. These results suggest that glucagon and glucocorticoids are closely associated with an enhanced NST, possibly in BAT, during cold acclimation.

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EFFECTS OF COLD EXPOSURE ON BODY TEMPERATURE IN LACTATING RATS. KYOKO IMAI-MATSUMURA[1], KIYOSHI MATSUMURA and TERUO NAKAYAMA. Faculty of Educ., Shiga Univ., Otsu, Shiga 520[1] and Dept. of Physiol., Osaka Univ. Med. Sch., Kita-ku Osaka 530.

We investigated the effect of cold exposure on thermoregulation in lactating rats. Colonic temperature (T_{co}) and oxygen consumption ($\dot{V}O_2$) were measured at an ambient temperature (T_a) of 25 °C and then at 10 °C for 30 min each. Experiments were performed in 6 virgin, 6 lactating (post-partum day 1 (D1), 7 (D7), 14 (D14) and 21 (D21)) and weaned (post-partum day 28) rats. At the end of cold exposure, the decreases of T_{co} in virgin, lactating D1, D7, D14, D21 and weaned rats were 0.4±0.4 °C, 0.3±0.7 °C, 0.4±0.5 °C, 1.0±0.8 °C, 1.7±0.9 °C and 0.7±0.3 °C, respectively. The change of T_{co} in lactating D21 rat was significantly large compared to virgin rats ($p < 0.001$). However, the $\dot{V}O_2$ in lactating D21 rat increased during cold exposure in the same manner as other rats. This suggests that the decrease of T_{co} induced by cooling in lactating D21 rat may be caused by an increase of heat loss.

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THE EFFECTS OF CUTANEOUS DENERVATION ON THE THERMOREGULATRY FUNCTION IN CONSCIOUS GOATS. ASAKI, Y. & JESSEN, C.*, Dept. Physiol., Tokyo Metropol. Inst. Gerontol., *Dept Physiol., der Justus-Liebig-Uni. Giessen.

Experiments were performed in two conscious goats to elucidate whether the outer layers of the body core contain thermosensitive elements which provide afferent signals to the temperature regulating system. A 0.2 m^2 area of the trunk skin was denervated and was either cooled or warmed by a water-perfused jacket at room temperature of 24 °C. The response to this stimulation was evaluated by determining the core temperature threshold at which metabolic rate passed the threshold level of 2.5 W/kg with decreasing core temperature. To manipulate general body core temperature external heat exchangers acting on arterial blood temperature through a chronic arteriovenous shunt were used. The core temperature threshold with cooling the denervated skin area was 0.4 °C higher than that with warming. These differences were statistically significant ($p<0.03$). It is concluded that these differences were due to temperature signals generated by thermoreceptors in the outer layers of the body core.

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COLONIC TEMPERATURE IN THE RMONEUTRAL ZONE IN RELATION TO THE RMO REGULATORY ABILITY IN HOT ENVIRONMENT. FURUYAMA, F. AND *FURUYAMA, M. Dept. Physiol. and *Dept. Pediatrics, Nagoya City Univ. Med. Sch., Kawasumi-cho, Mizuho-ku, Nagoya 467

Colonic temperature (Tco) and O_2 consumption were studied in thermoneutral zone in special relation to thermoregulatory ability at ambient temperature (Ta) of 42.5°C. Four control rats: Donryu, WKA, ACI, SD, and the heat tolerant rat strain were used. Their survival times at Ta of 42.5°C are known to be 78.1 min, 79.3 min, 70.8 min, 152.2 min and 311.2 min, respectively. Tco of the heat tolerant rats at Ta of 25°C was lower than the other 4 strains ($p < 0.01$). Hyperthermic Tco of the heat tolerant rats at Ta of 32°C was also lower than those of SD rats ($p < 0.05$) and the other 3 strains ($p < 0.01$). There was no significant difference in O_2 consumption at Ta of 24°C between the heat tolerant rats (0.132 ± 0.06 ml/$BW^{0.75}$) and ACI (0.142 ± 0.02 ml/$BW^{0.75}$). These findings suggest a possible difference in activity of heat loss system between the heat tolerant rats and conventional heat intolerant rats.

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SKIN SYMPATHETIC NERVE ACTIVITY CONTROLLING THE HEAT-INDUCED VASOCONSTRICTION IN THE HUMAN FINGER. NAGASAKA, T., HIRATA, K., NODA, Y., *MANO, T. AND *IWASE, S. Dept. Physiol., Sch. Med., Kanazawa Univ., Kanazawa 920, and *Dept. VI, Res. Inst. Environ. Med., Nagoya Univ., Nagoya 464

Finger blood flow (BF) and skin sympathetic nerve activity (SSA) to the glabrous side of the hand were measured during immersion of the hand in a water bath whose temperature (T_W) was raised by steps of 2°C every 10 minutes from 35 to 43°C. The experiment was conducted during the summer, in a room whose ambient temperature was 28 - 32°C. The subjects were 4 healthy males wearing summer clothes during the experiments. Finger BF through vessels located deep in the skin was measured using laser-Doppler flowmetry (ALF-2100, ADVANCE). The SSA was recorded directly from the median nerve at the wrist of the tested hand, using a tungsten microelectrode. With finger vessels already dilated at T_W of 35°C, finger BF decreased with a concomitant increase in the SSA as T_W rose to 39 - 41°C. At T_W of 43°C, however, finger BF and the SSA returned toward the control levels. This was also confirmed by a ramp rise of T_W from 35 to 43°C for one subject. From these results we conclude that, when the subject is in a warm state, blood vessels of the finger respond to local heating with vasoconstriction, and this finger vasoconstriction is evoked reflexively by the increased sympathetic outflow to the resistance vessels of the finger.

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The Effect of Acute Heat Stress on Regional Blood Flow and Thoracic Duct Lymph Flow in Rats. YAMADA, S. and HAYASHIDA, Y. Dept. of Systems Physiol., Univ. Occup. Environ. Hlth., Kitakyushu, 807.

Visceral and hindlimb blood flows were measured by a pulse Doppler flowmeter in conscious rats during acute heat stress. Visceral blood flow was measured in the renal or mesenteric artery. Hindlimb blood flow was measured in the abdominal aorta distal to the renal artery. Lymph flow was measured in the thoracic duct. Body temperature was raised with an infrared lamp by 2 °C. This resulted in a 33% increase in the regional blood flow of the hindlimb, while renal or mesenteric blood flow was decreased 19% and 34%, respectively. Lymph flow through the thoracic duct is directly affected by changes of regional blood flow. Given this assumption, it is calculated that the above changes in blood flow would result in a 21% decrease in lymph flow. Measured lymph flow through the thoracic duct was decreased 30%. These results suggest that the changes in visceral blood flow during acute heat stress exert the predominant influence on the rate of thoracic duct lymph flow in the rat.

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INVOLVEMENT OF SODIUM RETENTION HORMONES DURING REHYDRATION IN HUMANS
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We investigated the relation between involuntary dehydration and the mechanisms affecting Na^+ retention in the body, focusing on the renin-angiotensin-aldosterone system. We studied humans during dehydration and recovery while drinking tap water (H_2O-R) or 0.45% NaCl solution (Na-R). We measured plasma renin activity (PRA) and aldosterone levels (PA) prior to dehydration (control), after dehydration, and at 3 hr of rehydration. During the 3 hr rehydration period, subjects restored 51% of the water lost during H_2O-R, while they restored 71% during Na-R. Plasma volume (PV) was decreased about 5% after dehydration and restored by 174% of the loss during Na-R, and 78% of the loss during H_2O-R by 3 hr of rehydration. We found significant correlations between the change in PV and PRA and between PRA and PA. In both groups, PRA and PA significantly increased after dehydration, and decreased almost to the control level by 3 hr of rehydration when the PV deficit was restored. The rate of sodium excretion was correlated with PA in both groups. Thus, the renin-angiotensin-aldosterone system was driven to maintain PV regardless of the degree of rehydration. We concluded that during recovery from dehydration, retention of hypotonic fluid in the vascular space results in incomplete rehydration due to the removal of the drive for hormonal responses that act to retain sodium.

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CHANGES IN TOTAL VASCULAR COMPLIANCE BY HEAT ACCLIMATION. SUGIMOTO, E., HOROWITZ, M.*, OKUNO, T. AND MORIMOTO, T. Dept. of Physiol., Kyoto Pref. Univ. of Med., Kyoto 602 and *Dept. of Physiol., Hebrew Univ., Israel

Effects of hyperthermia(40°C) on blood volume (BV) and total vascular compliance (TVC) were compared between heat acclimated (3 weeks at 32°C and 50% R.H.) and non-acclimated control rats. Experiments were performed on conscious rats who were splenectomized and cannulated into the abdominal aorta and both jugular veins. Changes in BV and central venous pressure (CVP) were recorded at 30 s interval for about 1 h (10 min of control, 10 min of infusion of NaCl sol., 1.6% of body wt, and 40 min of recovery). TVC was calculated from the relation between changes in BV and CVP during the infusion. Body heating and hyperthermia induced a significant BV expansion, especially in control rats. TVC was similar in both control and acclimated rats under normothermic condition. Though hyperthermia did not affect TVC of control rats, it decreased significantly in the acclimated hyperthermic rats and so was the ability to retain infused fluid into the circulation. The data suggest that TVC plays an role in stabilization of BV of the acclimated hyperthermic rat when rapid BV changes takes place and serves to maintain heat exchange.

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EFFECTS OF AGING ON THE EFFICACY OF SWEAT GLAND TRAINING. OHNISHI, N., YAMASHITA, Y., IMAMURA, R., NATSUME, K., SUGENOYA, J., OGAWA, T. Dept. of Physiol., Aichi Med. Univ., Nagakute, Aichi, 480-11

Local sweat glands were trained by 2-hr immersion of the left arm in hot water of 42-43 °C for 14 consecutive days in winter in 7 old male and 7 old female subjects, aged 57 to 73, and in 14 young male and 19 young female subjects, aged 20 to 29. Seasonal difference in sweating activity was also examined in some of them. Sweat gland training caused marked increases in sweating response in the trained area to indirect heating, estimated by the arm bag method, in the young male (233±87%) and the young female (192±69%) subjects, whereas such increases in sweating response tended to reduce in the old males (140±38%) and the old females (140±43%). Sweating response was markedly increased in summer in the young male (257±99%), the young female(247±122%) and the old female (225±109%) subjects, but not in the old male subjects (118±30%). It is suggested that sweat gland training may be less effective for enhancement of sweat gland activity in the aged, although seasonal difference in sweating activity may persist in the old female.

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RELATIONSHIP OF TYMPANIC TEMPERATURE AND SWEAT RATE IN VARIOUS PARTS OF HEAD COOLING. YAMASHITA, Y., OGAWA, T., IMAMURA, R., OHNISHI, N., NATSUME, K., SUGENOYA, J. Dept. of Physiol., Aichi Med. Univ., Nagakute, Aichi 480-11

We previously demonstrated that face fanning lowered tympanic temperature (Tty) without a fall in esophageal temperature and induced a sustained decrease in sweat rate (SR). Presently we observed changes in Tty and SR during cooling of various parts of the head (face, scalp, forehead, eye, cheek, neck or nape) by fanning or blowing of cool air, or by placing an ice-bag. Tty lowered in most cases of fanning and blowing, accompanied by a decrease in SR. In many cases with an ice-bag, however, a transient decrease in SR was noted without a fall in Tty. Moreover, cooling a side of the head and heating the other side resulted in a fall and a rise in Tty on the respective side, accompanied by a difference in sweating responses in the bilateral forearms. These results suggest that cooling venous blood from the face and scalp effectively lowers the brain temperature, inducing a decrease in SR, although SR may respond transiently to a marked drop in skin temperature of the head. These observations support the credibity of Tty as indicator of brain temperature.

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SEX DIFFERENCES IN THE MECHANISM OF SWEAT REDUCTION INDUCED BY THERMAL DEHYDRATION. SUGENOYA, J., OGAWA, T., *ASAYAMA, M., YAMASHITA, Y., OHNISHI, N., NATSUME, K. Dept. Physiol., Aichi Med. Univ., Nagakute, Aichi 480-11, *School of Physical Education, Chukyo Women's Univ., Ohbu, Aichi 474

Characteristics of sweat expulsions were examined before and following the thermal dehydration (TD) in 8 young male (M) and 10 young females subjects (F). TD was induced by 12-h water and food restriction and 1.5 to 2-h sauna heating, and the body weight loss of 2.7 and 2.4% in average (difference was not significant) was obtained for M and F, respectively. The regression line relating the rate of sweat expulsions (Fsw) to mean body temperature showed a significant shift to the right following TD in 7 of the 9 experiments for M and 9 of the 10 experiments for F. The shift of the x intercept averaged 0.69 C in M and 0.51 C in F, and no significant difference was noted between the M and F. The regression line relating sweat rate to Fsw showed no consistent changes following TD in either M or F. Thus, the central sudomotor mechanism may play an important role in the occurrence of the sweat reduction during TD. It was concluded that the mechanism responsible for the sweat reduction is not different qualitatively between both sexes.

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EFFECT OF LOCALLY APPLIED ACETYLCHOLINE ON ANHIDROTIC ECTODERMAL DYSPLASIA (AED) IN THE HUMAN. HASHITANI,T., KANAI,M.* and SHIRAYA,N.*, 2nd Dept.Physiol., 1st Dept. Anat. and Dept. Pediat., Nagoya City Univ. Med. Sch., Nagoya 467

Anhidrotic ectodermal dysplasia (AED) is characterized by partial or complete absence of sweating and other epidermal appendages,together with a variable degree of dental aplasia. Affected children unable to sweat may experience episodes of high fever in warm enviroments and be mistakenly considered to have fever unknown origin. In 1982 Hatzis et al. reported that the hypoplastic eccrine glandular elements in AED may give rise to normal ecrrine glands both anatomicaly and functionally after repeated local application of acetylcholine.

In a 4 year old patient with AED, we applied acetylcholine (acetylcholine 10g + neostigmine 300mg + cold cream 90g), topically on the skin of the upper arm. After three months of the application sweat glands began to function and responded to thermal stimuli. Moreover, morphological developments of the sweat glands have been confirmed by electron microscopy.

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FEVER INDUCED BY TUMOR NECROSIS FACTOR. IRIKI, M., NAGAI, M., SAIGUSA, T., WATANABE, M., OSHIMA, H. , SHIMADA, Y.[2] Dept. Physiol., Yamanashi Medical College, Nakakoma, Yamanashi 409-38, [1]Dept. Pharmaceutical Sciences, Teikyo Univ., Tsukui, Kanagawa 199-01, [2]Tokyo Metropolitan Inst. of Gerontology, Itabashi, Tokyo 173

The role of tumor necrosis factor (TNF) in fever induced by the lipopolysaccharide (LPS), a effective component of the bacterial endotoxin, was investigated in conscious rabbits.
1) TNF injected intravenously at doses lower than 1 μg/kg induced fever with a single peak observed within two hours after the injection, whereas higher doses induced also a second peak after two hours. The rise of rectal temperature in the first peak was increased dose-dependently up to 1 μg/kg.
2) TNF activity in the blood was increased after 100 ng/kg LPS i.v.injection with the peak being seen one hour after LPS injection. The activity was evaluated with respect to cytotoxicity against L292 cells. 3) Intravenous injection of the antibody to TNF 60 min before, concurrently, or 60 min after injection of 100 ng/kg LPS had no effect on the first peak of LPS-induced fever, but significantly inhibited the second peak.

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FEVER INDUCED BY INTERLEUKIN-1ß (IL-1ß) AND SUPPRESSION OF THE FEVER BY INDOMETHACIN. HASHIMOTO, M. AND IRIKI, M., Dept. Physiol., Yamanashi Med. Col., Tamaho, Nakakoma, Yamanashi, 409-38

To investigate a characterization of the fever induced by IL-1ß, the pyrogenicity of recombinant human IL-1ß (rhIL-1ß) and recombinant rabbit IL-1ß (rrIL-1ß), and antipyretic effect of indomethacin (IM) on the fever induced by rhIL-1ß or rrIL-1ß were examined comparing with those of rhIL-1α. 1) RhIL-1ß or rrIL-1ß was injected intracerebroventricularly (icv) in conscious rabbits (2-3 kg) at an ambient temperature of 25±0.5°C. Dose-dependent increase in colonic temperature by 0.5 - 2.5 °C was produced by a single dose of rhIL-1ß of 10 - 1000 pg/kg. A single dose of rrIL-1ß of 33.3 - 1000 pg/kg produced increase in colonic temperature dose-dependently by 0 - 2.5 °C. Both rhIL-1ß and rrIL-1ß were about 3 to 4 times more potent than rhIL-1α in terms of the pyrogenicity. 2) RhIL-1ß was injected either icv (250 pg/kg) or intravenously (iv, 1 μg/kg). IM was injected icv (400 μg/rabbit) or subcutaneously (sc, 20 mg/kg) 15 min prior to IL-1ß injection. By IM given either sc or icv, fever induced by icv rhIL-1ß was inhibited remarkably. By IM given either sc or icv, fever induced by iv rhIL-1ß was inhibited moderately, and when IM was given both sc and icv, suppression of the fever was remarkable. Both fever induced by rhIL-1ß and rrIL-1ß showed similar quality as shown in our previous report on rhIL-1α fever in terms of its suppression by IM.

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CHARACTERISTICS OF FEVER AND ACUTE PHASE RESPONSE INDUCED IN RABBITS BY CYTOKINES; INTERLEUKIN-1, TUMOR NECROSIS FACTOR AND INTERFERONS. MURAKAMI, N., SAKATA, Y., WATANABE, T. AND MORIMOTO, A. Dept. Physiol., Yamaguchi Univ. School of Med., Ube, Yamaguchi 755

Characteristics of fever and acute phase response induced by recombinant human Interleukin-1 (IL-1), Tumor necrosis factor (TNF) and Interferon (IFN) were studied in rabbits.
1) Recombinant human IL-1α and IL-1β could reproduce the same pattern of febrile responses and acute phase responses induced with a crude endogenous pyrogen which was prepared in vitro from white blood cells of rabbits and was utilized in many experiments performed in our laboratory so far.
2) In addition to IL-1, other cytokines, TNF and IFN, could also produce a fever. However, acute phase responses developed with these cytokines were much different from those with IL-1 or were not induced at all.
3) These results indicate that the beneficial value of fever varied markedly depending on the kind of pyrogenic factor.

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ACUTE-PHASE RESPONSE AND METABOLITES IN THE ARACHIDONIC ACID CASCADE SYSTEM.
WATANABE, T., MORIMOTO, A. AND MURAKAMI, N. Dept. Physiol., Yamaguchi Univ. School of Med., Ube, Yamaguchi 755

It was investigated whether central arachidonic acid (AA) metabolites are involved in the development of the acute-phase response. Intracerebroventricular (ICV) injections of a cyclooxygenase inhibitor, indomethacin (INDO), or of a lipoxygenase inhibitor, nordihydroguairetic acid (NDGA), had no effect on the changes in the plasma levels of iron, copper and fibrinogen which were induced by ICV injection of endogenous pyrogen (EP). In addition, those changes were not induced by ICV injection of AA. In contrast, EP-induced hypozincemia was observed on pretreatment with NDGA, but not on pretreatment with INDO. However, plasma zinc increased after ICV injection of AA. Furthermore, ICV injection of EP alone or of EP with NDGA increased the leucocyte count 8 hr and 24 hr after the injection, while ICV injection of AA, or of EP with INDO induced leucocytosis 8 hr after the injection. These results suggest that AA metabolites do not participate in the changes in the iron, copper and fibrinogen, although they play a role in the changes in the plasma zinc and leucocyte count.

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LOCATION AND RESPONSIVENESS OF THALAMIC NEURONS IN RATS WITH COLD EXPOSURE.
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There are very few reports in which changes in activities of the ventro-basal thalamic neurons were observed, in detail, when cold stimulation was applied on the whole body of rats. In the present study, topographical location and responsiveness of rat thalamic neurons were examined with cold exposure. The responses of thalamic neurons were classified into two types. One is a switch-like response in which the activity abruptly increases at a skin temperature with skin cooling, and the other is a graded response in which the activity gradually increases with changes in the skin temperature on the exposure to cold. The recording sites of these neurons were histologically identified in the ventro-basal complex, ventrolateral thalamus and posterior thalamic group. More than eighty percent of the neurons responded to the skin cooling were found to be in the ventro-basal complex of the thalamus. However, there are no significant differences of the topographical location between two types of the neurons; neurons showing the switch-like response and the graded response.

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EFFECTS OF TEMPERATURE ON THE MEMBRANE PROPERTIES IN ISOLATED NEURONS OF PREOPTIC HYPOTHALAMUS.
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Our previous studies using tissue slice preparation revealed the existence of "primary" thermosensitive neurons having inherent thermosensitivity in the preoptic hypothalamus (POA). We investigated the thermoreceptive mechanisms of POA neurons using the whole-cell voltage clamp technique combined with the concentration clamp which allowed rapid changing of external solution within a few milliseconds. Neurons were isolated from the POA of neonate rats by enzymatic and mechanical treatments. The majority of recorded neurons showed a liner increase in inward current during warming (30 to 40 °C), but the Q10 was about 2. However, about 20% of neurons studied were markedly sensitive to warming and showed an increase in inward current to a rise in temperature with high Q10 in the hyperthermic range (35-40°C). This current increase in the hyperthermic range was reversibly blocked by application of tetrodotoxin. But, the inward current in none of the neurons showing Q10=2 was affected by tetrodotoxin. The results show that some neurons in the POA have highly temperature sensitive voltage-dependent Na^+ channel in the hyperthermic range, and these neurons are presumably "primary" warm sensitive neurons.

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EFFECTS OF TNF, IL-1 AND IFNλ ON THE PREOPTIC THERMOSENSITIVE NEURONS IN VITRO.
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The effects of the local application of recombinant human interferonλ (IFNλ) and interleukin-1β (IL-1β) and human tumor necrosis factor (TNF) on the unit activity of thermosensitive (TS) and thermally insensitive (non-TS) neurons in the hypothalamic slices of preoptic area of male rats. The perfusion of IFNλ (less than 5000 units/ml) decreased and increased the activity in 65% of warm units and 60% of cold units, respectively. A majority of non-TS units (71%) were not affected by IFNλ. IL-1β predominantly decreased the activity of warm units (63%) and increased the activity of cold units (67%), but had no effect on 63% of non-TS units. TNF also suppressed the activity in 59% of warm units but had no effect on 53% of non-TS units. The neuronal responses to IFNλ and IL-1β were preserved in a Ca^{2+} free/high Mg^{2+} solution, and therefore the effects are taken as being postsynaptic. The concurrent application of sodium salicylate (SALC) could not block the effects of IFNλ, but naloxone (NLX) antagonized the IFN effects. Conversely, the action of IL-1β and TNF on TS neurons were blocked by SALC, but not by NLX. The results suggest that IFNλ produces fever, at least partly, by the action on the opiate receptor mechanisms of preoptic TS neurons, and that IL-1β and TNF exert thermoregulatory effects by local production of prostaglandins.

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EFFECTS OF INTERFERONλ AND INTERLEUKIN-1 ON THE ACTIVITY OF VENTROMEDIAL HYPOTHALAMIC NEURONS.
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Single activity of ventromedial hypothalamic (VMH) neurons in tissue slices were investigated during perfusion of interferon-λ (IFNλ) and interleukin-1 (IL-1), which are known to be released from glial cells as well as from peripheral immunological cells. IFNλ, in concentration of less than 5000 units/ml which is comparable to that found in the brain after a viral infection, increased and decreased the activity of 64% and 13 % of 67 VMH neurons respectively. As we have observed in the preoptic neurons, the responses of VMH neurons to IFNλ were antagonized by concurrent application of naloxone, but not by that of sodium salicylate. The results are compatible with the previous finding showing the binding of IFNλ on the opiate receptors in the mouse brain (Blalock & Smith, 1981). Perfusion with recombinant IL-1β , in doses of 80-320 ng/ml, excited and depressed the activity of 38 % and 43 % of 42 VMH neurons, respectively. The actions of IL-1 on the VMH neurons were suppressed by sodium salicylate but not by naloxone, indicating the involvement of cyclooxygenation of arachidonate in IL-1's action. Since some VMH neurons which responded to IFNλ and/or IL-1 were found to respond to glucose, anorexia at the early phase of infections may be explained, at least partly, by the actions of these cytokines on the VMH neurons.

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EFFECT OF LOCAL INJURY TO CEREBRUM ON THE SWEAT OF RAT'S FOOTPADS.
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The object of this investigation was to search the cerebral region concerned in the spontaneous sweat of rat's footpads. After the cerebrum was injured locally by keeping an electrode, which had been inserted in it, at 60°C for 1 to 3 min, the sweat was examined for 3 weeks and the injured regions were examined with a microscope. The local injury of the frontal, parietal, occipital, or limbic cortex did not affect the sweat. The temporal cortex has not been examined. Two of 4 rats which were injured on both nucleus accumbens and preoptical area decreased the sweat. The injury of the septum or thalamus did not affect the sweat. The injury of both dorsomedial and ventromedial hypothalamic areas stoped sweating. But the injury of some regions containing the dorsomedial hypothalamic area alone did not affect the sweat. These results suggest that the ventromedial hypothalamic area is concerned in the sweat of rat's footpads. Since the anesthetized rats stop sweating, the cerebral cortex may be concerned in the sweat; but the local injury of the cerebral cortex did not affect the sweat.

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AFFERENT RESPONSES OF MUSCLE SPINDLE ENDINGS TO STRETCH AS FACILITATED OR SUPPRESSED BY STIMULATION OF NUCLEUS RAPHE MAGNUS OF RATS. SATO, H., 2nd Dept. Physiol., Nagoya City Univ., Sch. Med., Mizuho-ku, Nagoya 467

The previosu study demonstrated that γ motoneurons were weakly facilitated or strongly suppressed by electrical stimulation of the nucleus raphe magnus(NRM) of rats, suggesting that these effects were conveyed via the serotonergic descending pathways of the NRM and concerned in the control of cold shivering. To clarify which γ motoneuron is facilitated or suppressed by NRM stimulation, dynamic or static, and which muscle it is destined to, extensor or flexor, responses of muscle spindle primary (24) and secondary endings(4) to stretch of the muscle were analyzed in gastrocnemius et soleus and tibialis anterior of Urethane-anesthetized rats. It was found that 9(100%) of 9 primary endings in extensors were markedly but briefly facilitated, and 12(80%) of 15 primary endings in flexors were strongly suppressed for a long period(more than 30 min.) In these reciprocal effects of extensor-facilitation and flexor-suppression, the action of dynamic γ motoneuron was revealed to be dominant. It was suggested that cold shivering is controlled by the NRM via dynamic γ motor system.

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INHIBITORY EFFECT OF EXERCISE ON SHIVERING: DISTRIBUTION OF TERMINAL FIELDS OF FIBULAR MUSCLE AFFERENTS AND MOTONEURONS OF PECTORAL MUSCLE IN THE PIGEON SPINAL CORD. NOMOTO, S., Dept. Physiol., Tokyo Metropol. Inst. Gerontol., Itabashiku, Tokyo 173

The author previously showed that shivering in the pectoral muscle was inhibited by treadmill exercise or by electrical stimulation to a hindlimb muscle. Distribution of terminal fields of fibular muscle afferents and motoneurons of pectoral muscle in the spinal cord was studied by using WGA-HRP or choleratoxin-HRP in pigeons. Terminal labeling derived from M. fibularis longus was broadly distributed to segments between 18 and 28, and was concentrated in the ipsilateral dorsal horn (laminae I-IV and medial edge of lamina V). A few labeling was observed in the contralateral dorsal horn (medial edge of lamina V) in segments 21 and 22. Labeled motoneurons supplying M. pectoralis were found in ipsilateral ventral horn (ventrolateral portion of lamina IX) of segments between 12 and 14. Hence, the pectoral motor nucleus does not overlap the terminal field of fibular muscle afferents. So it is suggested that the above mentioned inhibitory effect was mediated by interneuron(s) located in segments between 18 and 28.

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THE EFFECT OF MONOAMINES ON THE RESPONSES OF DORSAL HORN NEURONES TO SOMATIC STIMULATION. NAGAI,M., WATANABE,M. AND IRIKI,M. Dept. Physiol., Med. Univ. Yamanashi, Yamanashi 409-38

It is well known that the activities of dorsal horn neurones(DHN) which respond to noxious stimulation of the skin are inhibited via descending serotonergic system. In the present experiments, we examined wheather microiontophoretic application of monoamines possess any effect on the responses of DHN to mechanical and thermal stimulation of the hindquaters of the urethane-anaesthetized rat. Serotonin(5-HT) inhibited the responses of DHN to warm stimulation of the scrotal skin in all neurones examined(4/4), and noradrenaline(NA) failed to exhibit any effect so far. On the other hand, NA inhibited the responses of DHN to tactile stimulation of the skin areas(2/5) or junctional flexion and extention of the hind leg(2/4). In some DHN , responses to mechanical stimulation were also inhibited by 5-HT, and enhanced by either NA or 5-HT. Thus, monoamines modulated the responses of about a half of DHN(13/25) to somatic stimulation. These results provide a possibility that signal transmission of nonnocuous somatic sensation is also modulated by monoamines and their descending processes.

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CHANGES IN HUMAN TYMPANIC MEMBRANE TEMPERATURE DURING FOREHEAD OR CERVICAL REGION COOLING.

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Tympanic membrane temperature (Tty), rectal temperature (Tre), skin temperature (Ts) on the forehead, buccal, hind part of ear or cervical region, subcutane temperature on the internal jugulal vein (Tc,part of int. jug. ve.) and sublingual temperature (Tsl) were simultaneously recorded.

The result of this study can be summarized as follows: 1) By cooling the forehead for 10-15 min, the fall in Tty was about 0.06-0.1 °C: and Ts, hind part of the ear was unchanged or increase slightly. 2) By cooling the forehead using an ice bag and beneath the head using an ice pillow for 15 min, shivering was observed within a few sec after cooling and Tty decrease about 0.1 C. Tc, part of the internal jugular vein increased 0.2-0.3 °C. The fall of Ts, forehead was about 0.4 °C and after cooling further it decreased about 0.6 °C. 3) By cooling the cervical region for 5-10 min, the fall in Tty and Ts, forehead was about 0.1 °C and 0.15-0.2 °C, respectively. 4) By cooling on the left side of the cervical region for 10 min, the fall of the left side Tty was 0.08 °C and after cooling further it was 0.03 °C. However, right Tty unchanged. The fall of the left side Ts, buccal and the right side Ts, buccal was 0.5 °C and 0.3 °C respectively.

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EFFECTS OF ANGIOTENSIN II AND ANGIOTENSIN III ON THE ACTIVITY OF PREOPTIC THERMOSENSITIVE NEURONS.

INOUE, T., HORI, T., NAKASHIMA, T. AND KIYOHARA, T. Dept. Physiol., Saga Medical School, Saga 840-01.

Brain angiotensin system, which plays a major role in osmoregulation and circulation control, has been suggested to be involved in thermoregulation. Microinjection of angiotensin II (AII) into the preoptic and anterior hypothalamus (PO/AH) produces a fall in body temperature, which is associated with a decrease in heat production and an increase in dry heat loss. In our previous study it was shown that microelectrophoretic application of AII excited and depressed the activity of the majority of warm-sensitive neurons and cold-sensitive neurons in the PO/AH respectively. This may explain the hypothermic effect of AII on the basis of AII's action on PO/AH thermosensitive (TS) neurons. In this study, we have investigated the effects of AII and AIII on the activity of PO/AH neurons in rat's tissue slices. AII and AIII (less than 1.7 μM) excited 14 of 22 and 15 of 16 warm-sensitive neurons, respectively, and their actions were reversibly blocked by saralasin. However, 24 of 29 and 17 of 24 non-TS neurons were not affected by AII and AIII respectively. Amastatin, an inhibitor of aminopeptidase A, blocked or depressed AII-dependent activity but no effect on AIII's action. Bestatin, an inhibitor of aminopeptidase B, enhanced the actions of AII and AIII. The results support the view that AIII may be the centrally active form of angiotensin.

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EFFECTS OF PROSTAGLANDIN E_2 ON THE ACTIVITY OF NEURONS IN THE PREOPTIC AREA AND THE AREA OF ORGANUM VASCULOSUM LAMINA TERMINALIS.

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It has not been determined how blood-borne endogenous pyrogens (EP) such as IL-1, interferons and TNF, eventually reach or otherwise signal their receptors in the brain. Recent studies have suggested a critical role of organum vasculosum lamina terminalis (OVLT) for fibrogenesis, as the entry site of EP or its active fragment or as the site of signal transduction of EP into second messengers like prostaglandins. To examine the latter possibility, we investigated the effects of prostaglandin E_2 (PGE_2), one of the most promising candidates of the final mediator of fever, on the activity of neurons in the OVLT and the preoptic anterior hypothalamus (PO/AH) of isolated tissue slices of rats. PGE_2, in doses between 2 and 18 pM, increased and decreased the activity of 30 % and 48 % of 40 OVLT neurons respectively. Similarly, 36 % and 34 % of 33 PO/AH neurons were excited and depressed by PGE_2. The thresholds for responses to PGE_2 were significantly lower in the OVLT neurons. In addition to the responses with rapid onset and rapid recovery, some OVLT neurons exhibited the responses of longer (more than 30 min) duration. Repeated applications of PGE_2 with short intervals resulted in tachyphylaxis. The neuronal responses were retained after synaptic blockade.

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THERMAL RESPONSIVENESS OF NEURONS IN THE VENTROMEDIAL NUCLEUS OF HYPOTHALAMUS.

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Single neuron activity was investigated for the thermal responsiveness in the isolated ventromedial nucleus of hypothalamus (VMH) in tissue slices in vitro. Out of 130 VMH neurons, 46 (35.4 %) neurons were warm-responsive and increased the discharge rate to a rise in tissue temperature and 4 (3.1 %) neurons were cold-responsive showing the opposite type of response to changes in temperature. During synaptic blockade in a Ca^{2+}-free/high-Mg^{2+} medium, warm-responsiveness was retained in 5 out of 10 units and cold-responsiveness was not lost in all the 2 units tested. In 2 of 10 units which had exhibited the warm-responsiveness in the control medium, positive temperature coefficients were converted into negative temperature coefficients in the Ca^{2+} deficient medium. Out of 17 units which had no thermoresponsiveness in the control medium, three units and one unit showed warm-responsiveness and cold-responsiveness, respectively, after Ca^{2+} removal from the medium. The results suggest that the thermoresponsiveness of VMH neurons is determined by the synaptic inputs from the other thermoresponsive neurons as well as by their own intrinsic thermosensitivity. The thermoresponsive neurons in the VMH may be involved in the control of non-shivering thermogenesis and thermally induced modifications of other homeostatic functions.

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EFFECTS OF INTRAVENTRICULAR PROTEIN SYNTHESIS INHIBITOR ON FEBRILE RESPONSE.

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It was investigated whether the temperature lowering process of febrile response is effected by endogenous antipyretics synthesized in the brain.

Fevers induced by intravenous injection of endogenous pyrogen (EP) or intraventricular prostaglandin E_2 (PGE_2) were significantly prolonged when protein synthesis inhibitor, anisomycin, was administrated intraventricularlly 30 min before or 1 hr after injection of EP or PGE_2.

Although it remains to be elucidated whether protein synthesis is involved in the production of antipyretic substances or the production of enzynes which break down or remove the pyretic substances, the present results clearly showed the involvement of protein synthesis in antipyretic mechanisms in the CNS.

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EFFECTS OF PROGESTERONE IN OVARIECTOMIZED RATS WITH AND WITHOUT ESTRADIOL TREATMENT.

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Single neuronal activities in the preoptic slice preparation from ovariectomized female rats were recorded and examined for response to progesterone (30ng/ml). Fourteen females had recieved estradiol treatment (20 μg/day for 3 days), while other 15 had been untreated. In the untreated rats, 12 (50%) of 24 warm sensitive neurons were inhibited, 2 (8%) were excited by progesterone; 5 (36%) of 14 thermally insensitive neurons were inhibited, 1 (7%) was excited by progesterone. While in the treated rats, 2 (10%) of 19 warm sensitive neurons were inhibited, 7 (37%) were excited by progesterone; 5 (25%) of 20 thermally insensitive neurons were inhibited, 1 (5%) was excited by progesterone. Among the preoptic warm sensitive neurons inhibited or excited by progesterone, significant differences could be seen between treated and untreated rats. These findings suggest that the effects of progesterone on preoptic warm sensitive neurons should be influenced by estradiol.

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EFFECT OF INDOMETHACIN ON BODY TEMPERATURE DURING EXERCISE IN RATS.

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There is a hypothesis that exercise-induced hyperthermia is a result of the elevation in thermoregulatory set point, mediated by prostaglandin as is the case in fever. Present study examined effect of the administration of prostaglandin synthesis inhibitor (indomethacin) on body temperature during treadmill exercise in rats. At 60 min after subcutaneous injection of sesame oil (control) or of indomethacin (15 mg/kg), rats started treadmill running. Exercise was performed for 30 min at the intensity of $\dot{V}o2$ Max 40～65 % (N=11) or 75～85 % (N=7). Rectal temperatures at the beginning of tail vasodilation during exercise and at the end of exercise were not significantly different between two groups in both exercise intensities. This result suggests that exercise-induced hyperthermia is not mediated by prostaglandin.

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EFFECTS OF 10%CO_2 INHALATION ON THERMOSENSITIVITIES OF PREOPTIC NEURONS IN ARTIFICIALLY VENTILATED RATS.

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In urethanized, paralyzed and artificially ventilated (AV) rats, the effects of 10%CO_2 inhalation on preoptic (PO) thermosensitive neurons were examined by regression of neuronal activity on PO temperature. The results were compared to our previous results in spontaneously ventilated (SV) rats in order to investigate whether the responses of PO neurons to CO_2 seen in SV rats were produced by CO_2-induced changes in respiration and circulation. Artificial respiratory frequency was 97±1 cycles/min. The decreases in heart rate during CO_2 inhalation were greatly suppressed in AV rats. In 9 of the 14 warm-sensitive neurons (64.3%), the slope of the regression line decreased significantly during CO_2 inhalation in AV rats ($P<0.05$). This modification of PO neuron thermosensitivity during CO_2 inhalation occurred more frequently in AV rats than in SV rats (7/23, 30%). In 1 cold-sensitive neuron, CO_2 inhalation did not significantly alter the slope of the regression line, but did significantly shift the firing rates upward ($P<0.01$).

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A ZEITGEBER OF THE CIRCADIAN PACEMAKER IN RAT PUPS: TEMPERATURE CYCLES. HONMA, S., HONMA, K. AND HIROSHIGE, T. Dept. Physiol., Hokkaido Univ. Sch. Med. Sapporo, 060

We reported that the circadian pacemaker of rat pups was reset by periodic food restriction during the early postnatal period. Because pups depend on mothers for the nutrition as well as the protection from heat loss, the entrainment to periodic food restriction is possibly due to the maternal rhythms driven by the food-associated oscillation. Therefore, entrainability of the periodic separation from mother and the periodic change in ambient temperature to pup's circadian pacemaker was studied.

Pups were blinded on the day of birth to exclude the influence of 24 h LD cycle. They were separated from mother for 4 or 2 h daily and 3 different temperature cycles (10, 22 or 30°C) were imposed until weaning. Spontaneous locomotor rhythm of pups was measured after weaning by an Animex, and the period and phase on the day of weaning were calculated.

Pup's circadian oscillation was entrained by daily 4 h separation. Out of 16 pups in each group, 15 pups entrained to the daily separation when exposed to 10°C, while 11 and 12 did when exposed to 22 and 30°C, respectively. The daily 2 h separation had no effect with any temperature cycles. It is concluded that the periodic separation from mother is a potent zeitgeber for the pup's circadian pacemaker, and the cold expo-sure during the separation significantly increased the entrainability.

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CIRCADIAN RHYTHMS OF WALL TEMPERATURE AND BER INTERVAL IN CANINE STOMACH AND THEIR INTERRELATION. FUJITANI, Y., HOSOGAI, M. AND OIKAWA, T. Dept. Physiol., Tottori Univ. Sch. Med., 86 Nishi-machi, Yonago 683

Stomach wall temperatures were measured through a thermister under conscious state of a dog and their values were printed out in every min with a personal computer. Also, the basic electric rhythms (BERs) of the stomach were measured. When standard diet was given from 12:00 to 13:00 once a day, that temperature falls early in the morning, shows a rise after feeding, remains in a lower level in the daytime and rises from the evening. By intravenous hyperalimentation (IVH), however, the temperature showed no particular circadian rhythm. BER intervals were irregular but in relatively constant level before feeding and were of a lengthening after feeding followed by sustained shortening, while no clear trend was found by IVH. In both power spectra, only slower components (170 min or so in period) were shown before feeding in the temperature changes and after feeding in the BER intervals. Crosscorrelograms between BER intervals and stomach temperatures revealed that the changes of the temperature appeared slowly by several min and inversly in directions compared with those of BER intervals.

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EFFECTS OF SHIFT-WORK EXPERIENCE ON BODY TEMPERATURE RHYTHM OF NURSES. OKUDAIRA,N., KANEMOTO,H.* AND HIROIKE,A.* Dept. of Physiology, Toho University, School of Medicine and School of Letters, Waseda University, Ohta-ku, Tokyo 143

To investigate the effects of shift-work experience on the body temperature and sleep-wake rhythms, 26 healthy nurses ranging in age from 21 to 28 were recruited for the 2-week study, in which they continued their typical irregular working schedules. They orally self-measured and recorded their body temperature every 4 waking hours. In addition, a daily sleep log was kept, in which the subjects indicated all the times they had slept over each 24-hour period, including naps. A least-squares analysis was used to fit a 24-hour cosine curve to the body temperature and sleep log data. The acrophase of the body temperature in 9 nurses, who had between 3 and 4 years' experience (mean ages 24.8), showed a maximum delay and its amplitude was significantly the least. On the other hand, the acrophase and amplitude in 6 nurses, who had up to 5 years' experience (26.5 years), tended to return to those of normal, healthy female nursing students. It is suggested that the nurses' body temperature rhythms might be affected in accordance with the length of their experience of irregular shift-work schedules, and that they adapt themselves physiologically and psychologically after around 3 to 4 years of experience.

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A HUMAN PHASE RESPONSE CURVE FOR LIGHT: T EXPERIMENTS. HONMA, K. AND HONMA, S., Department of Physiology, Hokkaido University School of Medicine, Sapporo 060.

A phase response curve (PRC) of the human circadian rhythm was obtained for light. 10 subjects spent 3 weeks alone in an isolation unit without knowledge of time, and their rest-activity cycles and rectal temperature rhythms were measured. During free-running, a light pulse of 5,000 lx was applied twice for either 3 or 6 hr, and a produced phase shift of the circadian rhythms was measured. The mean free-running period was 25.2 hr with SD of 0.4 hr. When the light pulse was applied at the early subjective day, the circadian rhythm phase-advanced. In contrast, there was no phase-shift and a slight phase-delay shift when the light pulse was given at the middle subjective day and the late subjective day, respectively. From the PRC shape, it is surmized that the human circadian rhythm is reset by light in the morning. The PRC has a very small phase-delay portion, which predicts that the circadian rhythm is difficult to entrain to a light-dark cycle with a period longer than 25.2 hr. In order to examine this prediction, T experiments with T equal to 26 hr were performed in 2 subjects. The light was given for 3 hr at 26 hr intervals. The circadian rhythm of one subject seemed to entrain to the light cycle, while the rhythm of the other subject failed to do it. The result is well explained by the PRC with a shallow phase-delay portion.

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ENTRAINMENT TO SKELETON PHOTOPERIODS IN THE CIRCADIAN LOCOMOTOR RHYTHM OF THE TOAD. OGASAWARA, T. AND TASAKI, K. Dept. Physiol., Tohoku Univ. Sch. Med., Sendai 980.

Entrainment to skeleton photoperiods of the circadian locomotor rhythm in the toad, Bufo bufo japonicus, was examined by using a running wheel method. Toads were entrained to 24 hr skeleton photoperiods, LD 1:12:1:10, LD 1:14:1:8 and LD 1:16:1:6 (L:200 lux white light, D:0.2 lux white light) and were mainly active in each longer subjective night. To 24 hr red light skeleton photoperiod was obtained a similar entrained pattern of activity.

These results suggest that two 1 hr light pulses in 24 hr photoperiod determine the pase of the circadian rhythm in the toad.

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PATTERN OF CHANGES IN LIGHT ENVIRONMENT DURING POLAR ROUTE FLIGHT. SASAKI, T., YAMASAKI, M. Dept. of Bioregulation, Kumamoto Univ. Medical School, Kumamoto 862

An eastbound flight results in a shorter day and an advance in the phase of Zeitgeber, and the biological rhythm is entrained generally by advancing the phase. In the circumpolar region, however, the periodicity of light-dark cycle, which works as the most potent Zeitgeber among others, changes in a complex manner according to the season. Therefore, the light environment to which polar route travelers are actually exposed shows a wide variety of LD change depending on the season and the time of day the travelers go through. So, by an eastbound flight in the Arctic, entrainment will not necessarily be accomplished by phase advance.

To prove this by simulation, computer programs were produced to locate the sun on the celestial sphere at any moment on any day in the current century, and then to compute its height and direction at any point on the earth. Given the flight time table and route, changing pattern of the light environment along the route is calculated hour by hour which is to be used to control the simulated environment.

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EFFECT OF VOLATILE SUBSTANCES FROM THE FOREST ON SLEEP AND CIRCADIAN RHYTHM. YAMAOKA, S., Dept. Physiol., Saitama Medical School, Moroyama-chou, Saitama 350-04

In spite of the increasing interest in psycological and physical effects of the forest, it is very difficult to find the physiological and fundamental study concerning the forest-human relationship. This study is one step to understand a part of this relationship. We examined the effect of some volatile substances from trees (phytoncides) on circadian sleep rhythm and wheel-running rhythm in Sprague-Dawley (SD) eye-enucleated rats. EEGs from frontal cortex, hippocampus and pontine reticular formation, and dorsal neck EMG used to monitor slow wave sleep(SWS), paradoxical sleep(PS) and alertness. The count of wheel running activity was recorded as spikes on EEG apparatus simultaneously with other polygraphic recordings. All of cedar leaves, α-pinene and cineol exposure resulted the increase of the amount of paradoxical sleep and the amplitude of circadian SWS and PS rhythm (in least square analyses), but could not observe any changes in period and phase of these circadian rhythm. In the additional study of male sexual behavior, α-pinene exposure significantly shortened the intromission latency and the post-ejaculation interval. From these results, it is suggested that the phytoncides may affect the modulating system of circadian rhythm or paradoxical sleep through the olfactory-limbic-hypothalamic pathway. Further investigations will be performed to complete this study.

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STRAIN DIFFERENCES IN EFFECTS OF RESTRICTED FEEDING ON CIRCADIAN ACTIVITY RHYTHMS BETWEEN TWO INBRED STRAINS OF MICE. ABE, H., KIDA, M., MANO, T. AND TSUJI, K.* Dept.VI, Res. Inst. Environ. Med., *Dept. Psychol., Nagoya Univ. 464-01

It has been reported that CS strain of mice, unlikely to the other strains, showed the unstable free-running period during continuous darkness condition. In order to search for the mechanisms of circadian rhythms of CS strain, the free-running rhythms of wheel-running activity of CS strain was compared with those of C57BL/6J strain under the restricted feeding (RF) condition in which a food access period was restricted for 2 hours at a fixed time of day. For CS strain, circadian activity rhythms free-ran during ad lib feeding before RF session. However, the rhythms were ceased to free-run by RF and phase relationships were established between the rhythms and RF. After elimination of RF, the rhythms free-ran again, but the initial phases of the rhythms did not correspond to the phases obtained by extrapolation from the rhythms observed before RF session. On the other hand, C57BL/6J strain did not show any change in the period of free-running rhythms during RF session, although anticipatory activity prior to food access period was observed. For all of control animals of both strains, their free-running rhythms were not affected by the periodic disturbances to be produced by the operations of RF. These results suggest that circadian rhythms of CS strain might be entrained to RF, and this strain might have a different mechanism of circadian rhythms from C57BL/6J strain.

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BODY TEMPERATURE RHYTHM: DEVELOPMENT OF CIRCADIAN RHYTHM OF BODY TEMPERATURE RHYTHM IN BLIND RATS. ISOBE, Y., Dept. Physiol., Nagoya City Univ. Med. Sch., Nagoya, 467

Development of body temperature rhythm (BT) was examined to clarify the ontogeny of BT rhythm. The rectal temperature was measured intermittently at 2 hr intervals throughout 26 hr in the blind and intact rats. BT rhythms of mother and pups were obtained during the nursing period and after the day of wean under the light-dark cycle(LD) and constant dark(DD). The individual rat's circadian BT rhythm was compared with their grouped data by the cosinor analysis. The mesor temperature became stable after the 5th week from birth. The earlier development of BT rhythm was observed in blind pups under the DD than in intact pups during the LD. The circadian period in blind rats determined by the shift of acrophase was shorter under the LD than under the DD. Overt circadian rhythm in both actogram and BT was not detected during the nursing period in the mother. Results suggest that pup's BT rhythm is entained by the LD cycle, and it is also modulated by some factors other than BT and activity rhythms of nursing mother.

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THE ROLE OF SEROTONIN ON THE STABILITY OF NEURONAL ACTIVITIES

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We previously reported that spontaneous discharge from many parts of the brain, such as the mesencephalic reticular formation, sensory cortex I, hippocampal pyramidal cells and hippocampal theta cells and ventrobasal complex of thalamus fluctuate during paradoxical sleep. In this study, we investigate the spontaneous activities from hypothalamus lateralis and basal forbrain area of head restrained cats and clarified that slow fluctuations during paradoxical sleep also exists in these areas. And from the examination of serotonin depletion with p-chlorophenylalanin administration, we concluded that the slow fluctuations of neuronal activities observed during paradoxical sleep are caused by the release from the serotonergic regulation. The serotonergic system has the role of stabilizing neuronal activities in central nervous system.

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EFFECTS OF DIFFERENT FORMS OF GARMENT ON CIRCADIAN RHYTHM OF HUMAN TEMPERATURE.

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This study was carried out to examine the effects of different skin temperatures in the extremities by wearing two different forms of garment on circadian rhythm of core temperature. Therefore, we tried to compare the rectal temperature rhythm between two different forms of garment: one covering the whole body area except for the head and the periphery (l-s), and the other covering the central body area alone (h-s). Six healthy females were served as subjects. The measurements were continuously made from 11:00 a.m. to 9:00 a.m. next day at an ambient temperature of 27.5 ± 0.5 °C and a relative humidity of 40 ± 10 %. Major results disclosed that the amplitude of rectal temperature rhythm was significantly larger in h-s than in l-s ($p < 0.01$), and both the acrophase and the first minimum of rectal temperature rhythm were earlier in h-s than in l-s.

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SWIMMING TRAINING INCREASES A TOLERANCE TO COLD. OHNO, H., GASA, S.*, YAHATA, T. AND KUROSHIMA, A. Dept. Physiol., Asahikawa Med. Coll., Asahikawa 078 and *Biochem. Lab., Cancer Inst., Hokkaido Univ. Sch. Med., Sapporo 060

Fifty male Wistar rats were divided randomly into five groups. Group S25, S30 and S35 rats were exercised by swimming up to 3 h/day, five times/week for 10 weeks in watar at 25, 30 and 35 ℃, respectively. Group CA rats were acclimated to cold by exposure to 5 ℃ for four weeks and the other group served as controls. After 2 h of cold air exposure at -5 ℃, the Tc dropped significantly in the untrained controls by -2.1 ℃, but not in the trained and CA rats. Calorigenic response to noradrenaline was much greater in the trained and CA rats than in the controls, indicating improvement in nonshivering thermogenesis; however, there was no definite difference in the changes of $\dot{V}o_2$ between S25 and S30 rats. The mass and protein content of the interscapular brown adipose tissue (ISBAT) in all swimmers as well as CA rats showed significant elevations after the experiment. In addition, the changes in the lysosomal enzyme values in the three tissues (ISBAT, liver and kidney) of swimmers appeared to be similar to those found in CA rats. During swimming training more enzyme molecules are synthetized in tissues, especially in ISBAT, so as to follow the enhanced demands of energy metabolism.

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INVESTIGATION OF LIPID METABOLISM IN REPETITIOUS SWIMMINGS OF RATS.

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To clarify characteristics of lipid mobilization in swimming, the differences between repetitious swimmings and immersions of rats at 35° C water bath were quantitatively and qualitatively investigated by gas-chromatography. The immersions enhanced lipilysis and caused accumulation of FFA in adipose tissue and serum, but the swimmings cancelled the accumulation and reversely enhanced the release. However, differences in fatty acid compositions of adipose tissue triglyceride (TG) and FFA and serum FFA were maintained during both experimental conditions. Liver TG in the swimmings decreased with decrease of the linoleic acid composition and the serum TG reversely increased with increase of the composition. Total phospholipids (TPL) of serum, liver and heart muscle decreased with number of the immersions, but the swimmings enhanced TPL of heart muscle. Cardiolipin (CL) of heart muscle and liver decreased with number of the both conditions, but that of skeletal muscle.The linoleic acid compositions of heart and skeletal muscle CLs increased significantly by the both conditions. Cholesterolester (Ch-E) in serum and liver by the immersions decreased, but serum Ch-E increased with remarkable increase of arachidonic acid composition by the swimmings.From these results, differences in enhanced lipid mobilization between the swimmings and the immersions were clarified.

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SEASONAL CHANGES IN AORTIC LIPIDS IN NON-EXERCISED AND EXERCISED RATS.

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Female Wistar rats, 4 weeks of age, were grouped into 4 (Ns, Nw, Es, Ew) of 14 to 20 rats each and were individually caged at 23±1 °C. The Ns and Nw were non-exercised. The Es and Ew were exercised on running wheel cages. The groups kept in winter were Nw and Ew. The other groups in summer were Ns and Ws. The entire experiment in each season ran for 12 weeks.

In the non-exercised rats (Ns, Nw), there were seasonal changes in all the measured values of aortic lipids except for those of aortic free cholesterol. The levels of total cholesterol, cholesteryl ester and triglyceride in the aortae of the Nw were greater than those estimated in Ns. The aortic phospholipid and free fatty acid contents in Nw diminished when compared with those found in Ns. Seasonal changes in the aortic lipids in the exercised animals (Es, Ew) were simillar to those observed in the non-exercised animals. The seasonal changes in the estimations in all the groups were expressed in terms of the respective ratios of the weight gain to the total caloric intake.

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Control mechanism of adenylate cyclase activity in adipocyte membranes from exercise-trained male rats.
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The control mechanism of adenylate cyclase activity in adipocyte membranes from exercise-trained male rats was investigated in detail. The trained rats ran on a rodent treadmill 5 days per a week for 8-9 weeks. Adrenaline-stimulated lipolysis and (-)-isoproterenol-stimulated adenylate cyclase activities were significantly greater in adipocytes and adipocyte membranes from exercise-trained male rats than in sedentary male rats, respectively. GTP-mediated inhibitions of forskolin (10 μM)-stimulated cyclase activities were observed in sedentary membranes, whereas the inhibitory actions of GTP were significantly reduced in trained rat. Treatment of membranes with islet-activating protein (IAP), a pertusis toxin, completely abolished the differences in GTP-inhibition of forskolin-stimulated cyclase activities between the two groups. Chorela toxin- or IAP-catalyzed ADP-ribosylation was examined next. The amounts of the inhibitory regulatory protein (41kDa/40kDa polypeptides) were about 40% less in membranes from trained rats than in sedentary membranes. The amounts of the stimulatory regulatory protein (a 45kDa polypeptide) was equivalent.

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THE EFFECT OF EXERCISE UPON THE GASTROINTESTINAL MOTILITY IN CONSCIOUS DOGS.
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The purpose of this study was to observe the changes in motility of the stomach and small intestine during exercise in conscious dogs. The chronic experimental preparations were done for the records of motility by implanting strain gauge transducer sealed with silicon rubber on the stomach, duodenum, jejunum and ileum under the condition of anesthesia (30mg/kg sodium pentobarbital). Three dogs were exercised on the treadmill at a speed of 3 to 5 km/hour for 1 to 3 min. Cardiovascular response in accordance with the exercise intensity was monitored by the heart rate (beats/min) converted from ECG. The results were that the amplitude of motility in the stomach decreased during exercise, and other tracts showed no obvious changes. These data indicate that the stomach may be dominantly influenced by the exercise-induced sympathetic nerve activity.

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OXIDATION OF MUSCLE GLYCOGEN AND LACTATE IN MICE AFTER STRENUOUS EXERCISE
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The purpose of this study was to investigate how much muscle lactate was oxidized and reconverted to muscle glycogen in mice after strenuous exercise to exhausion. Male ddY mice mice, 5 weeks of age, ran at a speed of 25 $m.min^{-1}$ for 20 min and 40 $m.min^{-1}$ for 5 min. Immediately after the exercise, 0.18 $\mu Ci.g^{-1}$ of [U-^{14}C]glucose was injected intraperitoneally. After injection of ^{14}C- glucose, significant ^{14}C was incorporated into muscle glycogen. Mice were divided into three groups. In RE (n=7), mice were sacrificed 24 hr after injection of ^{14}C-glucose. In EX (n=6), mice ran to exhaustion 24 hr after injection of ^{14}C-glucose at a speed of 57±1 $m.min^{-1}$, for 124 ±10 sec (Mean±SE), and were sacrificed after the strenuous exercise. In RC (n=7), mice ran to exhaustion 24 hr after injection of ^{14}C-glucose and were sacrificed after 60 min of strenuous exercise. Evolution of $^{14}CO_2$ expiration during 60 min of recovery after the strenuous exercise in RC was similar to that after injection of ^{14}C-lactate into aorta of rats after strenuous exercise to exhaustion. Mean ^{14}C-glycogen content in leg muscles in RC tended to be higher than that in EX, but significantly lower than that in RE. These results show that a major portion of glycogen which was converted to lactate during strenuous exercise was oxidized to CO_2.

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THE EFFECT OF VOLUNTARY EXERCISE AND THE INFLUENCE OF SALINE LOADING ON SYSTOLIC BLOOD PRESSURE AND VASCULAR LESIONS IN STROKE-PRONE SHR. TOMIDA,K.[1], ABE,T.[2], ASAMI,T.[2], FUKUDA,Y.[3]*, HIROTA,K.[4] 1)Wakayama University, Sakaedani Wakayama 640, 2) College of Arts and Science, University of Tokyo, Meguro-ku, Tokyo 153, 3)School of Medicine, Juntendo University, Bunkyo-ku, Tokyo 113, 4)Department of Exercise Physiology, Nippon College of Physical Education, Setagaya-ku, Tokyo 158

In this study were investigated the effect of voluntary exercise on resting systolic blood pressure and vascular lesions of stroke-prone spontaneously hypertensive rats (stroke-prone SHR) with 1% saline loading. Forty male stroke-prone SHR aged 7 weeks were assigned to one of 4 experimental groups, each was consisted 10 animals; sedentary control(S), sedentary with 1% saline loading(SS), exercised control (E), and exercised with 1% saline loading(ES). Animals were sacrificed at the 5th week. In the prehypertensive phase, resting caudal arterial systolic blood pressure was significantly lower in the E group than in the S group. However, after being loaded with 1% saline, the ES group showed higher resting systolic blood pressure than those of the SS group. In addition, the ES group revealed severer renal, myocardial, and cerebrovascular lesions than those of the rest of the groups.

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INDIRECT AMBULATORY MEASUREMENT OF BEAT-TO-BEAT ARTERIAL PRESSURE IN HUMAN FINGERS DURING EXERCISES. KAWARADA, A.*, SHIMAZU, H.*, ITO, H.* AND YAMAKOSHI, K.** *Dept. of Physiol. Kyorin Univ. School of Med., Tokyo 181, **Res. Inst. Appl. Electr., Hokkaido Univ., Sapporo 060

We designed volume compensation technique to indirectly determine beat-to-beat arterial pressure and its waveforms in human fingers, previously. It comprises a compression fluid-cuff with its pressure controller and a photo-plethysmograph to detect arterial volume change. Applied cuff pressure onto the finger is controlled by a servosystem connected to the cuff around the basal phalanx of a finger so as to keep the arterial volume constant at a reference level which corresponds to the arterial volume in an unloaded state. In this study, we have developed an ambulatory system to determine arterial pressure using this technique. Pneumatic pressure control system is adopted: The frequency response is flat up to 60 Hz. The weight of the cuff and actuator is 180 g, and the total weight including a recorder and power supply 2 Kg. Arterial pressure in ambulatory condition was successfully recorded during various exercises and stress tests, using this system.

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DIRECT MEASUREMENTS OF MUSCLE BLOOD FLOW IN HUMAN LOWER EXTREMITIES BY HYDROGEN GAS CLEARANCE METHOD. MAEDA,J., NISHIMURA,C.*, LEE,E.K.* AND TAKEMIYA,T. Div. of Physiol., Inst. of Health and Sports Sci., Univ. of Tsukuba. Tsukuba, Ibaraki 305.

In order to confirm the characteristics of muscle-native blood flow (ml/100g/min) in skeletal muscle, a wire type of hydrogen gas sensor(80μm in diameter) was applied for three types of muscles in human lower extremities. The resting blood flow of M.tibialis anterior, M.gastrocnemius and M.soleus (mean±S.E.,n) were 5.0±2.8(20), 3.8±1.6(27) and 4.9±2.5(22), respectively. There were no significant differences between them. Post-exercise hyperemia in the same muscles after plantar flexions exercise of 25%MVC(maximum voluntary contraction) were 4.5±0.8(3), 11.2±3.6(5) and 8.9±1.4(4), respectively. During the exercise, the heart rate was within a rise of 5-10 beats/min. Qualitative analysis of a clearance curve at rest showed that all were mono-exponential in M.tibialis anterior, and each 9% and 33% became bi-exponential in M.gastrocnemius and M.soleus. Although these results are essentially similar to those of literatures, but further comparative studies of resting blood flow in horizontal lying and up-right standing postures are necessary.

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EFFECT OF BREATH HOLDING ON HEART RATE DURING SUPRAMAXIMAL EXERCISE. AHN, B., NISHIBAYASHI, Y., *OKITA, S., MASUDA, A., TAKAISHI, S. AND HONDA, Y., Dept. Physiol. and *Chest Med., Chiba Univ., Sch. Med., Chiba 280

Breath holding(BH) is a maneuver often conducted during short-lasting streneous exercise, such as 100 m dash in sprinters. We investigated the effect of BH on heart rate(HR) during supramaximal exercise(415W) using a bicycle ergometer. HR and arterial oxygen saturation(Sao_2) were continuously observed during the 20 sec BH exercise and end-tidal Po_2 and Pco_2 were recorded before the exercise and at the breaking point. First, the subjects performed the BH test following room air breathing(Room air run). Then they conducted the BH after breathing 100 % O_2 for one min(O_2 run). Finally, arterial blood pressure(BPa) was continuously measured in both room air and O_2 runs. HR was progressively decreased from the latter phase of exercise in the room air run. This response, however, disappeared in the O_2 run. BPa tended to increase during the latter half period of the BH in the room air run. This response was also attenuated in the O_2 run.

Our study suggests that marked bradycardia demonstrated in BH during supramaximal exercise is ascribed mainly to activation of the peripheral arterial chemoreceptors due to oxygen desaturation and partially to elevated blood pressure as well as increased Pco_2.

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EFFECTS OF FOOD RESTRICTION AND PHYSICAL EXERCISE ON BASAL METABOLISM OF RATS. HARADA, K. AND *YONEMOTO, K. Lab. of Physical Edu., The Jikeikai School of Med., Chofu-shi, Tokyo 182 and *Lab. Sports Med., Jikei School of Med., Chofu-shi, Tokyo 182

Effects of food restriction and moderate physical training, in delaying the aging process, on basal metabolism of rats were studied. The Wistar-strain rats were bred at the room temperature of 22.0±2°C. They were separated three groups at 4 weeks of birth (free eating sedentary, food-restricted control and exercise). The first physical training was carried out by motor driven treadmill for 12 weeks at a speed of 25m/min for less than 15 min once daily and 6 times in a week. Trained rats were fed ad libitum as the sedentary control,thereafter their body weight at that time was kept constantly. The body weight of restricted control rats was adjusted the number of weight of exercise rats. Continuously, the second trining was carried out at the same load of two times per week. Basal metabolic rate of them were measured at 5-6 months after birth.Amounts of food intake in three groups did not change per body weight, however,ones per body surface area changed. Basal metabolic rate was highest in the restricted exercise group, significant change compared with sedentary.

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RENAL RESPONSES TO EXHAUSTIVE EXERCISE--MECHANISMS OF EXERCISE-INDUCED PROTEINURIA--. SUZUKI, M., MATSUBARA, S., AND IKAWA, S., Dept. Lab. Med., Jikei Univ., Sch. Med., Nishi-shimbashi Minatoku, Tokyo 105

The present study was done to investigate the mechanisms of post-exercise proteinuria for 170 healthy volunteers. Total protein(uTP), albumin(uAlb), β_2-microglobulin(β_2-M), lactic acid(uLA), pyruvic acid(PA), catecholamines(CA), Na, Cl, and pi concentration were analyzed in the urine collected following the exhaustive exercise. Furthermore, plasma angiotensin II(pAngII), blood LA and serum electrolytes were also measured. The maximal rate of protein excretion was observed 30 min after the exercise. The TP in excess of 200 mg/dl was showed in the 18 out of 170 volunteers(10.6%). Changes of uAlb were similar to those of uβ_2-M following the exercise($r=0.749$, $p<0.001$). The exhaustive exercise-induced proteinuria seemed to be of mixed glomerular-tubular type. A significant correlation was found between uAlb and uLA($r=0.824$) and also between uβ_2-M and uLA ($r=0.721$). In addition, uLA was found to have a significant negative correlation with urinary Cl concentration. The pAngII and uCA excretion increased in all of the cases after the exercise. However the increases in these hormones did not seem to be related to the urinary excretion of proteins. The results suggest that both the exercise-induced polyanions(e.g. LA and PA) and the reduction of renal blood flow might induce the change of glomerular charge, and enchance the transglomerular passage of macromolecules, and inhibit the reabsorption of macro- and micromolecular proteins in the proximal tubules.

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ANALYSIS OF LACTATE KINETICS DURING EXERCISE BY COMPARTMENT MODEL.
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To reveal the role of anaerobic energy supply during ramp exercise, we examined the lactate kinetics (LA-kinetics) using the compartment model. The original mathematical solution of the compartment model for LA-kinetics after exercsie was given by Zouloumian and Freund (1981). The model is based on the law of mass conservation in a volume. The main assumptions of the model are: 1) The total LA distribution space is composed of two compartments; working muscle and the remaining LA space (= blood), and 2) the rates of LA release (uptake) and utilization in each compartment are proportional to the LA contents. According to this model, we formulated the transfer function from energy supply of glycolysis (real LA production) to LA contents in blood (space). The coefficient of this transfer function was estimated using the time-serial data of LA after exercise. The real LA production in working muscle was estimated by the deconvolution of the time-serial data of LA in blood during ramp exercise and the transfer function (= impulse response). As the result, by the estimated patterns of real LA production, it was not clear whether or not the threshold phenomenon of glycolysis existed.

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NOMOGRAM FOR CALCULATION OF ENERGY EXPENDITURE OF TREADMILL WALKING.
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Equations were derived that predict the energy cost of treadmill walking of adult males and females in terms of subject's weight, walking speed and heart rate. The prediction from the speed was the most satisfactory with a mean deviation of -0.58%(male) and -1.26%(female) from values actually observed. The equations were E/B=0.0006732V**2-0.0549V+3.42 for male and E/B=0.0006342V**2-0.0489V+2.99 for female where E, B and V stand for energy cost(kcal/hr), body weight(kg) and speed (m/min), respectively. Equations in terms of heart rate were as follows; E/B=6.39W/R-4.15 or 7.08R1/R-4.78 for male and E/B=5.13W/R-3.49 or 5.26R1/R-3.25 for female where R, W and R1 are heart rates expressed in beats/min before walk, during walk and for the first 30sec after walk, respectively. The variability of the values obtained from the equations was within 5% of those actually observed. Using the heart rate after walk, the energy cost can be easily predicted without measuring the speed and the heart rate during walk, although the accuracy is a little inferior to others. Based on these equations, nomograms were developed.

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CHANGES OF THE SOMATIC-AUTONOMIC NERVOUS SYSTEM COUPLING IN THE MOTOR LEARNING.
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The purpose of this study is to examine how the somatic-autonomic coupling works in the motor learning using the coodinating tester.

The process of tracking diagrams by the tester was regarded as a motor learning from learning curves and the electromyogram(EMG) recorded from the acrominal part of m. deltoideus. The sustaining bursts of EMG during exercise were observed in the first trial. The active period of EMG during exercise was differentiated from the silent period in the 42nd trial. The R-R interval of the electrocardiogram during rest fluctuated from 800 to 900 ms. and during exercise approximately shortened to 500-600 ms. As learning progressed, the cardiac acceleration was enhanced in the anticipatory and the initial phase of the exercise. The respiratory rates during rest before exercise were 15 to 21 bpm and after exercise fluctuated from 12 to 36 bpm. Although the respiratory rates during exercise except for the first trial were 20-30 bpm, the rates in the first trial reached 30-36 bpm, which was regarded as the oriental reflex.

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MUSCCULAR MOTOR TIME(EMD) PATTERNS OF THE TRICEPS SURAE DURING VARIOUS EXERCISES AND POSTURE. NAGATA,A., Dept. Sport Sci.,Sch. Human Sci.,Waseda Univ., 2-Migashima, Tokorozawa-City 359

This study was conducted to assess the changes of electro-mechanical delay(muscular motor time, EMD) upon the evoked electromyogram of each medial side of the triceps surae muscle groups. EMD have reported to be 45-60msec delay time between muscular contraction and rising torque waves at ancient papers. Now, seven healthy subjects are practiced in the study. Bipolar surface electrodes detected electromyographic signals(digitized at 1,500Hz) by the electric stimulus, which were applied to evoked with the method of the current stimulus(4-25mA). Evoked electromyographic signals were H wave with lower stimulus(4-6mA), M1 wave with maximal intensity(18-20mA), and M2 wave with supramaximal stimulus(23-25mA). And voluntary contractions with two levels of torque were practiced upon auditory signals. The toeque was measured with the piezo-type torque sensor upon the plantar flexion of the ankle joint.

Analysis were consisted of calculating EMD of each experiment — this EMD were examined at time between the first EMG signals and the first rising movement of the torque signal — activiation lag time, and torque amplitude and voluntary orders. Correlations between EMD and the plantar contraction were found to be high, non-consisted with previous researches, and the true EMD value was appeared to be 15-7msec shortly, significantly.

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THE INFLUENCES OF VIBRATORY STIMURATION ON THE ERROR MAGNITUDE IN POSITION SENSE OF THE UPPER EXTREMITY. MIYAMOTO, S., SAWADA, Y. AND *AOKI, M. School of Allied Health Professions and *Dept. Physiol., Sapporo Medical College, S3, W17, Chuo-ku, Sapporo 060 Japan.

To investigate whether the error magnitude and the direction in finger positioning task change or not by sensory pertubation from cutaneous mechanoceptors and proprioceptors, vibratory stimuli of varying frequencies (30, 60, 100 & 300 Hz) were applied to the most effective portion (the spine of scapula close to the acromion) of pointing arm in healthy adults. The error magnitude and direction were measured with a specially devised protractor. The increments of error magnitudes in 30, 60, 100 and 300 Hz stimuli as compared with that without vibration were 1.7°, 1.7°, 2.3°and 2.7°in the dominant hand and 1.9°, 0.8°, 1.9°and 1.4° in the nondominant hand, respectively. The error shifted upward or downward in all stimuli except 100 Hz in the dominant hand which shifted downward. It is suggested that the cutaneous and subcutaneous mechanoceptors such as the Pacinian corpuscles, joint receptors and the muscle spindles contribute to accuracy of the position sense. In addition, by 100 Hz stimulus to the effective portion of the shoulder contralateral to the pointing arm, the error magnitude increased. Therefore sensory inputs from the contralateral arm also exert influences on the accuracy.

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INFLUENCE OF TAIL SUSPENSION HYPO-KINESIA AND EXERCISE TRAINING TO SERUM ENZYMES AND MINERALS IN RATS. NAKAYA, M., IKAWA, S.,°KOSUGI, K.* AND °TAKEUCHI, S., Space Medicine Lab. and Department of 1st Anatomy°, Jikei University School of Medicine, 3-25-8 Nishishimbashi Minatoku Tokyo 105

Eighteen female rats (Wister strain, 8week-old) were divided into three groups, i.e., Control(C), Tail suspension(TS) and Treadmill training(Tr). TS rats were put on suspender with the tail, and were suspended from rail of the cage. Tr rats were trained by treadmill. After four weeks exposure, blood was took from the abdominal aorta under ether anesthesia. Some viscera were taken off and weighed. Results were summarized as follows. 1) An increase of body weight in TS was less than that in other groups. 2) An average value of serum enzymes in TS was less than that in other groups at both CK and ChE. 3) The value of serum Ca in TS group was higher than that in others and that of serum Fe was the lowest in TS group. These results were thought to related with phenomena, Ca loss from bone and space flight anemia. 4) On visceral weight, the average value of TS was higher than that of others at heart,spleen, kidney and adrenal. 5) It is shown that four weeks exposure effects the serum matter and the viscera, above all in tail suspension group.

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COMPARISON OF MAXIMAL OXYGEN UPTAKE AND VENTILATORY RESPONSES DURING EXERCISE BY BICYCLE ERGOMETRY AT DIFFERENT PEDAL RATE.

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Twelve male and fourteen female subjects performed maximal exercise with pedalling rate of 40 and 80 rpm on a bicycle. The highest oxygen uptake attained in each test was measured and compared between the exercises of two different pedal rate.
No significant difference in male was noted between oxygen uptake determined at any pedal rate. However in female, it was confirmed that maximal oxygen uptake during 40 rpm is significantly less than maximal oxygen uptake attained in 80 rpm exercise.

On the other hand, ventilatory response to submaximal exercise(oxygen uptake = 1 l/min) with 80 rpm was not significantly different from that of 40 rpm.

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COMPARISON OF COLD VASOOSCILLATIONS FOR THERMISTOR AND LASER-DOPPLER METHODS. UEDA, G. AND TAKEOKA, M., Dept. of Environmental Physiology, Shinshu Univ. Sch. of Med. Matsumoto 390,Japan

The comparison between thermistor(TH) and laser-Doppler(LD) methods was attempted using rabbit ear central artery or the close capillary area. Cold was applied to a peripheral third of the ear. (1) When a carotid artery was completely occluded, LD curve which means blood flow decreased immediately and after the release it recovered showing the overshooting. This was not shown in the second time. When a peripheral part of the artery was occluded, TH showed an increase ,though LD indicated a decrease. (2) In the control period LD showed larger fluctuations than the TH recordings, sometimes showing sine wave-like undulations. Even when TH showed no sign of vasomotions during the cold exposure, LD could detect fine fluctuations. (3) When immersed into cold, TH curves declined by external influences. However, LD did not show decreases at all times, showing sometimes increases. Fluctuations could be found from the onset of the exposure. (4) Tissue level LD at capillary sites fluctuated obviously.

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COMPARISON OF PULMONARY CIRCULATION BETWEEN PIKA AND RAT. SAKAI,A., UEDA,G., YANAGIDAIRA, Y., TAKEOKA,M. AND*YOSHIDA,Y. Dept. of Environ. Physiol., and*College of Med. Tech., Shinshu Univ., Matsumoto 390

The study of Pika was conducted at 4 different altitudes; 4,460m(n=14), 3,300m(n=15), 2,300m(n=13), and 610m(n=10). Additionally, 10 rats at 2,300m, 8 rats at 1,600m and 10 rats at 610m were used as the comparative experiment for the Pika. All measurements were as follows ; pulmonary artery pressure(P_{PA}), the ratio of right to left ventricular weight (RVW/LVW), number of red blood cells(RBC), mean cell volume (MCV), hematocrit (Ht), blood viscosity(BV), red cell deformability(RCD), and oxygen consumption($\dot{V}O_2$). The principal findings are : (a) P_{PA}, RVW/LVW, and Ht in Pika showed significantly low values compared with those of rats in all altitude ranges;(b) the P_{PA}, RVW/LVW, and Ht increased with altitude in both Pika and rat, yet the extents of increase with altitude in Pika were respectively less than those of rat; and (c) by comparing the low altitude Pika with rat, MCV, BV and $\dot{V}O_2$ in Pika were shown to be lower than those of rat although no difference was found in RBC and RCD. These findings suggest that Pika has strong positive adaptability for high altitude.

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INHIBITION OF COLD VASOREACTIONS IN RABBIT EAR ARTERY. TAKEOKA, M. and UEDA, G Dept. Environ. Physiol., Shinshu Univ. Sc. Med., Matsumoto, 390

By immersion of both earlobes into -20 - 0 °C antifreeze liquid, regular type cold induced vasooscillations (CIVO) occurred on central ear arteries. The effect of local injection (inj.) of phenoxybenzamine (P.B.) under three different cold conditions was investigated. P.B. 0.05ml(0.5mg) was injected subcutaneously around a central ear artery of one ear and 0.05ml saline solution in other ear as a control. Thermistor pickups were placed on the central ear arteries and laser-Doppler pickups were placed on the tissue near the thermistors.

Results 1. RT 25°C, ST 10°C → Temperature (Temp.) of central ear artery ranges from 30 to 33°C: By a local inj. of P.B. 0.05ml(0.5mg), the temp. rise to 37 °C was seen and an increase of blood flow up to the double quantity was seen by a laser-Doppler method. No change was seen in an opposite saline-inj. ear. Next, the temp. fall by needle pricks of earlobe (30 pricks/10 sec) was blocked by P.B.

2. RT 25°C, ST -7°C → Temp. of central ear artery is 20 - 22°C: Only a small temp. rise (3°C) was seen by the inj. of P.B. Periods of CIVO didn't change. When P.B. inj. was followed by a movement, about 12°C rise was seen.

3. RT 20°C, ST -7°C →Temp. of central ear artery is 10 -16°C: Almost no change was seen even when a movement with transciently increased blood flow was caused by a P.B. inj.

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OXYGEN CONSUMPTION DURING FORCED ROTATING EXERCISES IN LONG- TERM COLD -ACCLIMATED RATS. YANAGIDAIRA,Y. AND UEDA,G. Dept.of Environmental Physiol.,Shinshu Univ.Sch. of Med.,Matsumoto 390

The study was carried out to investigate the effects of exercise training plus long -term cold exposure on nonshivering thermogenesis (NST) in male rats acclimated at two different environmental temperatures for 15 weeks. Sedentary rats were acclimated at 25°C (WA) and at 5°C (CA). Also, exercise-trained rats were acclimated at 25°C (WE),and at 5°C (CE). In a motor-driven rotating drum the training conditions were set at 6 ∿12rpm for 30min, 5 days/wk. The oxygen consumptions ($\dot{V}O_2$) during resting and exercising periods were compared each other among 4 groups every week. After 14 weeks, the measurements were repeated at three different environmental temperatures (25, 5 and -10°C). Throughout the experimental period, resting $\dot{V}O_2$ values were measured at 25°C in CA and CE. These were significantly higher than those of WA and WE at around the 6th and 12th weeks. The values of exercising $\dot{V}O_2$ were significantly higher in CE than in WE at the 2nd and 6th weeks. After 14 weeks, these were no significant differences among four-group $\dot{V}O_2$ values at 25°C or at 5°C. Only a value of resting $\dot{V}O_2$measured at -10°C in CE increased remarkably when compared to other -group values measured at-10°C. This result suggests that cold acclimated and exercise -trained rats led to increase NST in a -10°C environmental temperature.

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NONSHIVERING THERMOGENESIS (NST) AND ITS CONTROLING MECHANISM IN THE NEONATAL RAT. YAHATA, T. AND KUROSHIMA, A. Dept. of Physiology, Asahikawa Medical College, Nishi-kagura, Asashikawa 078

In order to evaluate the controling mechanism of ontogenesis of NST, changes in NA and immunoreactive glucagon (IRG) levels in brown adipose tissue (BAT) and its oxygen uptake induced by these hormones were investigated in the neonatal rats. BAT weight per unit body weight and relative mass of dorso-cervical (DC) BAT to interscapular (IS) one were higher around birth than the later stages of neonate. NA level in BAT were increased rapidly after birth and reached the adult's level about 1 week after birth, while IRG level in BAT was already high before birth, and higher in DC BAT than in IS BAT. High basal oxygen uptake by BAT in the early stage of neonate decreased gradually and reached the low level at the weaning stage. NA increased oxygen uptake 4 to 5 times during the period from 2 days to 2 weeks after birth, but less immediately after birth and at the weaning stage. The response to glucagon was the same as that to NA at early stage of neonate and at the weaning stage, but lower at the middle stage of neonate. The present results suggest that NST in BAT can be caused at very early stage of neonate and that glucagon may be a major factor to enhance NST during early period of neonate when the sympathetic nervous system does not fully function.

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BLUNTED FEBRILE RESPONSE TO INTRAVENOUS ENDOTOXIN IN STARVED RATS. SHIDO, O., NAGASAKA, T., AND WATANABE, T.* Dept. Physiol., Sch. Med., Kanazawa Univ., Kanazawa 920, and *Dept. Physiol., Sch. Med., Yamaguchi Univ., Ube 755

The effects of fasting on the febrile responses to intravenous (iv) injection of bacterial lipopolysaccharide (LPS) endotoxin of E. coli were investigated in rats. Ad-lib fed rats (C) produced a biphasic fever with an increase in the temperature difference between brown adipose tissue and colon and shivering activity (SA). Measurement by a direct calorimeter showed no particular change in heat loss. Rats starved for 4 days (F_4) responded to iv LPS with a monophasic fever accompanied by an increase in SA only. The maximal rise in colonic temperature (T_{col}) did not differ from the C-group. Subsequent 2-day fasting reduced SA and the maximal fever height. These results suggest that 4-day fasting reduces nonshivering thermogenesis and further food deprivation inhibits both shivering and nonshivering thermogenesis. Endogenous pyrogen (EP) injected iv produced a prompt rise in T_{col} followed by prolonged hyperthermia in the C-rats. In the F_4-rats, there was no second phase of fever due to iv EP. The injection of LPS, EP, and prostaglandin E_2 into the lateral ventricle (icv) evoked a similar extent of hyperthermia in the C- and F_4-groups. These results suggest that fasting reduces febrile response to iv pyrogens but not to icv.

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LOCAL EXERCISE PERFORMANCE WITH MUSCLE COOLING DURING HYPERTHERMIA. HIRATA, K., NAGASAKA, T., AND NODA, Y. Dept. Physiol., Sch. Med., Kanazawa Univ., Kanazawa 920

The effect of exercising muscle cooling on local exercise performance was studied during normothermia (NT), and during hyperthermia (HT) induced by sauna heating. Six male subjects performed hand-grip exercise at 20% of maximal hand-grip strength in sitting position in sauna box. Forearm was cooled at a rate of 140 $W \cdot m^{-2}$ in exercising (C_{ex}) or non-exercising (C_{nex}) sides, and warmed at a rate of 58 $W \cdot m^{-2}$ in exercising side (W_{ex}). Exercise started after 30-min rest in NT, and after esophageal temperature (T_{es}) increased by 0.5°C in HT, and continued until volitional exhaustion. During HT, mean exercise performance significantly improved in C_{ex} (12.0 $\pm$ 1.2 min) than in W_{ex} (8.0 $\pm$ 0.9 min). Exercise performance significantly improved (10.0 $\pm$ 0.9 min) in C_{nex}, which appeared to be attributed to skin cooling only. No significant difference of exercise performance was observed during NT with warmed or cooled exercising muscle. T_{es}, tympanic and skin temperatures, thermoregulatory and circulatory responses did not differ among the three muscle temperature conditions. Exercising forearm cooling improves exercise performance by 50% without appreciable changes in thermoregulatory and circulatory responses, a half of which is attributed to the direct effect of muscle cooling and the other is attributed to the effect of skin cooling.

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BASAL METABOLISM OF PUBERTAL BOYS AT SUCCESSIVE CHRONOLOGICAL AGES, TSUJITA,J*, MAYUZUMI,M** AND HORI,S* *Dept. Physiol., Hyogo College of Med. **Mukogawa Women's Univ. *1-1, Mukogawacho, Nishinomiya, 663

Measurements of basal metabolism(BMR) and physical characteristics were made on 12 pubertal boys from 12 to 14 years old in Kobe, in November 1986, May and November in 1987. The values of BMR per body surface area(BSA) showed great individual differences at all ages of adolescence. The average values of BMR per body weight throughout the adolescent years observed in the present experiment were greater than those reported in 1984. The absolute values of BMR increase with physical growth while BMR per BSA or body weight decreased gradually with aging. The rate of decrease in BMR per BSA tended to be greater with aging. The absolute values of BMR and BMR per BSA were smaller in bodys with retarded growth at the same age. BMR per BSA tended to be greater in November than in May. Probably due to seasonal variation in BMR. Correlation coefficient between BMR and body mass(0.67) was considerably greater than that between BMR and BSA(0.62) or body weight(0.60).

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THERMOREGULATORY AND CARDIOVASCULAR RESPONSES IN WET-SUITED SUBJECTS DURING UNDERWATER EXERCISE AT VARIOUS DEPTHS. IWAMOTO, J., MIKI, K., SAGAWA, S., TAJIMA, F., AND SHIRAKI, K. Dept. Physiol., Sch. Med., Univ. Occup. and Environ. Health, Kitakyushu 807.

Nine male subjects wearing 5-mm wet suits exercised on an underwater ergometer at work intensity of 2 and 3 met. The exercise was carried out in a water tank placed in a chamber which was pressurized to 2 and 2.5 atmospheres absolutes (ATA) by compressed air. The subject exercised for 2 h each at critical temperature (Tcw) at corresponding pressure. Measurements of temperature of the esophagus (Tes) and the skin, heat loss in the skin and the wet suits, insulation of the tissue (Itssu) and wet suits (Isuit), and cadiac output (CO) were made during rest and exercise. Itssu decreased as the intensity of the exercise increased. Although Tcw in the wet-suited subject increases as the depth increases (Park, Y.H. et al., J.Appl.Physiol. 64(5), 1988). Itssu was independent of the pressures. Convective heat loss underneath the wet suits decreased as the depth increased. This was probably attributed to a decreased water capacity between the skin and the wet suits. Heart rate and CO at corresponding exercise intensity decreased as the pressure increased. As the pressure increased, the overall heat dissipation became less than metabolic heat production during a given work intensity, however Tes was independent of the pressure. These facts lead us to assume that the heat produced during muscular exercise retaines in the tissue at high pressure due probably to a vasoconstriction of the efferent vessels in the muscle.

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CONTRACTION PROPERTIES OF HIP FLEXOR MUSCLES UNDER THE CONDITIONS OF MICROGRAVITY SIMULATED BY WATER IMMERSION. SUGAJIMA, Y., MITARAI,G. AND KOEDA, M. Dept. of Exercise Physiol., Fac. of Physical Educat., Chukyo Univ., Kaizu,Toyota, Aichi

It can be assumed that the relaxation of muscles under microgravity conditions results in a different set of muscular coordination for posture and movement control. In order to investigate this hypothesis the electrical activities of hip flexion muscles, i.e. iliopsoas(I), tensor fasciae latae(TFL), sartorius(S) and rectus femoris(RF) during voluntary isometric contractions were observed under the conditions of head out water immersion and compared with those obtained under the dry conditions without water immersion. The subjects were 7 healty 21-26 aged males. They performed a certain thigh flexion(120 degree) of the right leg with four different strength of contraction, that is, the maximal voluntary contraction(MVC), 75%MVC, 50%MVC and 25%MVC. During the performance, the subjects kept the upright standing posture without body sway by holding a frame appropriately equiped in the surround. The results obtainedshowedthat TFL, S and RF markedly decreased the electromyographic(EMG) activities under the water immersion, while I maintained the EMG discharges similarly with those under the dry conditions. This suggested that the coordination of muscle groups changes by microgravity. The participation of gravity on to the muscle contraction may be different due to the function such as adductor, abductor or flexor etc.

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STYDIES ON THE NORMAL THRUST FORCE OF A DIVER'S FIN-KICK IN 31 ATA, $He-O_2$ UNDERWATER ENVIRONMENT. YAMAGUCHI, H., SHIDARA, F, NARAKI, N., and MOHRI, M.
Undersea Science and Technology Dept., Japan Marine Science and Technology Center (JAMSTEC), Natsushima, Yokosuka 237

Swimming underwater with fins make a diver generate the thrust force up to 6.5kg constantly for several minutes in shallow depth. In the case of swimming at deeper zone, however, there has not been any reports in the past.

In this report, swimming performance capacity at the depth of 300m was tested and the physiological responses were compared between 1 and 31 ATA.

Water temperature was 26 ± 1 ℃ and the thrust loads applied to divers were 3, 4 and 5kg.

Through this experiment, it was found that the thrust performance up to 5kg could be completely achieved even in 31 ATA. Heart rate, respiratory minute volume and oxygen uptake showed similar regression line according to the addition of loads both in 1 and 31 ATA.

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VESTIBULO-SYMPATHETIC REFLEX IN MAN UNDER WEIGHTLESSNESS SIMULATED BY WATER IMMERSION. MANO, T., SAITO, M., IWASE, S., KOGA, K., ABE, H. & INAMURA, K., Research Institute of Environmental Medicine, Nagoya University, Nagoya 464-01

To clarify how the vestibulo-sympathetic reflex (VSR) is modified in man under weightlessness, the response of muscle sympathetic nerve activity (MSA) to caloric vestibular stimulation (CVS) was analyzed in standing humans during head-out water immersion. Subjects were 4 healthy males aged 20 - 27 with informed consent. To simulate weightlessness, thermoneutral water of 34°C was poured up to the neck of the standing subject. The MSA was recorded from the tibial nerve using a tungsten microelectrode, simultaneously with heart rate (HR), respiration, leg volume (LV) and horizontal nystagmus. MSA was analyzed quantitatively as burst rate. For CVS, cold water of 10°C, 50 ml was irrigated into the external meatus. The spontaneous MSA, HR and LV were reduced by head-out immersion, compared to those in dry state without water. The CVS increased MSA, HR and respiration, concomitantly with the nystagmic response, both under dry and immersion conditions. However, the MSA response (fractional change of burst rate) to CVS was higher during immersion than during dry state. When the MSA became markedly increased by CVS during immersion, vomiting occurred suddenly, followed by transient MSA suppression. In conclusion, the VSR is enhanced by water immersion. The enhanced VSR may facilitate the occurrence of vomiting under weightlessness simulated by water immersion.

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EFFECTS OF VESTIBULO-AUTONOMIC SYSTEM ON BLOOD PRESSURE RESPONSE DURING OSCILLATORY HEAD-UP AND HEAD-DOWN TILTING IN ANESTHETIZED DOGS. TERADA, N., HORIUCHI, J., AND TAKEUCHI, T. Dept. Physiol., Yamanashi Medical College, Tamaho, Yamanashi 409-38

Effects of vestibulo-autonomic system on cardiovascular adjustments during oscillatory head-up and head-down tilting (angle of 45° for 90 sec) was studied in anesthetized dogs. In intact animals, systemic blood pressure during both oscillatory head-up tilting (above 60cpm) and oscillatory head-down tilting (above 20cpm) fell significantly at an initial phase followed by a recovery toward the pre-tilting level. After labyrintectomy, however, the initial hypotension was augmented significantly during the oscillatory head-up tilting, but significantly diminished during the oscillatory head-down tilting. In the baroreceptor denervated dogs, these compensatory effects of the vestibulo-autonomic reflex system disappeared even in either intact or labyrinthectomized dogs. These results suggest that the vestibulo-autonomic reflex system is a prominent neural factor to compensate blood pressure changes during the oscillatory tilting. This factor of vestibulo-autonomic system modulates the systemic baroreceptor reflexes.

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ANALYSIS OF THERMAL ACCLIMATIZATION AND PYROGENIC RESPONSE IN PIKA (WHISTLE RABBIT). KOSAKA, M., MATSUMOTO, T., YANG,G-J., OHWATARI, N., TSUCHIYA, K., NAKAMURA, K. AND CHEN, C-M. Dept. of Environment. Physiol., Inst. of Trop. Med., Nagasaki Univ., Nagasaki 852

Pika's better heat conservation, higher metabolic rate, poor heat dissipation, high sensitivity to narcotics, poor pyrogenic response to exogenous LPS pyrogen (i.p.) and moderate response to LPS pyrogen (i.v.) were demonstrated in the previous report. In the present experiment, pika's heat loss ability and pyrogenic response to endogenous pyrogen (rh IL-1α) were precisely examined and discussed from the view point of heat acclimatization. (1) In the same experimental condition, rh IL-1α (2.0μg/kg·i.v.) induced high fever (ΔT:0.8-1.5°C) with short latent time (2-3min)compared to 20min of moderate LPS pyrogen fever (ΔT:0.7°C). (2) During heat exposure (30°C. 33°C, 35°C and 40°C, 60%rh), thermal panting was observed in rabbits, however,no increase in respiratory rate was observed in pikas. Noteworthily the rapid increase in rectal temperature of the two pikas was observed at heat exposure (40°C, 60%rh)and then finally the two pikas died after 90 min, and the lethal rectal temperature were 44.0°C and 43.1°C. Laboratory albino rabbits survived through this experiment. The ear surface area ratio to body surface area in pika was small compared to rabbit. And it was 7% in pika and 17% in rabbit. These results revealed pika's high pyrogenicity related to higher metabolic rate and the poor heat loss ability constituted by its small ear surface area and lack of thermal panting.

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PROPERTIES OF HEART-RATE/VENTRICULAR-EJECTION-TIME RELATION UNDER ACUTE HYPOXIA AND IN DE-ACCLIMATION PROCESSES AFTER HIGH-ALTITUDE EXPEDITION. MORI. S., WATANABE, S., TAKAGI, S. AND TAKABAYASHI, A.* Dept. Aerospace Physiol., Res. Inst. Environ. Med., Nagoya Univ., Nagoya 464, *Sch. Hygiene Med. Tech., Fugita-Gakuen Health Univ., Toyoake-shi 470-11

A steady, inversed relationship between heart rate (HR) and ventricular ejection time (VET) may become in disorder under severe hypoxia, since it is known that the relation is labile in the ischemic heart failure. A stepwise increasing high-altitude exposure in a hypobaric chamber was repeated for 3 to 5 successive days in 16 male subjects including 7 veteran mountaineerers (VM) and the cardiac output in rest and exercise were measured by an impedance method at each altitude. Above speculation could not be supported in the present analysis. However, when the VET/HR coefficients of the VM group were compared with those of the subjects never experienced high-altitude (NE), the day-by-day value was relatively stable in the individual NE but not in VM and the values were significantly higher in VM than in NE on the first day of the hypobaric experiments, though they became close to each other after the second day. According to the decay of variation in VM with the de-acclimation period, it was suggested that effects of high-altitude acclimation on cardiac function might persist for one year or more.

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BIOCHEMICAL CHANGES OF RATS DURING CHRONIC CENTRIFUGAL ACCELERATION.
Sudoh, Masamichi and IKAWA, Sachio Space Medicine Laboratory The Jikei University School of Medicine, Minato-Ku, Tokyo 105

Physiological responses to three week acceleration were studied in 12 female rats which were divided into three groups of 1G control, 1.6G exposure (1.6G) and 3.0G exposure (3G). Daily body weights, urine volumes, food and water intake were measured for three week acceleration. After the end of the experiment , we collected blood and measured serum enzyme activities, metabolites and minerals. Body weights in groups 1.6G and 3G decreased at the beginning of the experiment, but almost recovered to the pre-exposure level by the end of the experiment. Urine volume in both groups did not exhibit significant change. In terms of serum constituents such as Na, Ca, Cl and Ht, rats in both groups did not show significant difference, compared with the control group. This suggests any hemodilution or hemoconcentration did not occur. A decreaseof serum levels in inorganic phosphate, uric acid, LDH and CPK, and an increase in triglyceride were observed, with the greater levels in 3G than those in 1.6G.

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RESPIRATORY RESPONSES TO CO_2 IN HYPERBARIC HELIUM ENVIRONMENT(26, 51bar) IN CATS.
NARAKI,N, F.SHIDARA, Y.TAYA, Y.MIZUSHIMA, M.NAKANO, M.MOHRI,
Japan Marine Science and Technology Center, 2-15 Natsushima, Yokosuka 237

In hyperbaric air environments, ventilatory responses to CO_2 stimulation have been shown to be depressed by the increase of ventilatory gas density. CO_2 response tests in normoxic conditions with air at 1bar(gas density=1g/L) and with Helium at 26bar(4.5g/L) and 51bar(8g/L) were performed in unanesthetized cats. Ventilatory CO_2 responses were analyzed with spirogram measured with a whole body volume displacement plethysmograph during CO_2 elevation(0-70mbar), and the plethysmograph containing the animal was fitted into a hyperbaric chamber. Respiratory frequency, tidal volume and mean inspiratory flow slightly increased at 51bar compared with 1bar for CO_2 test, but the relative increase of these results from the base line (PCO_2=0mbar) during CO_2 elevation have not shown the significant difference between ambient pressures. In hyperaric helium environments of present study, the reduced ventilatory responses to CO_2 was not recognized. It seemed that the hyperbaric helium environment effected the respiratory control system.

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THE ROLE OF ADH, ANP AND ALDOSTERONE IN THE HYPERBARIC DIURESIS.
MIYAMOTO, N., MATSUI, N., INOUE, I., SEO, H., NAKABAYASHI, K. AND OHIWA, H., Res. Inst. Environ. Med., Nagoya Univ., Furo-cho, Chikusa-ku, Nagoya 464-01 and Undersea Medical Center, JMSDF, Yokosuka 239.

Urine flow, especially at night, increases under hyperbaria. To clarify the mechanism of this diuresis, a dry saturation dive experiment was carried out. Five male subjects were exposed to a 16-21 ATA helium-oxygen environment for 4 days. Blood samples were obtained in the early morning, once at pre-dive and post-dive periods, 3 times at 16-21 ATA. Eight-hour timed urine samples were collected during the whole experimental days. A typical hyperbaric diuresis was observed. Hematocrit rose at 16-21 ATA. The secretion of ADH was suppressed throughout the hyperbaric period at daytime, resulting in the decrease of the urinary osmolality. The secretion of ANP increased at night during hyperbaria and correlated with increases of both the nocturnal urine flow and urinary sodium excretion. The secretion of aldosterone decreased during the early phase of hyperbaria. These results suggest that the primary causes of the hyperbaric diuresis are the changes of both ADH and ANP secretion and that aldosterone modulates the diuresis.

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POSTURAL CONTROL OF FISH DURING PARABOLIC AIRCRAFT FLIGHT (II).

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Four kinds of goldfish, namely: normal, unilaterally labyrinthectomized (ULT) bilaterally labyrinthectomized (BLT), and blinded fish, were flown in a light aircraft. Two illuminating conditions, either a light from the top or from the side, were employed in this experiment. The behavior of the fish were videotaped and analyzed frame by frame.

During the hypogravity period of parabolic flight, normal and blinded fish showed diving responses. Although clear looping response of blinded fish was not observed, it may be due to the small size of fish tank. Dorsal light response of normal, BLT and ULT fish became prominent during hypogravity. The ULT fish, however, tilted about the its longitudinal body axis toward the operated side regardless of incident light. These findings suggest that the visual system plays an important role in stabilizing body posture, especially during hypogravity. For short periods of weightlessness, however, vestibular imbalance between the right and left side may emphasize a postural disturbance. This study was done with Drs. R von Baumgarten and J. Wetzig as the Japan-West Germany joint research project.

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EFFECT OF STATIC MAGNETIC FIELD ON NERVE ACTIVITY.

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The aim of this work is to investigate the infuluene of a static magnetic field upon the sciatic nerve activities, such as threshold, refractory period, conduction velocity (CV) or the responses to the repetitive stimulation. The nerve was isolated from bullfrog and was mounted in a recording chamber. Then the nerve was placed perpendicular to the magnetic field and was exposed at 7000 gauss (MFS) for 3 or 5 hrs. Both the threshold and the refractory period after MFS were not different from those before exposure. CV was increasing with time to about 103.5 % after 3 hrs and 106 % after 5 hrs. The increase of CV after MFS was 104.3 % and 102.3 % for 3 hr- and 5 hr-exposure, respectively. The effect of MFS for 3 hrs is little, however the CV after 5 hr-exposure seems to be smaller (compare 106 % with 102.3 %). It suggests that the MFS may supress the increase of CV. A pattern of a train of action potentials by repetitive stimulation with intervals within a range of relative refractory period was changed after MFS. It may mean that the recovery process after nerve activation is altered by MFS.

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RELATIONSHIP BETWEEN LOW FREQUENCY SWAY OF FOOT PRESSURE CENTER AND BODY FLUID CIRCULATION DURING STANDING IN MAN.

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The purpose of this study was to clarify the relationship between low frequency body sway and body fluid circulation (BFC) during static standing in man. METHODS: Subjects were 5 young healthy males. Sway of the foot pressure center (FPC) and fluctuations of hemodynamic regulatory functions were measured simultaneously. The latter parameters were intrathoracic blood volume (IBV), calf blood volume (CBV), heart rate (HR), venous pressure at the dorsum pedis (VPP), muscle sympathetic nerve activity (MSA) to the soleus, surface electromyograms of the soleus (EMG-s) and the tibialis anterior (EMG-t). RESULTS: One minute wave (1-MW) ranging 0.01-0.02 Hz was revealed in all parameters. Cross correlations among all parameters indicated high values, with coherency more than 0.7. The 1-MW's main component of the IBV or the FPC propagated to the other hemodynamic regulatory functions. If the phase of IBV decrease was defined as the first step, the order of phase difference was as follows. (1) IBV was decreased. (2) EMG-s was activated, or FPC was shifted on backward position. (3) MSA was activated, VPP was elevated and HR was increased 10-40 seconds later. (4) CBV was decreased. CONCLUSIONS: The 1-MW of body sway is closely related to the fluctuation in BFC. A sympathetic nerve reaction by the intrathoracic receptors may participate in the development of 1-MW.

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ANALYSIS OF THE POSTURE CONTROL SYSTEM FOR TRACKING MOVEMENT (II).

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The dynamics of posture control in humans during voluntary body tilting fore and aft were investigated. Subjects stood with the Romberg's position on a force plate were instructed to track a target spot displayed on a CRT by using the other moving spot revealed a position of the center of gravity. The target spots chosen were the sine wave of amplitude from 1 to 6cm and frequency from 0.2 to 0.9Hz. The gain characteristics of tracking movement revealed a peak at 0.5Hz in 1cm and 2cm and at 0.3Hz in 4cm and 6cm of the stimulus amplitudes. When the stimulus frequency was increased, the phase lag was progressed. The larger the stimulus amplitude , the more this delay decreased. The phase of movement of head(H), shoulder(S) ,waist(W), knee(K) measured by video tape were corresponded with each other. The ratio of displacement to height of each point was almost the same for the stimulus amplitude of 2cm . For the stimulus amplitude of 6 cm, each point of K, W and S took almost the same ratio except for 0.9Hz. Small movement of each point for 0.9 Hz may be counterpart of the active force of ankle rotation. In summary, the optimum range of the posture control for tracking movement was found in 0.3-0.5Hz frequency and 4-6cm amplitude.

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EFFECTS OF SIZE AND LOCATION OF THE VISUAL FIELD ON POSTURAL SWAY INDUCED BY OPTOKINETIC STIMULATION.

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We examined the body inclination to antero-posterior direction induced by vertical optokinetic stimulation. Each subject was stood on a force plate by Romberg's position, and instructed to gaze a fixation point on the screen at 1 m apart from his eyes. The random dotted pattern projected on the screen was moved to downward direction. The one eye of subject was covered and the other eye was restricted in the visual field by two types spectacle. The one was centrally holed spectacle (visual angle : 20, 30 and 40 deg), the other one was holed 40 deg in visual angle at a peripheral part. All subjects inclined anterioly during the stimulus in proportion to the size of visual field. Peripheral effect of 40 deg sized stimulation was not found clear difference between central and peripheral (upper and/or lower) part. Our observations suggest that the visual factor for postural stabilization might be affected rather the size of peripheral vision.

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EFFECT OF ATMOSPHERIC PRESSURE ON TISSUE INSULATION DURING WATER IMMERSION AT CRITICAL TEMPERATURE.

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Tissue insulation (Itissue) and skin heat loss (Htissue) were measured in 9 unprotected subjects immersed up to the neck in water of critical temperature (Tcw), defined as the lowest temperature a subject can tolerate at rest without shivering for 2 h, at 0.6, 1, and 2 atmospheres absolute (ATA). The Tcw at 0.6 ATA (32±0.4°C) was significantly higher ($P<0.05$) than that of 1 ATA (31±0.3°C) and 2 ATA (31±0.3°C). During 2-h immersion at Tcw no pressure-dependent difference was detected in esophageal temperature. Overall mean Itissue was 0.147±0.008, 0.162±0.005, and 0.153±0.007($°C.kcal^{-1}.m^2.h$) for 0.6, 1, and 2 ATA, respectively. The Itissue was at near maximum at Tcw and was independent of atmospheric pressure. The Itissue of the extremities (arm, hand, and foot) decreased significantly ($P<0.05$) at 0.6 ATA but Htissue was increased. As the result the extremity-to-trunk heat loss ratio significantly increased ($P<0.05$) to 1.4 at 0.6 ATA from 1.1 at 1 ATA. We conclude that high pressure (2 ATA) does not affect Itissue, Htissue, and Tcw. Hypoxia, however, facilitates heat transfer from the trunk to the limbs, probably due to a decreased countercurrent heat exchange in the limbs and leads to an elevation of Tcw.

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COLD EXPOSURE SUPPRESSES INSULO-ACINAR AXIS IN PANCREAS OF THE RAT. HABARA, Y. and ISHIKAWA, K., Dept. Physiol. and Dept. Anatomy, Asahikawa Med. College, Asahikawa 078

Effects of cold exposure on exocrine function of rat pancreas were studied by using isolated acini. In acini prepared from rats reared at 5°C for 2 weeks, amylase content when expressed per cellular DNA concentration was only 48% of that in normal acini obtained from rats kept at 25°C. Trypsinogen content per DNA was unchanged but was increased to 161% when expressed per cellular protein concentration. Secretory response of amylase stimulated either by cholecystokinin octapeptide (CCK8) or carbamylcholine (CCh) was suppressed in proportion to the decrease in acinar amylase content. A maximal response was obtained at 30 pM-CCK8 and 3 μM-CCh and was reduced by cold exposure to less than 50% of normal release. Trypsinogen release per DNA was unchanged but the release per cellular protein concentration increased in proportion to the rise in its cellular content. In cold-exposed rats, plasma insulin level was reduced to 55% of the level in control rats and insulin administration during the cold exposure restored the decreased acinar amylase concentration.

We assume from the present findings that the suppression of secretory response of amylase is mainly a result of decrease in acinar amylase concentration. A suppression of insulin effect on exocrine pancreas via a system termed insulo-acinar axis may strongly link to a diminution of amylase synthesis under the cold environment.

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CHANGES OF CARDIO-VASCULAR SYSTEMS OF ALERT RAT IN HYPER-GRAVITY CONDITION. UEKI, S., [1]NAKASHIMA, M. AND MATSUNAMI, K. Dept. of Neurophysiol., Inst. of Equilibrium Res. and [1]Dept. of Pharmacol., Gifu Univ., Sch. of Med. Gifu 500

We measured heart rate (HR) and respiratory rate(RR) of alert rats in hyper-gravity condition. We also measured the blood gas components after 5 min. or 10 min. exposure of hyper-gravity, i.e. pH, Pao_2, $Paco_2$, HCO_3^- and base excess(BE). The magnitudes of gravity were 6 or 8G. HR decreased in hyper-G exposure and did not return to initial values. RR also decreased in G exposure but returned to initial values rapidly after cessation of G exposure. pH tended to decrease. Pao_2 increased from 87.4±4.2 mmHg of the initial values to 102.9±5.7 mmHg after cessation of 10 min. exposure of 6G. But $Paco_2$ did not change at all. HCO_3^- decreased about 2 mmol/l after 10 min. exposure of 6G. BE tended to decrease. All values showed greater change for greater G exposure. Also changes in 10 min. exposure were greater than those in 5 min. exposure. Since the present results were possibly due to a rebound phenomenon, further study will be needed for the blood sample collected just during G-exposure period.

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CYCLIC CHANGES OF ESTROUS CYCLE IN RAT AFTER SATURATION DIVING AND DURING REPETITIVE AIR DIVING. TAYA, Y., NAKANO, M., NARAKI, N., SHIDARA, F., MIZUSHIMA, Y. and MOHRI, M. Undersea Science and Technology Dept., Japan Marine Science and Technology Center (JAMSTEC), Natsushima, Yokosuka 237

There is a need for more research into such questions as diving during menstruation, pregnancy and fertility after saturation diving.

In both male and female Wister Imamichi rats were exposed to 31-21 ATA N_2-O_2 and 31 ATA He-O_2 for 6 days and 5 ATA air pressure for 20 minutes per day (20 times/month) to study whether their functional fertility was affected. The results indicated that after exposure, about ninety percent of the female rats experienced changes in the duration of their estrous cycle in 31-21 ATA exposure groups. However, there was no evidence in the repetitive air diving group. Thereafter, the normal estrous cycle was restored and they could be normally fertilized. The offspring of exposure rats were normally bone. Sex ratio and litter size were found to be normal in each group.

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RESPONSES IN THE CARDIO-PULMONARY SYSTEM OF CATS EXPOSED TO -Gx ACCELERATION. SATAKE, H. AND MATSUNAMI, K. Dept. Neurophysiol., Inst. Equilibrium Res., Gifu Univ., Sch. Med., Gifu 500

The changes of cardio-pulmonary system were investigated when the centrifugal acceleration (-Gx; back to abdomen) exposed to anaesthetized cats (2.0±0.5 kg; n=6). The procedures of the experiment were the same as already reported. Heart rate (HR), stroke volume (SV) and respiratory rate (RR) were examined. Moreover, the cardiac response were analyzed in detail for the R-R interval of ECG during and immediately after the accelerative period for 400 sec from the onset. The -Gx acceleration caused increases of RR and HR except -2Gx load. A transient increase of SV was observed in the early period of the steady state. In many cases, R-R interval revealed a cyclic fluctuation in harmony with the respiratory rhythm. R-R interval started to decrease after the G-load was over 2G. The coefficient of variation (C.V.) of R-R interval increased transiently during an increasing phase of acceleration, and thereafter in the steady state of G-load, the C.V. returned to a similar value to the control. It is suggested that the changes of C.V. would reflect the fluctuation of R-R interval resulted from the respiratory rhythm. The fluctuation of R-R interval during the 1G-control period was larger than during the steady G-load period, nevertheless C.V. shows no remarkable difference between the two stage.

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ADAPTIVE CHANGES IN LIPID OF ERYTHROCYTIC MEMBRANE WITH GUINEA PIGS DURING EXPOSURE TO SIMULATED HIGH ALTITUDE. OSADA,H., KONDOU,Y. * AND SAKAI,A. * *

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Vital reactions of animal in high-altitude environment were examined from the viewpoint of environmental physiology. As for the movement of blood corpuscles, it has already been examined that under hypoxia the appearance of certain idiophathic phenomena such as red blood cell increase or platelet decrease etc. had been observed. In this report, therefore, studies on the movement of blood corpuscles were carried out from the variation of constituents in the lipid of erythrocytic membrane.

Result 1) Under hypoxia, significant rise of both free choresterol and phospholipids were recognized. 2) results of the fragility test showed the acceleration of hemolysis start point and the expansion of hemolysis width. In this experiment, under hypoxia, conspicuous disturbances in the constituent ratio of blood-corpuscle membrane were recognized.

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AUTONOMIC NERVOUS TONES AND TEMPERATURE REGULATION IN CHRONIC SPINAL RATS. TSUCHIYA, K. AND KOSAKA, M. Dept. of Environment. Physiol., Inst. of Trop. Med., Nagasaki Univ., Nagasaki 852

Male adult Wistar rats acclimated to 30°C were used in this study. The lower cervical cord was transected under pentobarbital anesthesia, and the spinal rats were reared at 30°C of room temperature. During the daytime, each conscious rat was placed in a loosely fitting cage, and heart rate (HR), rectal (Tre) and tail skin (Ttail) temperatures were recorded simultaneously in a warm room (30°C, 60%,r.h.). Cardiac parasympathetic (PT) and sympathetic (ST) tones were calculated by HR change after injection (i.p.) of atropine sulfate 1mg/kg or propranolol hydrochloride 8mg/kg. In a resting state, Tre (M.± S.E.) in control (spinal-intact rats) was 38.0± 0.1°C, and Tre in the 1st (1W), 2nd (2W) and 3rd to 6th (3-6W) week after the spinalization were 36.2± 0.1°C, 37.0± 0.2°C and 37.7± 0.3°C, respectively. HR in control was 369± 6 beats/min, and HR in 1W, 2W and 3-6W were 331± 14 beats/min, 361± 9 beats/min and 370± 11 beats/min, respectively. In chronic spinal rats, Ttail was higher than that in control. This suggests a decreased activity of the sympathetic vasoconstrictor in the tail. In control rats, PT and ST were 22.5% and 24.4%, while PT and ST in chronic spinal rats of 2W were 15.2% and 23.2%, respectively. These results suggest that the changes in both ST and PT may contribute to the recovery process of autonomic functions in chronic spinal rats.

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COMPARISON OF HEAT LOSS RESPONSES BY LOCAL HEATING OF THE PREOPTIC AREA AND ANTERIOR HYPOTHALAMUS AND THE RETICULAR FORMATION IN THE MEDULLA OBLONGATA WITH ARGON LASER IN RABBIT. OHWATARI, N. AND KOSAKA, M. Dept. of Environment. Physiol., Inst. of Trop. Med., Nagasaki Univ., Nagasaki 852

The heat loss responses such as increases in ear skin temperature and in respiratory rate were induced by local heating of the preoptic area and anterior hypothalamus (PO/AH) and the reticular formation in the medulla oblongata (MRF) with irradiation of argon laser guided with glass fiber (0.4mm in diamater) in 7 rabbits. And changes in respiratory rate (RR), heart rate (HR), temperatures of rectum (Tre), brain (Tbr), ear skin on the blood vessel (Tea'), ear skin (Tea) and abdomen (Tab) were compared when the minimal laser powers possible to induce heat loss responses in PO/AH and MRF were applied. The increases of temperature in the brain at 0,1,2,3, and 4mm apart from the irradiated center of argon laser were 2.8,2.6,1.5,0.9 and 0.5°C, respectively. The minimal laser powers to induce responses were 14.5mW of PO/AH and 19.0mW of MRF, and there was significant difference in both values. This difference may be due to thermal sensitivities of PO/AH and MRF. The decrease in HR during local heating of MRF was significant to compare with that of PO/AH. The enhancement of vagal activity and/or inhibition of sympathetic nervous activity might be caused. The differences of each value of indicators obtained from local heating of PO/AH and MRF were not statistically significant except laser power and HR.

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EFFECT OF THYROID HORMONE ON THERMAL SWEATING. MATSUMOTO, T., KOSAKA, M., YAMAUCHI, M. AND OHWATARI, N. Dept. of Environment. Physiol., Inst. of Trop. Med., Nagasaki Univ.

Hyperhidrosis with hyperthyroidism (Hyper) and dry skin with hypothyroidism (Hypo) are clinically well known. But, up to now, there is no general agreement concerning the effect of thyroid hormone on thermal sweating among the thermal physiologists. In this study thermal sweating of the patients of Hyper and Hypo was examined by capacitance hygrometry. In a chamber (25°C, 60%r.h.), local heat load (43°C water bath, 30min) was applied on the lower legs to induce sweating. Sweat onset time in Hyper and control were 10.6 ± 5.2 and 15.6 ± 5.0min (Mean ± SD), respectively. Total sweat volume in both group were 66.06 ± 26.24 and 47.95 ± 31.25mg/capsule, and increase of oral temperature at sweat onset time were 0.20 ± 0.16 and 0.10 ± 0.08°C, respectively. In Hypo more than several years, no sweating was observed during 30min heat load. In one case, sweat onset time was 56 min where oral temperature rose 0.5°C. In the other, no sweating was observed even though 0.9°C increase in oral temperature during 51min heat load. But, in Hypo less than 2 weeks, short sweat onset time and large sweat volume were observed. In short term Hypo, thyroid function (T3, T4, TSH and FT4) was the same as the value of long term Hypo. From these results, two suggestions are drawn; one is that thyroid hormone enhances sweating via thermoregulatory mechanism, and the other is that thyroid hormone action at intracellular level may change slow compared to thyroid hormone regulation in plasma level.

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〔会　報〕

日本生理学会昭和63年度第1回常任幹事会議事録

日　時：昭和63年4月3日(日)　午後2時～6時
会　場：和歌山県民文化会館
出席者：加藤正道，佐藤　誠，西山明徳，熊田　衛，新島　旭，本田良行，本間三郎，伊藤正男，酒井敏夫，島津　浩，高橋国太郎，竹内　昭，塚田裕三，登坂恒夫，本郷利憲，入来正躬，入沢　宏，金子章道，富田忠雄，永坂鉄夫，久野　宗，中馬一郎，中山昭雄，藤本　守，岡田博匡，堀　泰雄，石河延貞，大村　裕，西彰五郎，望月政司(教室史編集委員長)，中野昭一(教育委員長)，松下　宏，辻本　毅，辻　繁勝(当番幹事)
欠席者：広重　力
議　長：松下　宏(当番幹事)

＜報　告＞

1. 庶務報告（伊藤庶務幹事）：会員について，昭和63年1月～3月の期間入会151名，退会74名，会員総数3,551名（一般会員3,285名，特別会員30名，名誉会員3名，準会員233名）であることが報告された．学士院賞を受賞された大村　裕常任幹事に対し，祝辞が述べられた．昨年11～12月に逝去された評議員田北周平，特別会員戸塚武彦，評議員東　健彦の三氏に対する追悼の辞が述べられた．

第14回日産学術研究助成に小野武年富山医科薬科大学教授「記憶と時間，場所及び環境変化認知の脳内機構」990万円の採択が報告された．昭和63年山田科学振興財団研究援助助成に木下喜博，東田陽博，宮下保司の三氏を推薦した．日本学術会議第14期会員推薦人予備者に熊田　衛常任幹事を推薦した．第65回日本生理学会大会（和歌山）記念市民公開講演会（昭和63年4月2日）の主催，第6回バイオメカニズム学術講演会（63年9月）及び第6回国際肥満学会（63年9月）への協賛を追認した．日本医学会より次期日本医学会評議員及び連絡委員（任期63年4月1日より2年間）各1名の推薦の依頼があった．

2. 会計報告（本郷会計幹事）：昭和62年度決算の報告がなされ，会計監事（島津，竹内）の会計監査を受けた旨報告があり了承された．

3. 日本生理学雑誌編集報告（酒井編集幹事）：日本生理学雑誌50号の発行と編集状況について説明がなされた．例年ではあるが年初の発行は遅れがちであること，現在2号の発送が完了した段階であり第66回日本生理学会大会の第1報は3号に掲載する予定である旨の報告がなされた．

4. J. J. P. 編集報告（本田委員長）：J. J. P. 編集状況について，論文の投稿と返却または辞退の割合は従前と変わらないが，改稿論文提出の遅れもあって発行が遅れ昨年末と本年初頭の2号の頁数は薄いものとなった．しかし，昨今投稿数は増え回復の兆しにあること，昨年度海外からの投稿が増えたにも拘らず採択率の低いことなどが報告された．J. J. P. 昭和62年度決算について，円高による外国購読料減少にも拘らず頁数減による製作費の減少と国内購読の伸びにより，赤字予算に反して繰越が生じた旨の報告がなされた．

5. 教育委員会報告（中野委員長）：第65回大会における教育シンポジウムは，4名のシンポジストにより“統合カリキュラムの中での生理学教育を考える”と題して行われる．懸案の「生理学実習書」改定について，アンケート調査報告書をまとめ日生誌に投稿したこと，実習書改訂に関する小委員会（入来委員長）によりbasicとadvanced courseに分けて昭和63年度中に上梓したい旨報告がなされた．

6. 研究費委員会報告（新島委員長）：科学研究費について，日本学術会議第7部より「中枢統合機能」が分科細目増の要望の第一位に推されていること，昭和63年度の科学研究費総額は前年比8.4％（38億円）増で，重点領域研究，独創的先端技術，一般研究BとC，奨励研究A，海外学術研究などの充実が挙げられていることが報告された．民間からの研究助成について，さらに調査研究が行われる旨述べられた．

7. 動物実験に関する委員会報告(塚田委員長)：「生理学領域における動物実験の基本的指針」(委員長原

案）を委員会において審議のうえ一部改訂し委員会試案としてまとめられたので，追加資料として提出した旨報告された．本年10月末，グリプス教授（ジュネーブ）の来日を機会に次回の委員会と小グループ講演会を開く予定である旨述べられた．

8. 評議員選考委員会報告（本間委員長）：評議員候補者53名全員を推薦することが報告された．

9. 日本生理学教室史編集委員会報告（望月委員長）：日本生理学教室史下巻は8月までに全原稿の初校を終え本年末に刊行される予定であること，発行部数1,000部，1部定価15,000円を予定し，10月以降に注文書を送りたい旨報告された．

10. 生理科学研究連絡委員会報告（本間研連委員長）：生理科学研究連絡委員会は，昭和63年1月29日日本学術会議会議室で行われIUPSへの本年度分担金(8,700$)が認められたこと，同日，実験動物研連との合同委員会がもたれたことについて報告された．

11. 国際生理科学連合報告（伊藤 IUPS 理事）：第31回IUPSヘルシンキ大会（9～15/7/1988）について，プログラム案が紹介された．日本人会員からはPitts Lectureに星教授が，Invited Lectureには2名が指名され，Congress Symposiaの座長には5名が起用されている旨説明された．

12. 第66回（昭和64年）日本生理学会大会の準備状況（堀当番幹事）：4月5，6，7日の3日間，岡山大学津島キャンパス（教養部）で開催を予定し，演題受付は例年通り無制限とすることが報告された．宿泊は日本交通公社に委託し，充分余裕のあるベッド数が確保されている旨説明がなされた．

13. 第65回（昭和63年）日本生理学会大会に関する報告（松下当番幹事）：演題発表数819題の内，口演614題，ポスター展示205題であること，大会参加申込者数1,455名，当日参加申込者149名，合計1,604名であり，そのうち生理学会新入会者は138名であることが報告された．

＜議　題＞

1. 前回議事録の承認：前回の議事録が示され承認された．

2. 昭和63年度予算案：本郷会計幹事より予算のたて方，費目は従前と同じとの説明があり，予備費からの教育委員会活動費（20万円）と生理研連シンポジウム支持費用（10万円）の支出，国際交流基金からの神経科学ワークショップ（バンコック）派遣講師の旅費支出等を含め承認された．

3. 評議員推薦について：53名全員の推薦が承認された．

4. 日本医学会評議員および連絡委員の選出：評議員に酒井敏夫幹事，連絡委員に馬詰良樹評議員が再選された．

5. 大会抄録号に関する件：現在，日生誌8，9合併号として刊行中の大会抄録号をJ. J. P. Supplementとして刊行する計画が，本田 J. J. P. 編集委員長より提案された．部数4,000（全生理学会会員＋海外購読分），刊行および国内郵送費4,162,000円（原稿用紙代，英文校閲費および通信費以外は生理学会予算による），編集（当番幹事，日生誌およびJ. J. P. 編集委員会の共同），実施（第66回大会号より）などの提案に対して，学会会則4条改訂と日生誌8，9号の補充の必要性（酒井編集幹事），生理学会予算逼迫の可能性（本郷会計幹事）等が指摘された．然し年来の懸案でもあり，場合によっては会則改訂の必要はあるが（島津会則委員会委員長），第66回大会より実施するため今大会の評議員会，総会に提案することに決した．

6. J. J. P. の投稿規定改訂に関する件：人体及び動物実験に関するEthical Approval(案)が本田編集委員長より提示され，委員会において若干字句修正のうえ，J. J. P. 投稿規定に追加されることが承認された．

7. 生理学領域における動物実験の基本的指針について，塚田動物実験に関する委員会委員長より委員会案の主旨説明がなされ，日生誌に掲載し会員の意見を集約することを前提として了承された．

8. 第67回日本生理学会大会開催地について：宮崎医科大学，石河延貞，美原　恒両教授のお世話で宮崎において開催されることが承認された．

第65回日本生理学会評議員会・総会議事要旨

日　時：昭和63年4月5日(火)　午後5時～6時30分
会　場：和歌山大学一般教育棟 G101 講義室
出席者：約300名
議　長：松下　宏，辻本　毅，辻　繁勝

議長は開会にあたり，恒例に従い評議員会・総会を並行して行うことを提案し，承認された．議題に入る前に逝去された戸塚武彦特別会員，並びに青木　健，東　健彦，五十島長太郎，尾崎俊行，大畑　進，斎藤十六，田北周平各評議員に対する追悼の辞が述べられ，黙禱が捧げられた．さらに，大村　裕幹事の学士院賞，入沢　宏幹事の紫綬褒章の受賞に祝辞が述べられた．

＜評議員会・総会報告＞

1. 庶務報告（伊藤庶務幹事）
   - 昭和62年12月末現在の会員数は一般会員3,286名，特別会員30名，名誉会員3名であること(表1)，又63年3月現在で評議員数が1,084名に達したことが報告された．
   - 第2回塚原仲晃記念賞が九州大学野間昭典教授に送られた．
   - 第14回日産学術研究助成に富山医科薬科大学小野武年教授が採択された．
   - 生物物理学講習会，日本宇宙生物科学第1回大会，第8回及び第9会バイオメカニズム学術講演会，第2回生体生理工学シンポジウム，第11回人間熱環境シンポジウム，第3回筋収縮のエナジエテイックス国際シンポジウム，第6回国際肥満学会を協賛する旨報告された．
   - 本年4月2日，和歌山市において，第65回日本生理学会大会を記念する和歌山市民講演会が生理学会主催で開催された．
   - 日本医学会評議員および連絡員の改選が行われ(任期2年)，評議員に酒井敏夫幹事，連絡員に馬詰良樹評議員が再選された．
   - 長崎大学熱帯病医学研究所を共同利用研究所として改組する計画について，生理学会からも要望書を文部大臣あてに送る．
2. 会計報告（本郷会計幹事）
   - 昭和62年度決算報告（表2）について説明がなされ，会計監事の監査を受けた旨報告があり，承認された．
3. 日本生理学雑誌編集報告（酒井編集幹事）
   - 日本生理学雑誌49巻の編集報告（表3）と50巻の編集・発行状況の説明がなされた．50巻の発行は現在やや遅れぎみであるが，なるべく同月同号で発行したい旨報告された．
4. J. J. P. 編集・会計報告（本田委員長）
   - J. J. P. 論文投稿状況の報告がなされた．国内からの投稿数に就いては大きな変化はないが，

表1　日本生理学会庶務報告
(昭和62年12月末現在)

会　員			
一般会員			3,286名
特別会員			30名
名誉会員			3名
準会員			
学校図書館			121部
研究所・書店			118部
寄贈及び交換			
外　国			22部
国　内			13部
合　計			3,593部
特別会員(30名)			
井上　章	井上清恒	伊藤真次	
伊藤　龍	市岡正道	内薗耕二	
岡　芳包	勝　義孝	勝木保次	
黒津敏行	斎藤幸一郎	銭場武彦	
高木健太郎	問田直幹	冨田恒男	
名取禮二	中村治雄	永井寅男	
長嶋長節	西田　勇	西丸和義	
福田邦三	福原　武	松田幸次郎	
三田俊定	簑島　高	山田　守	
吉井直三郎	吉村壽人	若林　勲	
名誉会員(3名)			
Sir John Eccles			
Ichji Tasaki			
Chandler McCuskey Brooks			

表2　日本生理学会昭和62年度決算報告

(自 昭和62年1月1日　至 昭和62年12月31日)

収　入

	62年度予算	62年度決算	増減	備考
(1) 前年度繰越金	1,829,784円	1,829,784円		
(2) 昭和62年度収入	29,120,000	32,285,606		
(内訳)				
会費	21,380,000	23,916,000	＋	
購読料	2,030,000	2,202,000	＋	
論文掲載料	1,600,000	1,176,602	－	
広告料	1,800,000	2,340,800	＋	13件
会誌分冊売	40,000	39,710	－	
預金利子	70,000	65,214	－	第一勧業銀行
日本医学会奨励金	200,000	100,000	－	
印税	200,000	444,500	＋	
論文表題集	1,700,000	1,840,000	＋	
雑収入	100,000	160,780	＋	教室史上巻他
(1)+(2) 合計	**30,949,784**	**34,115,390**		

支　出

(内訳)	62年度予算	62年度決算	増減	備考
会誌印刷代	13,000,000	12,356,144	－	49巻12号～50巻11号
会誌発送代	2,900,000	3,014,166	＋	同上
編集会議費	130,000	121,950	－	日本生理学雑誌
校正料	300,000	300,000		同上
原稿査読料	25,000	15,000	－	同上
大会援助費	500,000	500,000		和歌山医科大学
事務室使用料	2,275,512	2,446,116	＋	12ヶ月
事務室光熱費	320,000	306,953	－	
通信費	850,000	795,330	－	
事務費	850,000	647,762	－	
備品	150,000	255,620	＋	ワープロ，机他
会合費	200,000	333,920	＋	常任幹事会，委員会
旅費	1,500,000	1,791,610	＋	同上
人件費	3,400,000	3,414,479	＋	アルバイト含む
社会保険	250,000	232,839	－	
職員退職金積立	100,000	100,000		
論文表題集	1,700,000	1,617,670	－	
国際交流基金	250,000	250,000		
雑費	100,000	43,740	－	製本他
予備費	2,149,272	1,917,353	－	名簿製作に関する費用他
合計	**30,949,784**	**30,460,652**		
昭和62年度繰越金総額		3,654,738		
合計		**34,115,390**		

表3　日本生理学雑誌49巻(62年度)編集報告

49巻1～12号(8・9号合併)発行11回
49巻総頁数　741頁

＜内訳＞	編
原著	6
短報	1
総説	7
教育	2
学会抄録	8
会報	12
広場	6
追悼	1
その他	4
お知らせ	21
大会号	815題

尚，業績表題集は別冊として刊行.

海外からの投稿が増加している旨報告された.

- J. J. P. 決算報告がなされ，本年度から購読料の値上げ(8,000円から9,000円へ)を既に実施していること，現在の発行部数は国内配付1,145，海外配付410で1,600部である旨説明された.
- 日生誌の英文抄録号をJ. J. P.誌のsupprementとして発行することが常任幹事会で決まったので，明年度の第66回大会から実施する旨報告された．編集は当番幹事，日生誌，J. J. P. 誌の3者で行い，英文の添削のための添削料の徴収が必要だが，その他の詳細に就いては明年度大会のセカンド・サーキュラーでお知らせする予定である旨説明された.
- 時代の趨勢として，J. J. P. 誌でも論文投稿規程の中に，人体実験および動物実験に関する倫理規定を加える必要があり，投稿規程にEthical Approvalを追加することが報告され諒承された.

5. 教育委員会報告（中野委員長）
   - 教育委員会主催で4月5日行われた教育シンポジウム「統合カリキュラムの中での生理学教育を考える」が盛況であった旨報告された.
   - 先般実施された広重・入来両教授の生理学実習書改定に関するアンケート結果を根拠として，生理学実習書の改定を行うことが決められた旨報告された．今回は，学生用のBasic Courseと教官用のadvanced Courseに分け別の本として発行する予定であり，編集責任者は両方共に現教育委員の中から選ぶが，advanced Courseに就いては従来からの編集哲学を尊重する意味で，従来の編集責任者とも相談して改定を行う旨説明された.
6. 選挙管理委員会報告（竹内委員長）
   - 昭和62年8月に科学研究費の審査委員の候補者の選挙が行われ，その結果指名された候補者の氏名は日生誌に掲載された通りである旨報告された.
7. 研究費委員会報告（新島委員長）
   - 科学研究費分科細目に「中枢統合機能」を増設することを学術会議に申請中のところ，現在，重点項目として審議が行われている旨報告された.
   - 63年度科学研究費の概算要求額が決まったが，昨年度より8.4%増となり，特に重点領域研究，一般研究B，C，若手研究者用の奨励研究などの充実に向けられるものと説明された.
   - 民間からの研究助成金に就いて，委員会が，それぞれの内容の調査を行っており，資料が集まった段階で報告したい旨説明があった.
8. 動物実験に関する委員会報告（塚田委員長）
   - 生理学領域における動物実験に関する基本的なガイドラインを作るための委員会試案を作成した旨報告された．この案の作成にあたっては，国際的に通用するものであること．出来るだけ簡単なものであること．生理学には動物実験が必須であることの3視点に留意したとの説明があり，近々，日生誌のブルーページにこの案が掲載される予定なので，多くの会員から御意見を寄せられたい旨要望し諒承された.
9. 評議員選考委員会報告（本間委員長）
   - 評議員候補者53名（表4）を推薦することが報告され諒承された.
10. 日本生理学教室史編集委員会報告(望月委員長)
    - 日本生理学教室史下巻の原稿が，昨年10月に至り全部集まり，編集を行って印刷所に送付した．現在，医学，歯学関係の初校が終わっており，8月頃には再校になる旨報告があった．発行部数は上巻と同じく1,000部，1部定価15,000円とし，販売方法は本年末に刊行予定なので，10月頃から各教室あてに注文書を発送したい旨報

表4　昭和63年度日本生理学会新評議員名簿

(敬称略)

氏名	所属	氏名	所属
三木　健壽	産業医大・助手	有田　秀穂	筑波大・基礎医学系・講師
内田　勝雄	山形大・医・助手	児玉　逸雄	名大・環医研・助教授
渋谷　　泉	山形大・医・助手	村山　伸樹	熊本大・工・助教授
下内　章人	国立療養所山形病院・医員	伊藤　真一	熊本大・医・助手
戸塚　　武	愛知コロニー・心身障害研・室長	丸　　栄一	防衛医大・助手
石田　行知	三菱化成生命研・主任研究員	松本光比古	岩手医大・講師
北野慎一郎	東京女子医大・助手	高島浩一郎	岩手医大・助手
能勢　　博	京都府立医大・講師	菱田　不美	昭和大・教養部・教授
船橋　広三	岐阜大・医・助手	河谷　正仁	昭和大・医・講師
渡辺　和子	岐阜大・医・講師	松尾　龍二	大阪大・歯・講師
橋本　真明	山梨医大・助手	坂本　尚志	旭川医大・講師
吉岡　芳親	岩手医大・助手	古山　俊介	日大・松戸歯・教授
水野　義雄	大同工業大・助教授	寺田　信幸	山梨医大・助手
浦野　博秀	福井医大・助教授	有馬　利昭	防衛医大・助手
成瀬　　達	生理学研・助手	三川　　隆	生理学研・助手
青木　貴子	岐阜女子短大・講師	妹尾　広正	徳島大・医・助手
越田　　信	名市大医・衛生技師	佐野　敦子	徳島大・医・講師
玉置　陽子	大阪大・医・助手	中張　隆司	大阪医大・助手
紫藤　　治	金沢大・医・助手	宮本　　学	大阪医大・助手
佐々木和彦	岩手医大・医・講師	七條喜一郎	鳥取大・農・助手
妹尾　久雄	名大・環医研・助教授	竹村　京子	関西医大・助手
佐々木康人	広島大・歯・助手	堀　　雄一	杏林大・医・助手
宇佐美彰朗	東海大・体育・助教授	当間　　忍	千葉大・医・助手
木村　　弘	千葉大・医・内科・助手	野島　一雄	高知医大・助手
西林　賢武	千葉工大・助教授	古川　直裕	川崎医大・助手
里村　洋一	千葉大・医療情報部長	白井　幹康	国立循環器病センター・室長
小室　　仁	東京医歯大・助手		

告された．なお，初校時の加筆訂正に就いては内容，量をあまり変えない範囲で可能であるとの説明があった．

11. 生理科学研究連絡委員会報告（本間日本学術会議第7部長兼研連委員長）

- IUPS への本年度分担金 $8,700を支払ったが，この額はアメリカに次いで二番目に多額で，デレゲートとして5名派遣出来る旨報告された．
- 62年10月31日に近畿生理学談話会と同日に大阪大学に於いて，生理科学連合主催によるシンポジウム「細胞生理学から見た情報伝達」が行われた旨報告があった．
- 第14期学術会議に対して生理学会から議員候補として伊藤幹事，推薦人として本間幹事，本郷幹事，推薦人予備者として熊田教授をそれぞれ申請した旨報告された．又，6月9日には推薦人会が開かれ生理科学分野の各候補から1名を選ぶことになっている旨説明があった．

12. 国際生理科学連合報告（伊藤 IUPS 理事）

- 次回の IUPS 大会は，フィンランドのヘルシンキで64年7月9日から15日迄開催される旨報告があった．プログラム最終案によると，インバイテッドレクチャー67件，コングレスシンポジウム 108 件が計画されているが，そのうち星教

表5　日本生理学会昭和63年度予算

（自 昭和63年1月1日　至 昭和63年12月31日）

		収　入	
(1)	前年度繰越金	3,654,738円	
(2)	昭和63年度収入	29,390,000	
	（内　訳）		備　考
	会費	21,960,000	(会費7,000円×3,374×0.9＋臨時会費)
	購読料	1,920,000	(準会費9,500円×224×0.9)
	論文掲載料	1,200,000	
	広告料	2,000,000	
	会誌分冊売	40,000	
	預金利子	70,000	(第一勧業銀行)
	日本医学会奨励金	200,000	
	印税	200,000	(生理学実習書，用語集)
	論文表題集	1,700,000	
	雑収入	100,000	
	(1)＋(2) 合計	**33,044,738**	

	支　出	
（内　訳）		備　考
会誌印刷代	13,000,000	(49巻12号～50巻11号)
会誌発送代	3,000,000	(同　上)
編集会議費	130,000	(日本物理学雑誌)
校正料	300,000	(同　上)
原稿査読料	20,000	(同　上)
大会援助費	500,000	(岡山大学)
事務室使用料	2,502,984	(12ヶ月)
事務室光熱費	310,000	(同　上)
通信費	850,000	(会誌外通信)
事務費	700,000	(コピー，事務雑費)
備品	100,000	(宛名カード用ひきだし)
会合費	350,000	(常任幹事会，委員会)
旅費	1,800,000	(同　上)
人件費	3,600,000	(アルバイト含む)
社会保険	250,000	
職員退職金積立	100,000	
論文表題集	1,700,000	
国際交流基金	250,000	
雑費	100,000	
予備費	3,481,754	
合計	**33,044,738**	

授がピッツ記念レクチャラーに指名されたのをはじめ合計4名の日本人がレクチャラーになっており，シンポジウム座長にも5名の日本人が起用されている旨説明された．

13. 第66回（昭和64年）日本生理学会大会の準備状況（堀当番幹事）

- 4月5，6，7日岡山大学津島キャンパスの岡山大学教養部で開催予定，演題受付は無制限とすることが報告された．又，宿泊は日本交通公社に委託するが，A，B，C級のホテルが2,400室，宿泊可能であり，会期中の宿泊に関しては充分余裕が有るとの説明がなされた．

14. 第65回（昭和63年）日本生理学会大会に関する報告（松下当番幹事）

- 演題発表数819題の内，口演614題，ポスター展示205題であること，大会参加申込数1,455名，当日参加申込者149名，合計1,604名が参加したことが報告された．又，生理学会新入会者が138名あったことも報告された．

＜議　題＞

1. 昭和63年度予算（本郷会計幹事）

- 収入，支出共に昨年の実績と大きな変化はないが，支出として事務室の使用料値上げにともなう額が計上されたこと，又，本年秋に開催される神経科学ワークショップへの3名の講師派遣費$2,000を来年度，国際交流基金の中から支出することに就いて説明がなされ承認された．（表5）．

2. 新評議員推薦

- 選考委員会推薦の候補者が承認された（表4）．

3. 特別会員推薦

- 松本淳治，横山正松，須田　勇の3氏について特別会員としての推薦があり，それぞれの推薦者代表より略歴，業績等の紹介，推薦理由の説明があり，総会の賛同により承認された．

4. 会則の付則および内規(6)の一部改正について

- 表6の如く，現行部分（左側）を改正（右側）することが承認された．

5. 第67回（昭和65年）日本生理学会大会開催について

- 宮崎医科大学，石河延貞，美原　恒両教授のお世話で宮崎で開催されることが承認された．

評議員会・総会終了後，前回当番幹事本間三郎氏より，今大会当番幹事に謝辞が述べられた．

表6

日本生理学会会則，附則 「常任幹事に関する事項」（現行）	同 「常任幹事に関する事項」（改正案）
全国8地区に分け各地区の評議員の互選によって常任幹事を定める．地区およびその定員は下表による．任期は3ヶ年とし重任を妨げない．選挙の際選挙管理委員会を設け選挙事務を委嘱する．選挙の結果は日本生理学雑誌上に報告する．	全国を8地区に分け，常任幹事は各地区の評議員の互選により選出される．地区及び定員は下表による．任期は3年とし重任を妨げない．各地区の評議員は，地区の定員に担当する数以内の氏名を所定の投票用紙に記入して投票を行う．投票は無記名とする．投票用紙に同一氏名を複数記入した投票は無効とする．得票数同数の場合は入会順，年長順に順位を決定する．欠員を生じた場合は，常任幹事会の議を経た後，次点者を以てこれにあてることができる．この場合の任期は前任者の残任期間とする．選挙事務は選挙管理委員会に委嘱する．選出された常任幹事の氏名は日本生理学雑誌上に報告する．
日本生理学会会則の内規　(6)（現行）	同内規　(6)（改正案）
6) 本会に次の常置委員会をおく． 日本生理学雑志編集委員会，The Japanese Journal of Physiology 編集委員会，評議員選考委員会．	6) 本会に次の常置委員会をおく． 日本生理学雑誌編集委員会，The Japanese Journal of Physiology 編集委員会，評議員選考委員会，選挙管理委員会．

アンダーラインの所が主な改正案を示す．

事務局から

1989年6月9日～14日ヘルシンキで開催される第31回国際生理科学連合の最後のアナウンスメントのパンフレットが日本生理学会に届いております.

必要の方は，事務所にご連絡下さい.

なお国際生理科学連合の会員名簿が出来ました. 49ヶ国24,000名の生理学者の名前がリストアップされております. 日本生理学会でまとめて注文した分がありますので，御入用の方ははがきで日本生理学会にお申込み下さい. 価格は1冊1,600円です.

支払いは，第一勧業銀行本郷支店 普通預金1332610 日本生理学会 本郷利憲宛にお振込み下さい.

日本生理学会会費払込みについてのお願い

昭和63年度会費7,000円未納の方に振替用紙を添付してあります. ご多忙のところお手数ですが，お払込み下さいますようお願いいたします. 所属などご変更の場合はその旨ご連絡下さい. 本会の年度は1月～12月となっております. 次年度より退会の場合は前年度の11月末日迄に文書でお申出下さるようお願いいたします.

尚 JJP の購読料を生理学会会費と一緒に払込まれる方がおられますが，JJP は日本学会事務センター扱いで，本会とは異なります. お間違いのない様よろしくお願いいたします.

日 本 生 理 学 会
〒113 東京都文京区本郷 3-30-10 布施ビル
電話 (03) 815-1624
振替口座 東京 3-86430

日本生理学会評議員 特別会員 昭和大学名誉教授 井 上 清 恒君は，昭和63年7月27日にご逝去されました. ここに謹んで哀悼の意を表します.

〔編集後記〕

第65回日本生理学会大会は，当番幹事和歌山県立医科大学生理学教室の松下　宏学長，辻本　毅，辻　敏勝両教授により，意欲に満ちた計画の下に盛会裡に行われた．演題819題という大きな学会運営に，思う存分の手腕を振われ，お陰で会員一同学会出席の楽しみを満喫しました．心からお礼申し上げます．

さて，日本生理学雑誌第50巻8-9合併号(1988)は，一つの日本生理学会における記念号として後々までも語り継がれることになるでしょう．長いこと定着してきた大会の抄録が掲載されるのは，本号を最後として消えて行くからです．次大会の抄録は，Jpn. J. Physiol. の Supplement として国際場裡にデビューすることになります．会員各位の研究成果が，迅速に報道され且つ priority の確保を願う声は，相当の以前からありました．大会抄録が，和文から英文による編集に改って(第56回大会，1979年)からも9年の経過があり，この間に多くの議論が持たれたことは衆知の通りであります．日本生理学雑誌が，大会の抄録を掲載して50巻を迎えたことは，歴史的に大きな役割を演じて今日に至ったことを意味します．

大会抄録が他誌に移されたからと云って，機関誌としての義務が終ったわけではありません．年度毎の当番幹事の日本生理学会大会を終えての言葉，大会記念写真，常任幹事会，総会並びに評議員会記録は，是非共掲載されるべきであります．また，大会抄録が Jpn. J. Physiol. に移されても，学術発表の内容が解る様な姿を遺しておくべきでありましょう．例えば，予稿集のプログラムにある和文演題は，予稿集で終ることなく，日本生理誌に転載することにより，抄録は無くても大会の特長なり雰囲気は，後々までに伝えられるでありましょう．こうなると，予稿集の生命は，学会当日だけに終らず，フロッピーで鶴岡印刷に渡して下されば，どの様な形にも日本生理誌上に延長されることになります．

JJP 大会抄録に関連して，すでに50巻6号，224頁(1988)に，日本生理誌及び Jpn. J. Physiol. の両編集委員は抄録号編集委員になることを報じました．従って，JJP, Supplement には抄録号編集委員全員の御名前を掲げることになります．御了承下さい．

第31回国際生理科学会議 (HELSINKI JULY 9-14, 1989) の情報が次々と入って来ております．ヘルシンキ大会の展示委員会から biomedical science 並びにこれに関する technology に参加の希望がありました．Exhibition Announcement および registration form は以下でお求め下さい．

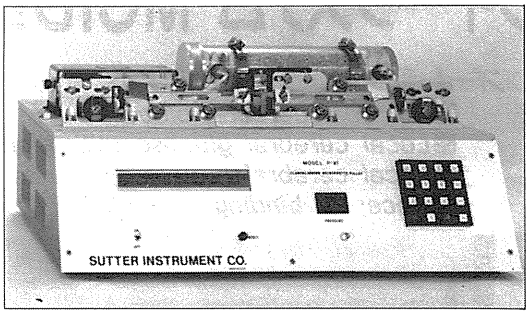
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(酒井敏夫)

編　集　委　員

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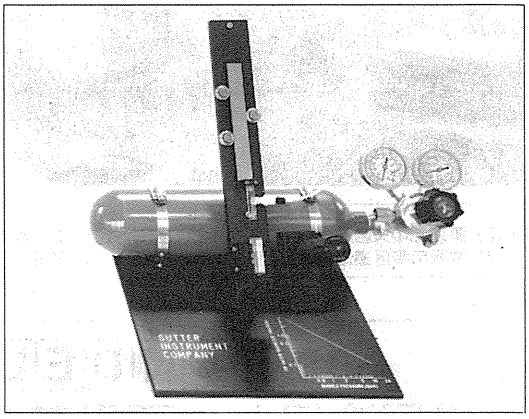
マイクロ・インジェクション手法にとっては，良好な微小電極の入手が必須条件です。



米国サッター社製プラーP-87型は，下記1，2の電極を1台で作成します。

1. 細胞内に注入するための先端部が鋭利な電極。
（標準で0.06ミクロンを出荷の際に引き，SEMにての写真を添付してきます。）
2. ホールドさせるための先端部を鈍化させ，陰圧にて吸収する電極。

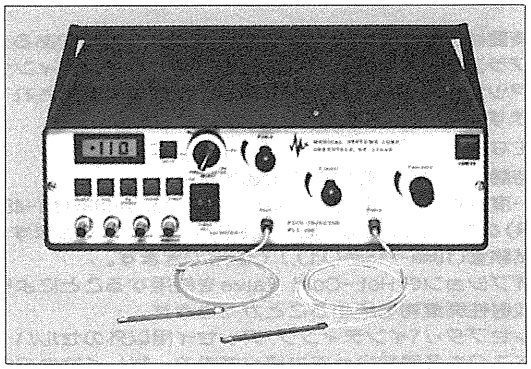
マイクロ・インジェクション手法にとっては，チップ径の測定が必須条件です。



米国サッター社製チップ径測定装置LW-87型は，従来の電極抵抗値より推測する方法に比べ正確で、下記の特長があります。

1. ガラス電極を破壊せずにチップ径の測定ができる。
2. 電子顕微鏡での測定が必要ありません。
3. 電極の材質や形状，とくに内径／外径比に影響なく測定できます。

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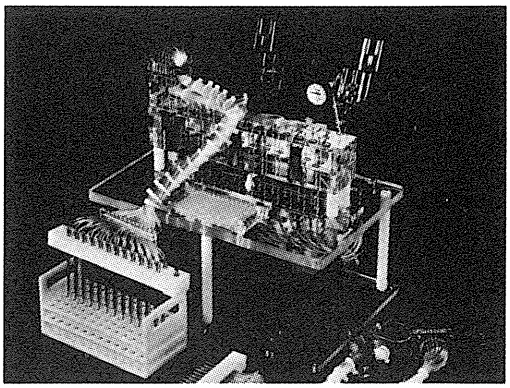
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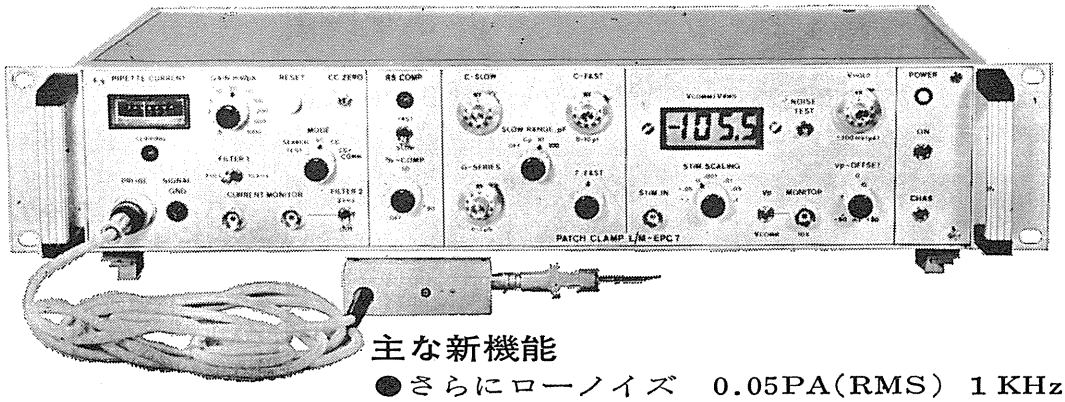
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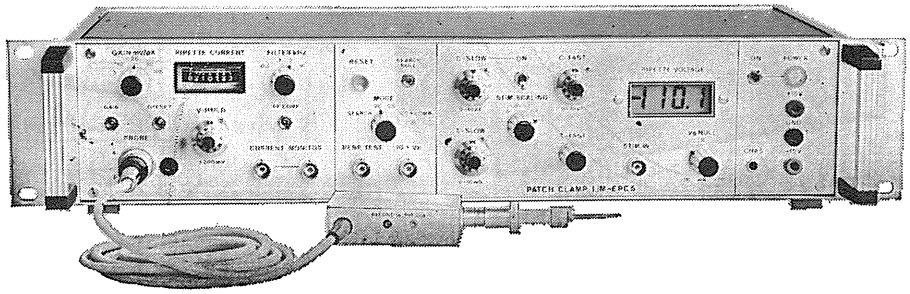
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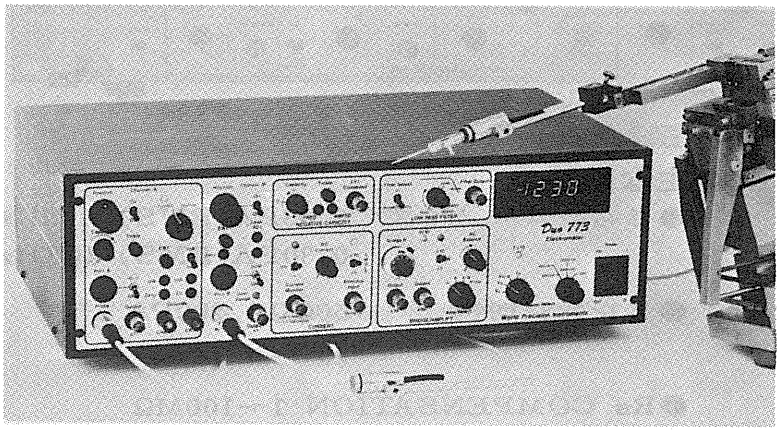
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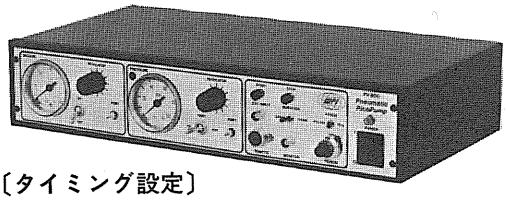
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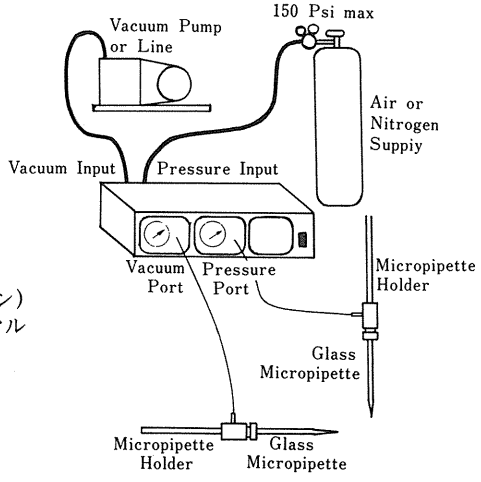
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〔タイミング設定〕

期間モード	GATED（入力シグナルによる） TIMED（内蔵時計による）
パルス始動	手動、外部入力及びフットスイッチ（オプション）
パルス幅	TIMEDモードで10msec～10sec（10回転ダイヤル設定）最低設定幅は設定圧による。 (ex. 8msec at 0 psi, 3msec at 100psi)
精度	フルスケールの0.1%
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MICROSLICER

DTK-3000W

生理・薬理学の分野において、主に電位差測定にラット、ネコなどの新鮮脳切片(200～500μm)が用いられています。従来は、カミソリの刃をつかった手作業、あるいは未凍結切片作製用のミクロトームを使用していましたが、切片の厚さが一定しなかったり、切片作製に膨大な時間がかかり、大きな切片や薄い切片が切りにくいという難点がありました。「マイクロスライサーDTK-3000W」は、これらの欠点を克服し、先生方のニーズにこたえるべく開発されました。

【特　長】

- ラットはもちろんネコ・サルの全脳までも貼付可能なワイドな試料台(70×70㎜)。
- 新鮮脳で約50μm、固定(ホルマリン・グルタール等)組織で10μmの均一な薄さで連続切片作製可能。
- 試料台の任意上昇(5～1,000μm)の自動化により、作業時間が一層短縮され、また操作性が格段にアップ。

【姉妹機】

DTK-1000・DTK-2000・DTK-3000

堂阪イーエム

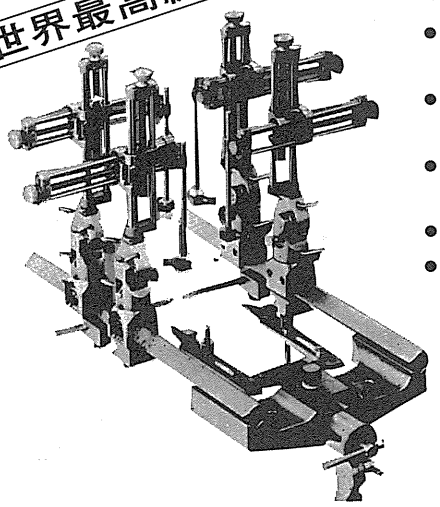
本社・工場/〒601-11 京都市左京区静市市原町1032の3
電話 (075) 741—3069

DKI 米国David Kopf社　　Meiwa

実験動物用ステレオタクシック装置

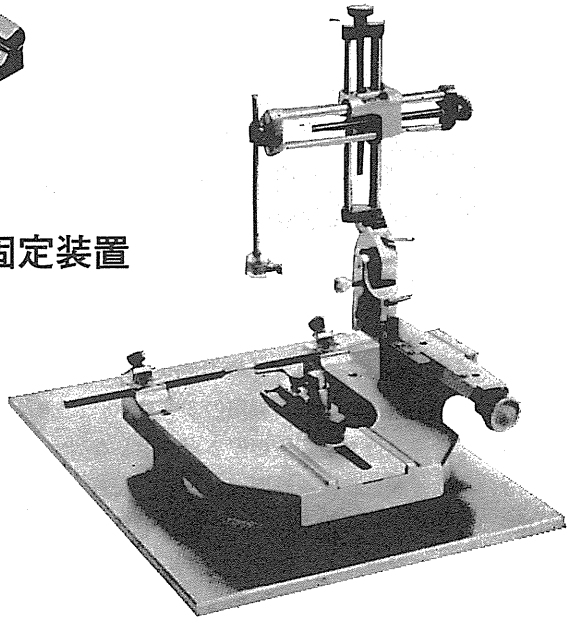
米国DKI社は、実験動物用脳定位固定装置及び関連機器の製作に関して世界のリーダーシップとしての役割を果しています。同社のねらいは進歩的な学者に、精巧で信頼できる研究用器械を提供することにあります。これらの装置は現在世界中で数多く使われています。

世界最高級品!!



#1504 犬・猿用脳定位固定装置

- 犬、猫、猿、うさぎ用からラット等の小動物にいたるまで附属品の交換で適用できます。
- 素材は特殊合金で精密加工してあり、長年酷使しても歪はなく精度は保証されています。
- 電極の位置設定及び復元は従来不可能とされていたほどの正確さでできます。
- 電極挿入の角度調整は自在です。
- メンテナンス・フリーです。



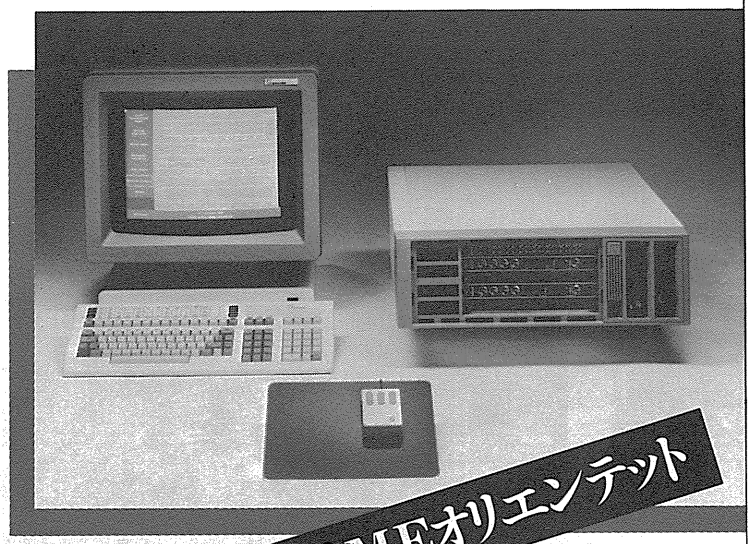
#900 小動物用脳定位固定装置

- ラット、マウスの研究に最適です。
- 操作が簡単で精度の高い万能の装置です。
- エレクトロード・マニプレーターは3方向とも0.1ミリの副尺付です。長年の使用にもマニプレーターにくるい・がたつきはありません。
- フレイムの反対側にも別のマニプレーターをつけることもできます。

盟和商事株式会社
大　阪：大阪市住吉区千躰2－4－25
〒558　TEL　代表（06）674－2222番(代)
東　京：東京都新宿区西新宿6－12－4（コイトビル）
〒160　TEL　代表（03）344－3901番

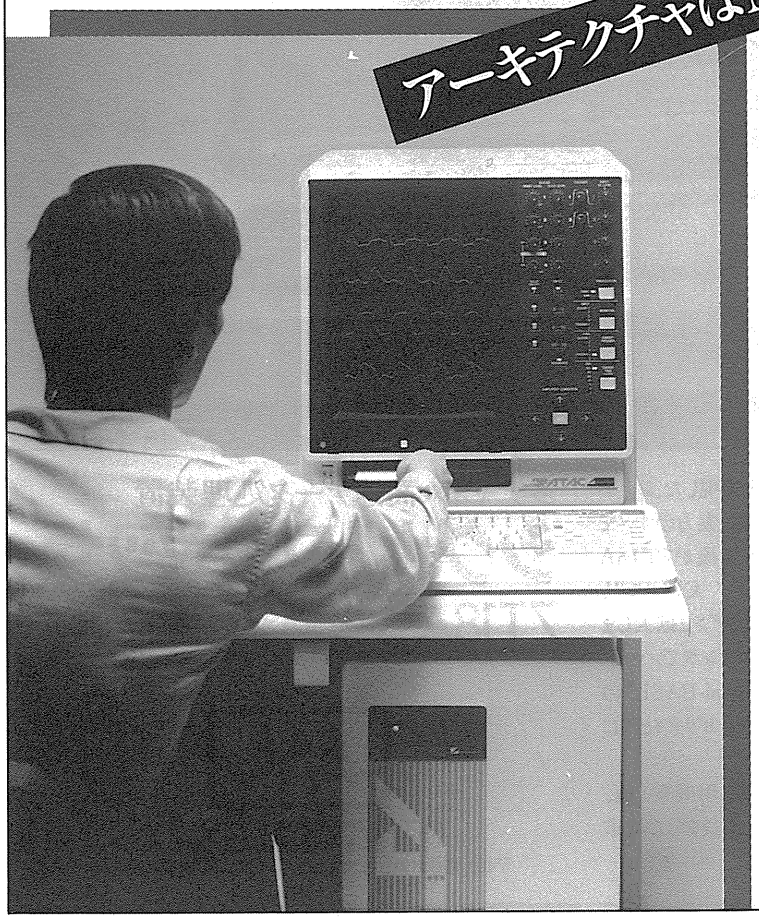
生体信号の高速リアルタイム処理は日本光電におまかせください。

医用データ処理装置（MASSCOMP）MC-5400・5500



- 1 μsの連続高速AD変換が可能
- データ取り込みは驚異の256chが可能
- 32ビットCPUを核にマルチCPU方式を採用
- 専用高速メモリバス、周辺にはマルチバスを配したデュアルバス構造を採用
- UNIXでリアルタイムを強化したRTU™オペレーティングシステムを採用
- 独立したグラフィックプロセッサにより、解析結果をカラーで高速ディスプレイ（1152×910分解能）
- 5.5インチフロッピィディスクとハードディスク（71～272Mバイト）を内蔵

アーキテクチャはMEオリエンテット



医用データ処理装置 ATAC-3700

- 1 μsの高速AD変換を実現
- フーリエ変換処理は高速20ms/1024点
- ランダムスキャン方式で実時間処理波形や入力信号をモニタ
- 豊富な波形処理命令語を持つ BASIC 言語を標準付属
- 3.5インチ1.2Mバイトフロッピィディスクを2基内蔵
- 高性能なアナログコンディショナを16チャネル装備可能

エレクトロニクスで病魔に挑戦する

NIHON KOHDEN

日本光電

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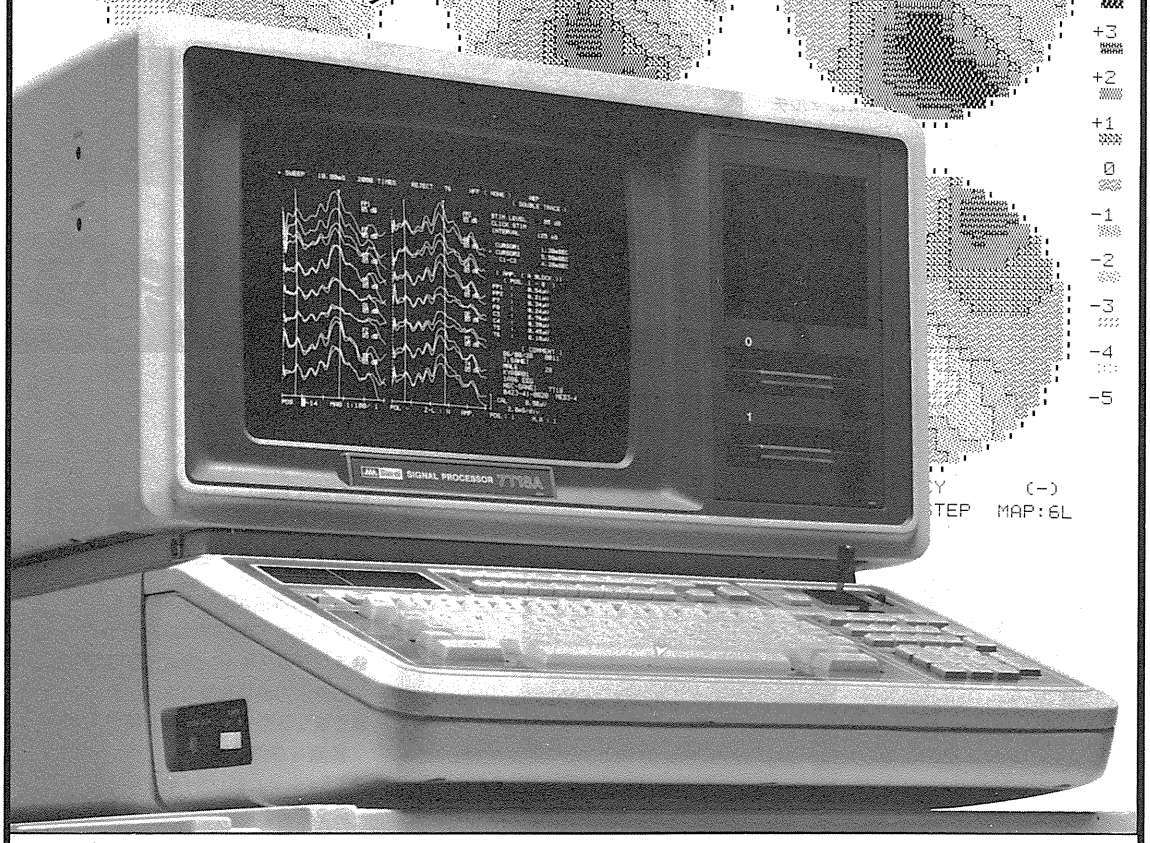
☎03(953)1181

先進技術を医療に

Human-touch Technology

おかげさまで40年。

スピードが、グラフィックが、生体信号処理をかえた。



オンラインの多チャネル生体信号処理を実現した、シグナルプロセッサのベストセラー7T17。その実績と実力のすべてを受け継ぎながら、一段と成長した最新鋭機が7T18Aです。定評ある処理スピードはさらに向上、実装メモリも4Mバイトにパワーアップして適応領域がグンと拡大しました。きめ細かな画面表示はサーマルプリンタでハードコピーがとれます。生体信号処理用Signal-BASICの特殊コマンドが強化され、優れたフレキシビリティと共に高次の解析をサポートしています。

※三栄レポートNo.38（Signal-BASICの応用例集）他、各種資料が用意されております。担当営業員までご請求ください。

多チャネル高速データ処理装置

シグナルプロセッサ

7T18A　医療用具承認番号60B第1891号

日本電気三栄

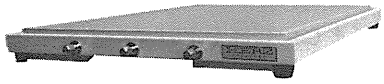
〒160 東京都新宿区大久保1-12-1 ☎03(209)0811(代表)

HERZ

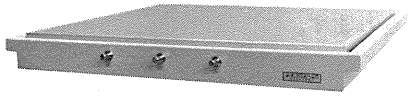
「最先端技術」に直結する「ヘルツの防振システム」

HERZ「卓上型空気ばね式防振台」「大形空気ばね式防振台」「光学実験台・フラットベンチ」は、国公立試験研究機関、大学及び民間各産業における基礎技術開発また、工場における品質管理・検査等、先進産業に大きく貢献しております。

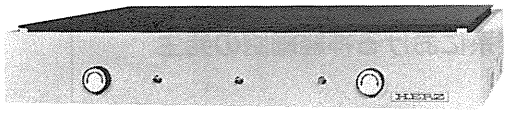
研究室や工場検査室で簡便に使用できる「卓上型空気ばね式防振台」は、過去5年間で3,000台を上回る納入実績を誇っており、また「大形空気ばね式防振台」に使用される「光学ベンチ」は、社内生産をしているため国内外で最大の「10m×2m」までの面積まで製作しております。



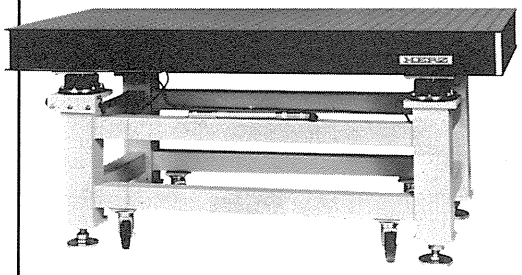
●卓上型空気ばね式防振台 ST-45



●卓上型空気ばね式防振台 ST-65



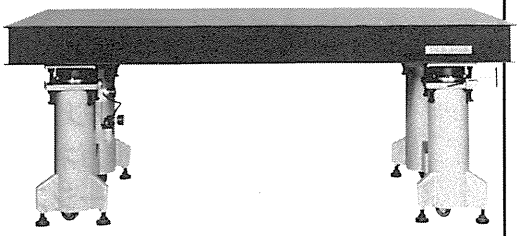
●卓上型空気ばね式防振台 LHA-300



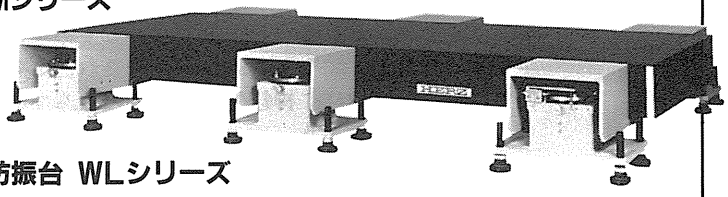
●大形空気ばね式防振台 LA·LMシリーズ



ダンピングフリー（固有振動数コントロール付）
●大形空気ばね式防振台 DFBシリーズ



ダンピングフリー（固有振動数コントロール付）
●大形空気ばね式防振台 DFシリーズ



大重量機器搭載用
●大形空気ばね式防振台 WLシリーズ

「空気ばね式防振台」「フラットベンチ」のカタログご請求、お問い合わせは営業部宛ご連絡下さい。

ヘルツ工業株式会社

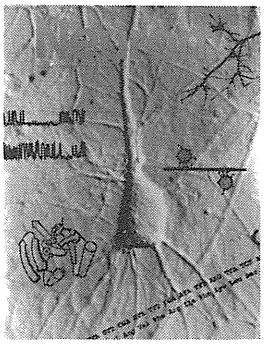
営業部 〒252 神奈川県藤沢市遠藤1739-1番地
TEL. 0466(88)1301　FAX. 0466(88)3273
本　社 〒252 神奈川県藤沢市遠藤1980番地
工　場 TEL. 0466(88)3311

創刊'88

Cell Press, Inc.

神経生物学の新しい展開!

NEURON



Editors : Zach Hall, Jim Hudspeth, Lou Reichardt

月　刊　法人¥59,000/年　個人¥32,000/年

NEURONは、めざましい発展をとげている分子生物学および細胞生物学的な神経学の研究に主眼を置き、神経細胞学にとって重要な論文を幅広く掲載しています。又、Cell 誌と同様に、速報性を備え、論文や評論は12週間以内にカバーされます。

NEURONには次のようなテーマの論文が掲載されます。

- ●神経細胞の遺伝子および蛋白質の分子生物学
- ●脊椎および無脊椎動物の神経系における神経細胞の発生
- ●イオン系の組織と作用
- ●感覚情報の伝達
- ●細胞および分子レベルでの神経の可塑性
- ●神経遺伝学と神経疾患の細胞および分子レベルでの研究
- ●ニューロン、グリア、およびレセプターの細胞骨格
- ●軸流動とオルガネラの選択
- ●エクソサイトーシスと分泌
- ●刺激因子の同定とその役割
- ●細胞表面の分子およびレセプター
- ●シナプシスのシグナル伝達の第２次メッセンジャー

評論は、またNEURONの重要な部分であり、毎号、神経生物学の主要な発展に関する評論やミニ評論が掲載され、この分野及び関連分野の発展動向に関する情報は、神経生物学者のみならず、多くの研究者の関心をひくことになりましょう。

■1988年「円」価格は、版元の都合で変更されることがありますので、予めご了承下さい。
■お問い合わせは直接本社「マーケティング部」までお願いいたします。■カタログご請求下さい。

〈日本総代理店〉ユサコ株式会社

本　社〒105 東京都港区新橋１丁目13番12号堤ビル　☎(03)502-6473
営業所：大阪☎(06)344-6624　名古屋☎(052)931-2601
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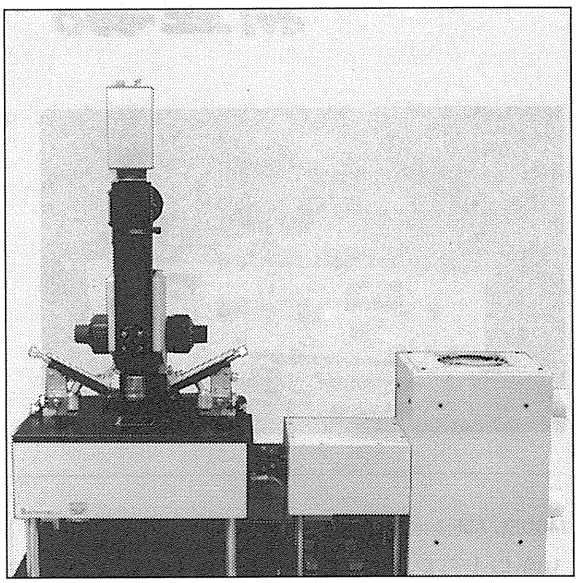
USACO®

新製品

細胞内カルシウムイオン濃度計測

蛍光顕微測光システム

M-1000 , M-500 シリーズ



当社にて開発された新方式のモノクロメータの採用と、微弱蛍光測定用に特に開発された光減衰率の非常に少ない顕微測定装置は、新世代の細胞内情報の測定システムです。

特　長

1.新方式のガルバノミラー採用に依りPH,DNA定量、蛍光抗体測定にも応用でき、新しいプローブにも対応できます。
又、当社開発の膜電位電流解析ソフトと組み合わせる事に依りカルシウムイオン濃度とカレントとの相関関係を知る事ができます。

2.３種類の測定に対応できます。
2波長励起1波長蛍光測光　(Fura 2)
1波長励起1波長蛍光測光　(Quin 2)
1波長励起2波長蛍光測光　(Indo 1)

3.超高感度カメラとフォトマル測光の使用により、カルシウムイオン濃度の二次元的な変化と高速変化の測定が可能です。

4.石英ファイバーを利用する事に依り臓器表面のカルシウムイオン濃度の測定も可能です。

5.豊富なカルシウムイオン濃度解析ソフト
擬似カラー表示,
濃度変化のグラフ表示,
濃度分布の経時変化表示,
濃度分布の３次元解析,
水平・垂直分布濃度表示
(M-1000型対応)

6.豊富なライブラリーソフト
細胞動態計測ソフト,
細胞形態計測ソフト,
細胞内微弱蛍光測定ソフト,

株式会社インターデック・ジャパン

〒532 大阪市淀川区宮原２丁目14-10
中尾ロイヤルビル8F
PHONE(06)397-3681(代)

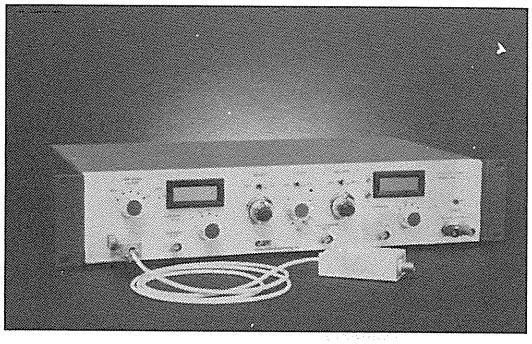
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横浜西口Kビル2F
PHONE(045)311-7911(代)

資料請求券
M-1000
M-500 シリーズ

グッドニュース

General Bio-Engineering社より

Large-Current Whole-Cell Clamp 新登場。

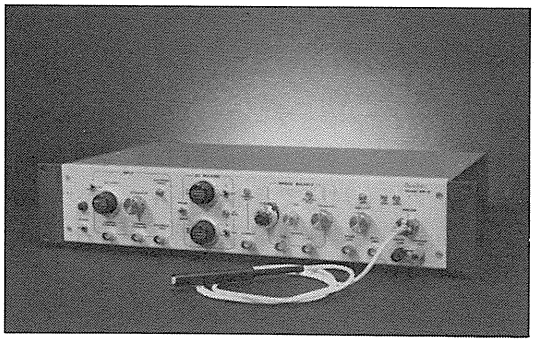


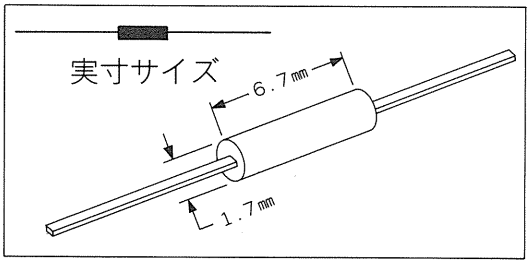
MODEL HAY-1 Whole-cell Clamp

ノイズを極限まで減らして面倒な周波数補償を不要にした使いやすい1,000nAの大電流Whole-cell Clampが可能です。シリーズ、レジスタンスの補正も容易で心筋のNaチャンネルの研究にも最適です。微小電流用プローブもあります。

MODEL AM-2 (Single型)

10年以上の長期にわたって不変の支持を誇るバイオダインエレクトロニクス社のAMシリーズ微小電極用増幅器。電極挿入を容易にするプッシュボタン発振器などいろいろ便利な機能が喜ばれています。差動型のMODEL AM-4もあります。





生理学用アンプ、pHメータ等の科学機器に欠かせないハイインピーダンスアンプに最適な精密超高抵抗器。10MΩから10GΩまでローノイズ。シャント容量を0.08pFに押さえてあり、負性温度係数、超高抵抗にもかかわらず、大きさは1.7㎜×6.7㎜という超小型ですからプローブの設計も容易です。

お問合せは

ゼネラル バイオ エンジニアリング社総代理店

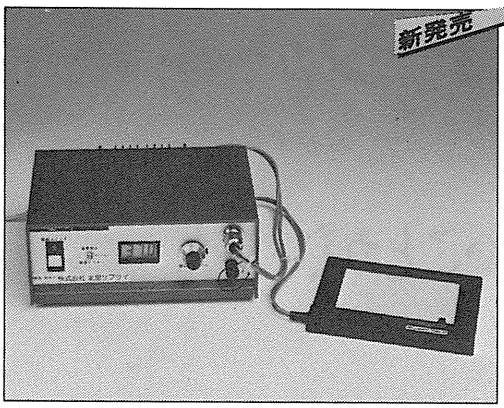
宮満産業

岩手県宮古市宮町３丁目10—16

TEL 0193—64—1965

FAX 0193—64—1964

至適温度で生体組織の顕微鏡観察が容易。



顕微鏡用透明加温板

マイクロウォーム・プレート®

デジタル表示
設定温度モニター付 **DC-MP10DM**　特許出願中

【特徴】

■フィードバック方式による精密温度コントロール。
■徹底的なシールドによる電気的ノイズカット。

【用途】

■各種細胞の定温培養状態の観察や電位測定。
■精子の活力検査や受精卵培養状態の至適温度下での観察。
■生体組織に対する薬理作用の観察。
■小動物(マウス、ラット)の生体電流測定。

⊙保温カバーケース(CO²混合ガス導入口付):オプション

- 温度設定　室温～50℃(±0.2℃at37℃)
- 温度表示　デジタル(1/10℃)
- 加温板寸法　DC-MP10DM/84×106㎜(厚サ1㎜)

安定した一定温度の透明加温板!

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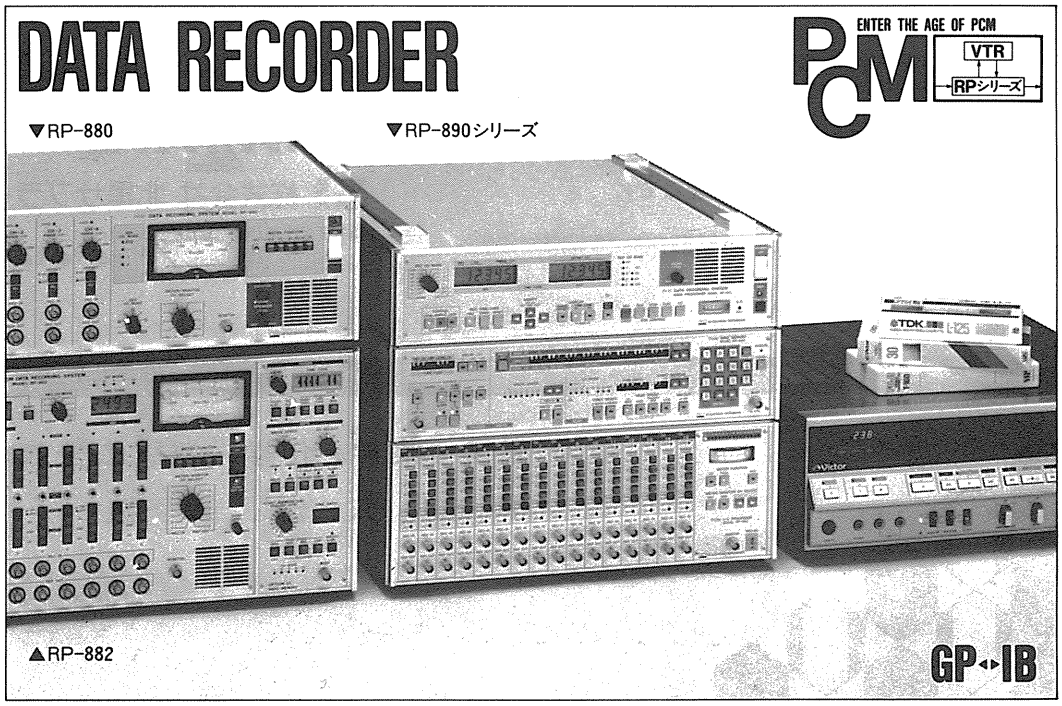
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エヌエフのデータレコーダがPCM方式なのは、PCMにしか出来ないことが、いろいろあるからです。



エヌエフの《PCMデータレコーディングシステムRPシリーズ》なら、

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❹取扱いが簡単。〔ゼロ点調整などが不要だから〕

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《PCMデータレコーディングシステムRPシリーズ》には、

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■4チャネルメモリ内蔵

４チャネル同時に記憶可能。
（２チャネル時1024ワード、４チャネル時512ワード）

■4波形セーブ可能(1チャネル)

異なる条件下での波形の相互比較が容易にできます。

■メモリ読み出し時のX軸拡大可能(×5)

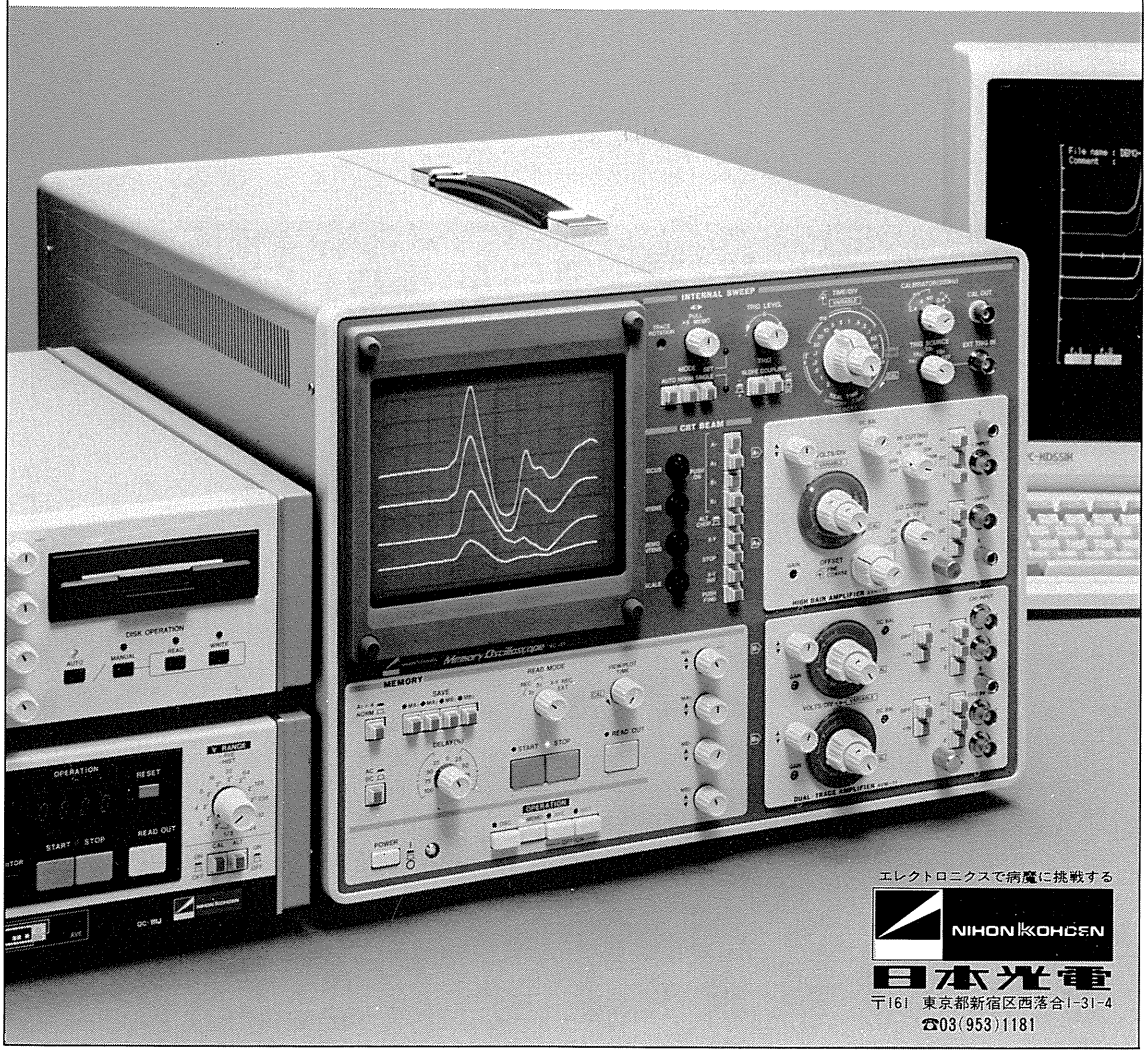
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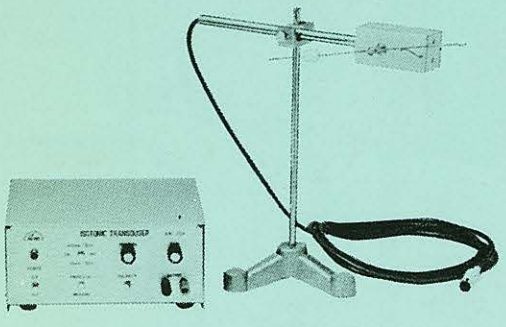
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