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PCMデータ・プロセッサー
—PCM-DP16型—



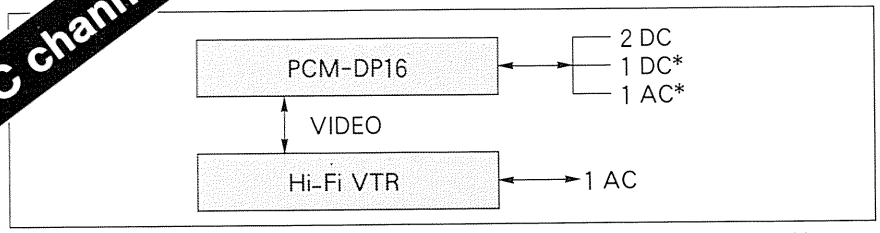
PCM-DP16型はカレントクランプ、パッチクランプ、ボルテージクランプを含めた生理学現象のあらゆるアナログデータをPCM信号に変換する装置です。
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また、市販のVTRテープを使って長時間の記録が可能なので、大量のデータを安価に記録できます。

特　長

1．SN比が良く(80dB程度)記録データが劣化しない。
2．周波数特性が良い(DC～15KHz)。
3．長時間の記録ができる(最大でVHS 8H、β 5H、8ミリVTR 4H)。
4．記録密度が高い(0.3Gbyte/H)。
5．入出力レンジが±10Vあるのでコンピューターの A/D 基板との接続が容易。
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AC*チャンネルは音声記録用として使用できます。

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『生理学教育の中で「死」をどのように捉えるか』

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中馬一郎(大阪大・医・生理)

中野昭一(東海大・医・生理)



第64回　日本生理学会大会　　昭和62年４月１日～３日　於 千葉大学西千葉キャンパス

第64回日本生理学会大会を終えて

第64回日本生理学会大会
当番幹事　本間三郎・本田良行

第64回日本生理学会大会（第22回日本医学会総会第三分科会）を昭和62年4月1日から3日までの3日間，千葉大学西千葉キャンパスにおいて開催いたしました．天候の不順にもかかわらず，多数の生理学関係者（1,627名）が大会に参加されましたことに心からお礼申しあげます．

本大会の準備にあたっては，生理学会の伝統を踏まえ，シンポジウム・特別講演などの特別企画は最小限とし，一般研究発表（口演，ポスター発表）が円滑かつ充実して行われるように配慮いたしました．第60回日本薬理学会総会が同じ千葉大学で同時期に行われたのを機会に，両学会研究者に共通の話題についての合同シンポジウムを開催いたしました．これが唯一の特別企画となりました．両学会の会場が離れていたための不便もありましたが，生理学会会場で行われた合同シンポジウム（循環，神経ペプチドの生理と薬理）には多数の聴衆が集まり，これらの分野についての関心の強さおよび研究者数の多さを物語るものと思われました．ご協力頂きました諸先生に厚くお礼申しあげます．毎年行われている教育シンポジウムでは，今回は生理学研究者の立場から『死』の問題をどのようにとらえるかについての検討を行いました．生命現象を扱う私達自身にとって，このような根本的な問題についての深い洞察が必要な時期にきているといえます．

本大会の一般演題申し込み総数は815題であり，このうち4題の取消がありましたが，口演621題，ポスター190題が10会場にわかれて発表されました．申し込み時点においても口演発表希望が圧倒的に多く，ほぼこれにしたがってプログラムを編纂いたしました．この傾向はここ数年変わらないように思われます．分野（分類）別の演題数は多い順に次のとおりでした．循環（59題），細胞生理（52題），視覚（47題），興奮性膜（41題），体温調節・発汗（40題），自律神経（36題），能動輸送（36題），シナプス・終板（35題），以下呼吸，脳幹，心筋などの順です．これらの中には境界領域の研究発表が多く，今回も踏襲した従来の分類に改善の余地があると思われます．例えば数項目に分散している各種自律機能の中枢性制御に関する発表を，新たな一，二の分類にまとめることも可能かもしれません．また，分類別の発表演題数にここ数年の継続した増減がみられ，研究対象や各分野別研究者数の変遷を窺い知ることができました．発表演題数のきわめて少ない分類項目を，他の項目に吸収する試みも今後必要と言えましょう．口演発表時間10分，討論5分，スライド10枚以内という規定は今後も維持されるものと思われます．ポスター発表に関しては，種々の意見があると思います．しかし，全く自由に討論できる場を提供した今回のような単純な形式でも十分成果をあげうるものと判断されました．

各分野別の集会・研究会も13のグループ・ディナーとして行われ，この形式の集会が定着したかに思われますが，それだけに新鮮さに欠け，一考を要する時期に来ているようです．大会事務局としては，会場のみを用意し，集会の運営は世話人の先生方におまかせ致しました．したがって各研究者がどのグループに属しているのか，また適当なグループがないためディナーに出席しておられない研究者などの実態を把握することはできませんでした．また各グループにわかれるために多少閉鎖的になる可能性があり，さらに集会の運営に問題を生じている懸念もあるようです．本来の目的である会員相互の交流の場として，若手を含めた多くの研究者が意欲をもって参加できるよう，今後この問題についての幅広い議論が行われることを期待します．

総会・評議員会にはかつて無いほどの多数の参加があり，時間の制約にもかかわらず十分な議論が行われたものと感謝しております．

大会の運営に関しましては，経費節減のため各種のサービス業務を極力削減せざるをえず，また，大会事務局が全くの手仕事で行ったことも多く，このため多くの不便とご迷惑をおかけ致しました．ここに無事大会を終了できましたことは，参加されました会員各位のご理解および大会運営にご協力頂きました関係各位のご厚情の賜物と深く感謝いたします．

今後も生理学会大会が，ますます盛会となり，実り多い研究発表の場となりますことを期待して止みません．

THE 64th ANNUAL MEETING
OF
THE PHYSIOLOGICAL SOCIETY OF JAPAN

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April 1 — 3, 1987

Chiba University School of Medicine

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PHYSIOLOGY–PHARMACOLOGY JOINT SYMPOSIUM

[JS–1(1)~JS–4(4)]

JS-I Development and regeneration of synapse

JS1-1 Interactions between nerve and target cells during synapse formation in culture. Hiroshi Kuromi. Department of Neuropharmacology, Brain Research Institute, School of Medicine, Chiba University, Chiba 280, Japan

During synapse formation, nerve fibers come to innervate appropriate target cells. When the target cells are contacted by appropriate nerves, neurotransmitter receptors accumulate at the nerve-contact sites. The present study was performed on the cultured cells to elucidate the mechanism and molecular basis for the receptor accumulation and the specific innervation at the synapse during development. I.The process of aceetylcholine receptor(AChR) accumulation was examined by taking sequential fluorescence photographs in Xenopus cell culture. When the muscle cell was contacted by an appropriate nerve, large preexisting AChR cluster(high density of AChRs) at the extrajunctional region dispersed before AChRs accumulated at the nerve-muscle junction. During AChR cluster formation at the nerve-muscle junction, small AChR clusters emerged from the background and increased in size. They did not migrate as clusters from the extrajunctional regions. Diffusely distributed AChRs moved laterally in the muscle membrane so fast that diffusion was not rate-limiting for AChR cluster formation. Concanavarin A prevented rapid diffusion of AChRs as well as nerve-induced receptor accumulation. Passive diffusion-trap mechanism is compatible with all of observations during receptor accumulation at the nerve-muscle synapse. II.The smooth muscle of chick expansor secundarirum is innervated exclusively by sympathetic nerves. Isolated sympathetic nerve cells adhered to the dish coated with the smooth muscle-conditioned medium(SMCM) but not the dish coated with skeletal muscle-conditioned medium(SKCM). Sympathetic neurites preferentially extended down tracts of substrates obtained from SMCM, but did not enter into tracts of substrates obtained from SKCM. These results suggest that target cells release some substances which affect the adhesion and growth cone migration of innervating nerve cells.

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JS1-2 Development of the spinal neurone circuit. Norio Kudo. Department of Physiology, Institute of Basic Medical Sciences, University of Tsukuba, Ibaraki 305, Japan.

The developmental process of reflex and descending pathways to lumbar motoneurones was studied electrophysiologically and morphologically in rat fetuses ranging in age from embryonic day (E) 14.5 to postnatal day 1. The physiological study was performed in vitro using an isolated spinal cord preparation. Stimulation of the 4th lumbar (L4) dorsal root evoked a reflex response in the L4 ventral root at and after E16.5. The segmental latency of the ventral root potential was markedly shortened between E17.5 and E18.5 and essentially unchanged at the later stages. A morphological study using the horseradish peroxidase (HRP) orthograde tracing technique revealed that the collaterals issued from the L4 dorsal root fibres began to project to the gray matter at E15.5-E16.5. A group of collaterals entered the motor nucleus and ramified there at E18.5. Bouton-like structures appeared on the terminal branches in the motor nucleus at this stage. It is thus concluded that the polysynaptic reflex first appears at E16.5 and the monosynaptic reflex at E18.5. The effect of stimulation of the first cervical (C1) spinal cord on lumbar motoneurones was also examined. The response in the L4 ventral root following stimulation of the ventrolateral funiculus of the C1 cord first appeared at E16.5. After synaptic transmission in the cervical and thoracic spinal cord was interrupted by removing calcium ions from the perfusing solution in these regions, the synaptic effect on motoneurones in the lumbar spinal cord, where normal solution was perfused, did not change. In our morphological study, the descending fibres originating from the lateral vestibular nucleus and the medullary and pontine reticular formation reached the lumbar spinal cord at E14.5-E15.5. Consequently, the effect evoked by stimulation of the C1 spinal cord could be due to descending fibres projecting to the lumbar spinal cord. These results indicate that the function of both neuronal circuits involving the spinal reflex pathway and the descending pathway in the lumbar spinal cord starts at the same stage, i.e. E16.5, five days prior to birth.

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JS1-3

DEVELOPMENT AND SYNAPTIC PLASTICITY OF VISUAL CORTICAL CIRCUITRY

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The dispute between Nature versus Nurture theory concerning visual cortical plasticity has been one of the most exciting topics in neuroscience. In the dispute during the last two decades it has been established that photic responsiveness of visual cortical cells is still immature in newborn kittens and develops under the influence of the visual environment (Hubel & Wiesel, 1963), If visual experience is restricted to a certain visual pattern during the period of rapid development in photic responsiveness, the responsiveness develops only to that pattern (Hirsch & Spinelli, 1970; Blakemore & Cooper, 1970), suggesting that the cortical cells learn the responsiveness through visual experience. The present study was designed to study plastic changes underlying the learning of photic responsiveness. Changes in synaptic transmission were investigated in slice or whole animal preparations of the visual cortex, after electrical stimulation of the visual pathway (white matter, WM; lateral geniculate nucleus, LGN; or optic chiasm, OC). The effects were consistent between three types of experiments (with WM stimulation in the slice preparation and with LGN and OC stimulation in the whole animal preparations): 1) activation of the visual pathway potentiated synaptic transmission at both first (geniculo-cortical) and second stages (cortico-cortical synapses), 2) potentiation was greater at the cortico-cortical (about 6-fold) than the geniculo-cortical synapses (2-fold), 3) potentiation occurred more slowly but lasted longer (for more than 10 hours) in the cortico-cortical than the geniculo-cortical synapses (a few hours), 4) potentiation occurred only in kittens at so called critical ages (around 4th week). Developmental study also indicated that the cortico-cortical transmission was absent before and developed during the critical ages. Therefore, there was remarkable potentiation in the cortico-cortical synapses under conditions of experimental activation of the visual pathway and visual experience during normal development, which suggests that photic responsiveness is learned at the cortico-cortical synapses.

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JS1-4. Enkephalinergic inhibitory and cholinergic excitatory regulations on neurotransmission in superior cervical ganglion reinnervated by peripheral vagal fibres in cats. Kazuyoshi Kurahashi, Toshihiro Okamoto and Motohatsu Fujiwara. Department of Pharmacology, Faculty of Medicine, Kyoto University, Kyoto 606, Japan.

It has been shown that distribution of the soma of the vagal sensory neurons are not only at the nodose ganglion (NDG) but also at the peripheral vagal trunk in cats, and the distribution of enkephalin in the nucleus of the solitary tract has been demonstrated immunohistochemically. The purpose of the present experiment is to elucidate pharmacological nature of neurotransmission in superior cervical ganglion (SCG) reinnervated by the peripheral vagal fibres containing sensory neurons in cats. The heterologous cross-anastomosis between the cranial end of peripheral vagal trunk and the caudal end of SCG was performed. Operated cats were kept for 2-4 months. Then cats were subjected to functional test, to check the reinnervation of peripheral vagal fibres to SCG: when centrifugal stimulation was applied to the vagal trunk on intact side, the nictitating membrane and pupil of the operated side responded to the stimulation, these were regarded as signs of the successful reinnervation of peripheral vagal fibres to SCG. The successfully operated cats were subjected to the acute experiments. The contraction produced by electrical stimulation of the artificial preganglionic trunk (peripheral vagus) was inhibited dose-dependently by close arterial injection of hexamethonium (1 to 10 μg) and atropine (1 to 10 μg) to the SCG. The injection of naloxone (0.3 to 3 μg) to the SCG enhanced the contraction in response to stimulation of the artificial preganglionic trunk and the injection of enkephalin (1 to 10 μg) to the SCG inhibited the response in a dose-dependent manner. Naloxone (10 μg) antagonized the inhibitory effect of enkephalin. The reinnervated SCG was perfused with choline (10^{-5}M) and physostigmine (1.5×10^{-5}M) containing solution. The spontaneous release of ACh in the perfusate was not detectable and the stimulation of the artificial preganglionic trunk caused a definite release of ACh. Perfusion with enkephalin (10^{-6}M) did not affect the release of ACh. It was concluded that the pharmacological nature of sensory fibres in the peripheral vagal trunk might be both cholinergic and enkephalinergic, and suggested that cholinergic excitatory and enkephalinergic inhibitory fibres might play an important role at the nuleus of solitary (central end of these sensory fibres) to transmit peripheral signal to higher centers.

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JS1-5

Enhancement of Ia synaptic transmission in motoneurons by section of peripheral sensory fibers. Y. Miyata, Department of Pharmacology, Faculty of Medicine, Tokyo Medical and Dental university. Tokyo 113, Japan.

When impulse activity of sensory fibers is chronically eliminated by local application of tetrodotoxin (TTX) to the peripheral muscle nerve, monosynaptic Ia excitatory postsynaptic potentials (EPSPs) evoked in motoneurons by stimulation of the disused sensory fibers are known to be enhanced 2 weeks later. In contrast, the monosynaptic EPSPs are significantly depressed 2 weeks after section of the peripheral sensory fibers. Nerve section also results in the loss of sensory impulse activity. A question that may be posed is how the loss of sensory impulse activity per se, caused by nerve section and by TTX application, brings a reverse effect on central synaptic function. To test this question, the medial gastrocnemius (MG) nerve in the hind leg of Wistar rats was cut near the muscle under Nembutal anesthesia, and Ia monosynaptic EPSPs elicited in spinal motoneurons by stimulation of the MG nerve were recorded 1-30 days after the operation. As previously reported, the monosynaptic EPSPs were substantially depressed 2 weeks or more after nerve section. However, this depression was found to be preceded by enhancement of the EPSPs. The EPSP enhancement was discernible on the day after nerve section and reached the maximal level on the 3rd postoperative day. The increased amplitude was 3.4 times larger than the control and could not be accounted for on the basis of changes in the motoneuron input resistance. Evidently, peripheral nerve section induces two distinct effects on central synapses. The initial EPSP enhancement may be attributed to the loss of sensory impulse activity, whereas the subsequent synaptic depression may be due to some factor associated with the loss of peripheral axonal continuity.

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JS1-6 Regeneration of central neural pathways. Saburo Kawaguchi. Department of Physiology, Institute for Brain Research, Faculty of Medicine, Kyoto university, Kyoto 606, Japan

In contrast to the current concept of abortive regeneration of mammalian central axons, occurrence of marked, functionally active, regeneration of the cerebellofugal projection was proved in the cat after transection of the decussation of the brachium conjunctivum (BCX). For complete transection of the BCX and marking the lesion, an edged U-shaped wire was implanted into the brain stem base at the midline. Later, horseradish peroxidase was injected into the cerebellar lateral and interpositus nuclei to label the cerebellofugal projection arising from these nuclei. By this procedure, axonal regeneration was proved by demonstration of labeled fibers passing through the area enclosed by the U-shaped wire; and the origin, course, and destination of the regenerated fibers were identified unambiguously. Functional connectivity of the regenerated cerebellothalamic projection was tested electrophysiologically by recording potentials from the cerebral cortex on stimulation of the cerebellar nuclei in the same animals examined morphologically. The cut ends of axons began to swell as early as 15 min after transection and the swollen endings became growth cones in 14-24 hours. In successful regeneration, fibers tipped by growth cones crossed the lesion in 3 days and distributed dense terminals in the thalamus by 19 days. Most of the regenerated axons took a course similar to that of the normal projection and terminated in the normal projection areas, whereas a small proportion of fibers showed an aberrant course and termination. In all animals in which marked axonal regeneration occurred, cerebellocerebral responses, as in intact animals, were evoked in the frontal motor and parietal association cortices. Having convincing evidence for the occurrence of successful regeneration, we can say that years of pessimism about the failure of mammalian central axons to regenerate are giving way to new optimism about their regrowth potential. Repairing of neural tracts after brain injury may not be an insubstantial dream.

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JS-2 Pharmacology and physiology of regulation of respiration

JS2-1 Pharmacological and physiological study on central control of respiration.

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The recent views as well as the essentials of previous important experimental results on the anatomical localization, functional and neuronal organization of the central respiratory mechanisms, classically expressed as the respiratory centers, in the brain stem were critically reviewed and discussed placing special emphasis upon the neural mechanisms responsible for the rhythmogenesis in the brain stem.

The rhythmic eupnea-like activity originated in the medullary neural mechanisms is dominant with respect to the spontaneity (Hukuhara Jr., 1973, 1976) over other rhythmic activity described in the pons and the spinal cord (Cohen 1979; Hugelin, 1973; Coglianese et al., 1977). These stably discharging bulbar neurons exhibited only the least value of the degree of correspondence between their unit activities and the phrenic HFO. This suggests that significant correlation of the phrenic HFO activity to the respiratory rhythm generating process may be less probable.

The neural network for the central respiratory mechanisms may involve various types of respiratory neurons having different role in the regulatory function (Hukuhara Jr., 1973). The above-mentioned different stability of respiratory neurons strongly suggest that there may exist the different degree of functional correlation of individual respiratory neuron to the neural mechanisms for the respiratory rhythmogenesis. A model of the neuronal organization of the central respiratory mechanisms in the brain stem involving 4 subpopulations of respiratory neurons: primary; satellite; input; and output respiratory neurons, was proposed. Respiratory neurons with higher stability mentioned above may be playing an essential role as the member of the primary respiratory neuron population, which are characterized in their specified relations to the rhythmogenesis in generating the respiratory rhythms in the bulbar mechanisms. Thus, 4 bulbar inspiratory and 5 expiratory neurons discharging stably with a smaller coefficient of variation for the burst period and with a larger correlation coefficient of puse-density auto-correlation of their unit activity were exclusively found only in the lateral region of the bulbar reticular formation. This new finding is pertinent and supports the view proposing an existence of the primary neuron system consisting of primary neurons within the bulbar part of the entire neuronal network of the central respiratory mechanisms in the brain stem.

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JS2-2 Pharmacological and physiological studies on synaptic interconnections between bulbar respiratory neurons.

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Bulbar respiratory neurons receive waves of excitatory (E) and inhibitory (I) post-synaptic potentials (PSPs) during the neural respiratory cycle. These IPSPs and EPSPs contribute importantly to periodic fluctuation of membrane potentials characteristic of each type of respiratory neuron. In particular, periodic IPSPs, readily identified by a reversal of membrane potential fluctuation after injection of chloride ions and by a low input resistance, appear during the inactive phase in many respiratory neurons. However, the pre-synaptic source of these inhibitory inputs has not been established in many cases. Further, little is known regarding the identity of trans-synaptic chemical mediators responsible for these IPSPs.
Spike-triggered averagings of membrane potential revealed that the high incidence of correlations occurred between action potentials of early inspiratory (EI) unit in the retro-facial nucleus (RFN) and IPSPs of postinspiratory (PI) neuron in the contralateral ventral respiratory group (VRG) area. This IPSP wave was oscillating with a period of 10 - 12 msec characteristic of a high frequency oscillation (HFO) in membrane potential. The results document the phase relation between these two groups of neurons.
Pharmacological properties of glycine and gamma-aminobutyric acid (GABA) were examined by intracellular recording and extracellular iontophoresis. Both amino acids hyperpolarized the membrane of augmenting inspiratory (AI) and PI neurons in VRG. This effect was converted to depolarization either when the membrane was hyperpolarized by current clamp or after injection of chloride ions. The action of glycine was blocked by strychnine, and that of GABA by bicuculline. Strychnine and bicuculline depolarized AI and PI neurons, increased spike frequency of AI neurons during inspiration and prolonged the period of spiking in PI neurons. In some PI neurons bicuculline selectively depolarized the membrane during inspiration and increased input resistance during that phase. The results suggest that GABA mediates inspiratory IPSPs in PI neurons, and that both GABA and glycine participate in tonic and phasic post-synaptic inhibition of AI and PI neurons.

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Courtesy of The Japanese Pharmacological Society.

JS2-3 Pharmacology and physiology of the central mechanisms for respiratory reflexes with special reference to the reflex inhibition of phrenic discharge caused by shocks to the superior laryngeal nerve (SLN). Yuji Sakai. Department of Pharmacology, Faculty of Medicine, Saitama Medical School, Saitama 350-04, Japan.

The central mechanisms for respiratory reflexes have been extensively studied in the past three decades, though those for the protective reflexes from upper airway seem to be relatively neglected. The potency of a given respiratory reflex in an altered state of breathing, which may be caused both physiologically or pharmacologically, should be also evaluated. The lateralized responses of the phrenic nerve to single shocks of the SLN (Berger & Mitchell, 1976) and their role in the inspiratory termination (Iscoe et al., 1979) have been described in the cat. The inhibition of phrenic discharge thereby produced has a short latency and has been related to a kind of protective reflex from the larynx. Hence, the SLN-phrenic reflex was used as a test system to study how a central depressant drug affects a respiratory reflex. Most experiments were done in the rabbit, which was vagotomized, paralysed and ventilated artificially with oxygen-rich gas mixture, and began after inhalation of halothane was discontinued. The peri-stimulus time histogram of phrenic discharge and inspiratory single shocks to the SLN enabled a quantitative evaluation of the inhibitory reflex.

When the rate of ventilation was either increased or decreased, the resulting hyper-capnia reduced the reflex inhibition in association with an increase in basal phrenic discharge and the hypocapnia enhanced the reflex inhibition of the discharge. Halothane and diethylether, when they were inhaled, reduced the reflex inhibition to some extent. The halothane-induced change was partly reversed by increasing the level of CO_2. Morphine and pentobarbital, administered intravenously, had a more pronounced effect on the reflex and their effect was reversed by a subsequent dose of either the opioid antagonist, levallorphan and naloxone, or the analeptic dimorpholamine. On the contrary, both drugs enhanced the reflex inhibition, when train shocks were delivered to the SLN. This effect seems to be well correlated to a simultanous decrease in the post-inhibitory excitation of phrenic discharge.

On the basis of a dynamic mechanism of reflex integration, it may be concluded that all respiration-depressant drugs tested have a more or less marked inhibitory effect on the central mechanism for the reflex inhibition.

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JS2-4 The peripheral chemoreceptors in the control of respiration.

Teijiro Natsui. Department of Physiology, Teikyo University School of Medicine, Tokyo 173, Japan.

The carotid bodies have been well known as the peripheral chemoreceptors that are sensitive to change in the chemical composition of the arterial blood. Their afferent nerve fibers pass through the carotid sinus nerves to join the glossopharyngeal nerves and to the medulla oblongata. A characteristic of the carotid bodies is that they contain large sinusoids with an extremely high rate of perfusion. Because of this, the oxygen needs of chemoreceptor cells can be met mainly by dissolved oxygen alone. Stimulation of the peripheral chemoreceptors produces an increase in ventilation. The carotid bodies are stimulated physiologically by an increase in carbon dioxide tention, and by reduction in pH and specifically by a reduction in oxygen tension of the arterial blood. An unified theory has been offered to explain the mechanism of chemoreceptor excitation by a common stimulus. It states that the excitation of chemoreceptors by physiological stimuli results from an increase in hydrogen ions within the receptor cells. The carotid body is made up of cell clusters in an abundant connective tissue. There are two distinct types of cells. Type I (glomus) cells, which are in synaptic contact with nerve endings, are characterized by dense-cored vesicles, and Type II cells, which also have a close relationship to nerve endings, surround the glomus cells. A possible receptor mechanism of the carotid body reduced from these structures is that the glomus cells release a neurotransmitter in response to stimuli, which initiates action potentials in the afferent fibers terminating on the glomus cells. Several hypotheses have been proposed to explain the receptor mechanism of the carotid body. However, none of them could explain all the results obtained by physiological and pharmacological studies. Thus, it is still not yet clear which structure is the actual chemoreceptor; nor is it known what the effective stimulus to the receptors is. The peripheral chemoreceptors are fast-responding detectors of the arterial oxygen tension. However, they play a minor role in the regulation of normal breathing because the carbon dioxide drives from the central chemosensitive areas normally insure a proper supply of oxygen. It has been, therefore, suggested that the peripheral arterial chemoreceptors in air-breathing animals might be the survival of a reflex essential to the control of respiration in water-breathing animals.

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Courtesy of The Japanese Pharmacological Society.

JS2-5 Respiratory chemosensitivity of the medulla oblongata.
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This paper summarizes the current concept of the medullary respiratory chemosensitivity.
1. Carbon dioxide (CO_2) is a potent physiological stimulus to breathing. Respiratory stimulation due to CO_2 persists even after denervation of the peripheral arterial chemoreceptors, which indicates that other chemosensor(s) responding to CO_2 influences ventilation. Winterstein hypothesized that H^+ is the unique central stimulus for respiration and that CO_2 acts on chemoreceptor(s) somewhere in the brain only by increasing H^+ concentration.
2. Loeschcke, Koepchen and their coworkers demonstrated that the responsible structures localize in the superficial layer of the ventral medulla oblongata. Much of respiratory response to CO_2 was suggested to arise from stimulation of the ventral medullary areas by increasing H^+ concentration of the brain extracellular fluid. Histological and electrophysiological examinations, however, failed to show the existence of special H^+-receptor cells in the surface layer. Local applications of acid solution or cholinergic drugs increase the discharge frequency of the ventral medullary neurons and stimulate respiration. The increase in neuronal discharge by H^+ depends upon intact synaptic connections in the surface layer. The application of procaine or cooling the surface, on the other hand, initiates profound depression of respiration and circulation. The dependency of sympathetic vasoconstrictor activity on the medullary surface pH has also been demonstrated.
3. Although the ventral medullary surface was seen as a primary H^+ receptor site in earlier studies, there is a possibility that experimental access to the ventral medulary surface provides a 'window' on the lower brain stem through which we may see many functions of the ventral medullary neurons, synapses and pathways. H^+ and drugs likely modulate the synaptic transmission in these neuronal networks for the respiratory and cardiovascular regulation. Recent evidence revealed that neither ventilation nor discharge frequency of ventral medullary neurons uniquely correlates with H^+ concentration when the acid base parameters of the brain extracellular fluid are altered. The ventral medullary surface, therefore, is not a uniform H^+-dependent source of respiratory drive, but areas of heterogenous structures with different functional significance.

Reprinted from The Japanese Journal of Pharmacology, Vol. 43, Supplementum P 51 ;
Courtesy of The Japanese Pharmacological Society.

JS2-6 Cybernetics of chemical regulatory system of breathing; Some implications concerning exercise hyperpnea. Yoshimi Miyamoto Department of Information, Faculty of Engineering, Yamagata University, Yonezawa 992, Japan.

Introduction of the concept of control theory into physiology has opened new possibilities of analyzing homeostatic mechanism of living system. Grodins and his associates have been the first to analyze the respiratory control system in terms of cybernetics (1). Such a model conveniently described by the classic control theory fits well to the experimental results so far as the inhalation of CO_2 is considered as disturbance, but no one has hitherto succeeded to explain exercise hyperpnea by the chemical control mechanism since PCO_2 (or pH) dose not appreciablly change from its resting level. A number of hypotheses has been presented so far, of which cardiodynamic hypothesis proposed by Wasserman and his associate (2) has specially attracted during the last decade. Recently, Miyamoto et al. (3) have demonstrated that $\dot{Q}$ increases simultaneously with $\dot{V}_E$ when exercise begins. An alternative explanation for the exercise hyperpnea has been proposed by Yamamoto et al.(4); $PaCO_2$ is not constant but fluctuate in synchronization with respiratory cycles. The carotid body may be stimulated by the respiratory oscillation of $PaCO_2$ evenif its mean level remains constant. It has recently been confirmed experimentally that the maximum amplitude of $dPaCO_2/dt$ is in a proportional relationship with $\dot{V}CO_2$ during exercise (5). If this holds true, the combination of both the hypotheses of cardiodynamic and CO_2 oscillation, i.e., "fast" chemical control process, would provide an adequate explanation for exercise hyperpnea. We estimated both the kinetics of $P\bar{v}CO_2$ and $\dot{Q}CO_2$ ($\dot{Q} \times P\bar{v}CO_2$) at the begining of exercise onset from simultaneous measurements of $\dot{V}CO_2$, $\dot{V}_E$, and $\dot{Q}$ using Fick equation. $\dot{Q}CO_2$ would increase immediately when exercise begins before noteworthy increase in $P\bar{v}CO_2$ takes place. It has been suggested that carotid body could be a unique sensor for the $\dot{Q}CO_2$ change since $\dot{V}_E$ damped in hyperoxia and augmented in hypoxia despite that $\dot{Q}CO_2$ remains unaffected. The transition of $P_{ET}CO_2$ from rest to exercise was hypocapnic in hypoxia, normocapnic in normoxia and hypercapnic in hyperoxia. Such a circumstance can not be explained by the feedback mechanism in which $PaCO_2$ and PaO_2 are considered as control variables, but another mechanism such as oscillation of these gases should be taken into consideration. (1) Ann.N.Y.Acad.Sci.109,852(1963), (2) J.Appl.Physiol.36, 457 (1974), (3) J.Appl.Physiol.52, 1198 (1982), (4) J.Appl.Physiol.15,215 & 807 (1960), (5) J.Physiol (London).329,57 (1982).

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JS-3 Circulation: Refresher course

JS3-1

VENTROLATERAL MEDULLA AS A CENTER FOR TONIC AND REFLEX CONTROL OF SYMPATHETIC VASOCONSTRICTOR DISCHARGES AND ARTERIAL PRESSURE - A REVIEW. KUMADA, M., TERUI, N. AND SAEKI, Y. Institute of Basic Medical Sciences, Univ. of Tsukuba, Ibaraki-ken 305

The ventrolateral medulla (VLM) is a region near the ventral surface of the medulla extending between the caudal pole of the facial motor nucleus and the rostral portion of the inferior olive. Electrical or chemical stimulation of the VLM causes an increase in efferent renal nerve activity (RNA), representing vasoconstrictor discharges, and a pressor response, whereas bilateral destruction of cell bodies in that region eliminates tonic RNA. Furthermore, VLM neurons are responsive to inputs from various peripheral and central sources which include arterial baro- and chemoreceptors, spinal and trigeminal somatosensory nerves, afferent renal fibers and the posterior hypothalamic area. Some of the VLM neurons reflexly control sympathetic discharges through descending bulbospinal axons innervating the region of sympathetic preganglionic neurons. VLM neurons are sensitive to excitatory and inhibitory amino acids such as L-glutamate, glycine, GABA and taurine. Noradrenaline and clonidine affect directly their neuronal activity. Thus, the VLM is a likely candidate for the cardiovascular center which tonically and reflexly controls sympathetic vasoconstrictor discharges and arterial pressure. It also is a site of drug action that affects neural control of the circulation.

JS3-2

MOVEMENTS OF CROSS-BRIDGES DURING CONTRACTION OF MAMMALIAN HEART MUSCLE. MATSUBARA, I. Dept. Pharmacol., Sch. Med., Tohoku Univ., Sendai 980

The behaviour of myosin heads in cyclically contracting heart muscle was studied by the X-ray diffraction method. From the intensities of the principal equatorial reflections the fraction of myosin heads in the vicinity of the actin filaments was calculated. The fraction increased as the tension developed during the systolic phase, reaching the maximum level of 70% at the peak of contraction. During the diastolic phase 50% of myosin heads remained near actin. However, these heads did not seem to produce any significant force since a change in their number did not affect the diastolic tension. The effect of calcium concentration on the movement of myosin heads was studied using chemically skinned heart muscles. During the maximum contraction at pCa 5.0 to 4.4, 80% of heads were found in the vicinity of actin. An unexpectedly large fraction was associated with actin at lower calcium concentrations; at pCa 6.2 to 5.8 where the average tension was less than 20% of the maximum, the average fraction was almost half of that during the maximum contraction. These results suggest that, at low calcium concentration, a significant number of myosin heads may be attached to actin without producing tension.

JS3-3

CALCIUM CHANNELS IN CARDIAC MUSCLES. OCHI,R. Dept. Physiol. Sch. Med., Juntendo Univ., Tokyo, 113

Extensive patch-clamp analyses of cardiac calcium channels have elucidated gating processes of activation and inactivation, existence of multiple gating modes and existence of two kinds of channels. We studied the beta-adrenergic modulation of L-type calcium channel gatings by recording single channel currents from isolated guinea-pig ventricular cells using 50 mM Ba-containing pipettes under cell-attached configuration. Clamp steps applied repetitively at 2 Hz produced blank sweeps as well as current-containing sweeps consecutively in clusters. With mean currents from total sweeps 0.1 to 1 uM-isoproterenol (ISO) produced the increase in its amplitude mainly by decreasing blanks and made the time course of decay during depolarization slower, typically from 250 to 500ms, by affecting the inactivation process. The time constant of restoration estimated from the single channel currents was 100-200 ms at -80mV. Thus, blanks appeared more numerously than expected from the rates of voltage-dependent inactivation and deacvtivation. Repetitive depolarizations with short pulses have revealed the existence of a voltage-independent slow gating process which is modulated by beta-stimulants to allow more current-containig sweeps, and thus the increase in the total Ca current.

JS3-4

CONTRACTION AND RELAXATION OF VASCULAR SMOOTH MUSCLE. ENDO, M. AND IINO, M. Dept. Pharmacol., Fac. Med., Univ. Tokyo, Tokyo 113

Physiological contraction of vascular smooth muscle is mostly mediated by raised cytoplasmic free Ca ion concentration. Among the subcellular and molecular mechanisms of whole contraction and relaxation processes, discussion is focused on those of Ca mobilization upon stimulation. Ca is physiologically mobilized either by an influx from extracellular space through voltage-dependent Ca channels or by a release from an intracellular Ca store. Ca influx through receptor-operated Ca channel may also be important under some experimental conditions. Morphologically, Ca store appears to be the sarcoplasmic reticulum, but not the cytoplasmic surface of the cell membrane as sometimes assumed. In skinned fiber experiments, Ca can be released from the store either by Ca ion itself or by inositol trisphosphate. The inositol trisphosphate-induced Ca release is dependent on Ca ion concentration in a submicromolar range, which is not high enough to activate the Ca-induced Ca release. The physiological significance of these Ca release mechanisms was discussed.

JS3-5

FUNCTIONAL AND MORPHOLOGICAL CHARACTERISTICS OF VENOUS SYSTEM.
OHHASHI, T., Dept. of Physiol., Sch. of Med., Shinshu Univ., Matsumoto 390

We have undertaken to study regional and species differences in mechanical characteristics of venous walls, morphological principles in the distribution of venous valves, pharmacological responses of venous smooth muscles to vasoactive agents, and the distribution and density of aminergic nerve fibers by use of isolated human, monkey, dog and rabbit veins. There were marked regional differences in the venous distensibility. The non-uniform distensibility of venous walls was understood in terms of local differences in the architecture of elastic fiber components and the content of smooth muscle cells in the venous walls. In all the veins, venous valves with bicuspid were always observed at the positions of venous angles and inguinal ligaments, but were not found in the superior and inferior caval veins. From these functional and morphological points of view, the venous system may be divided into three groups as follows;(1) trunk, (2) portal, and (3) peripheral venous group. Responses of venous smooth muscles seemed to be classified following such three venous groups. Aminergic nerve fibers were most densely innervated in the venous walls of inferior trunk veins such as abdominal caval vein and common iliac vein. Thus, the trunk veins may play a major role in the neural regulation of venous return. No species difference was observed in the distribution pattern of aminergic nerve fibers in the venous system.

JS-4 Physiology and Pharmacology of neuropeptides

JS4-1

THE ROLES OF NEUROPEPTIDES IN THE SPINAL CORD. OTSUKA, M., YANAGISAWA, M. AND NUSSBAUMER, J.C. Dept. Pharmacol., Fac. Med., Tokyo Med. & Dent. Univ., Bunkyo-ku, Tokyo 113.

We have developed an isolated spinal cord-peripheral nerve preparation of the newborn rat, in which it is possible to record spinal reflexes from a lumbar ventral root in response to stimulation of the ipsilateral saphenous or obturator nerves. Single shock weak intensity stimulation of a saphenous nerve induced a fast conducted afferent volley in the L3 dorsal root and a fast depolarizing response in the ipsilateral L3 ventral root. A stronger stimulus applied to the saphenous nerve resulted in a slowly conducted volley in the dorsal root and a slow depolarizing response in the ventral root. The latter slow response probably represents a nociceptive C-fiber reflex. The slow ventral root potential (v.r.p.) evoked by saphenous nerve stimulation was depressed by a tachykinin antagonist, Spantide, (16 μM), suggesting that substance P and neurokinin A are involved as neurotransmitters in this nociceptive reflex. The saphenous nerve-evoked slow v.r.p. was also depressed by endogenous neuropeptides, Met-enkephalin, dynorphin (1-13), galanin and somatostatin.

JS4-2

NOCICEPTIVE TRANSMISSION AND NEUROPEPTIDES. SATOH, M. Dept. of Pharmacol., Fac. of Pharmac. Sci., Kyoto Univ., Kyoto 606

In the present studies, the roles of substance P (SP) and calcitonin gene-related peptide (CGRP) in the primary afferents in acute and chronic nociception were examined using non-inflamed (control) and adjuvant-induced polyarthritic (PA) rats.

In PA rats, the immunoreactive SP (iSP) level in the L4-5 dorsal root ganglia (DRG) significantly increased. Intrathecally injected colchicine increased the iSP levels of DRG much more in PA rats than in control rats. Basal release of iSP from the DH was increased in PA rats. These results suggest that the biosynthesis and axonal transport of SP in and release of SP from the primary afferents are facilitated in PA rats.

Intrathecal CGRP (5nmol/rat) in PA rats produced a hyperalgesia to mechanical stimulation, which was inhibited by a SP-antagonist. CGRP enhanced capsaicin-induced iSP-release from the DH. CGRP elevated the uptake of Ca^{2+} into the synaptosomes from the DH. The number of maximum binding sites of CGRP to the synaptosomes was increased in PA rats. These results suggest that CGRP plays a role in the promoted nociceptive tranmission in the lumbar DH of PA rats through increasing SP-release.

JS4-3

OPIOID PEPTIDES. OKA, T. Dept. of Pharmacol., Sch. of Med., Tokai Univ., Isehara 259-11

[Met^5]-Enkephalin has been shown to be inactivated by three enzymes, both bestatin- and amastatin-sensitive aminopeptidase, both thiorphan- and phosphoramidon-sensitive endopeptidase-24.11 and captopril-sensitive peptidyl dipeptidase A, in isolated preparations such as guinea-pig ileum and mouse vas deferens. Additionally, these enzymes have been indicated to be membrane-bound ones and located very close to opioid receptors. Moreover, enkephalin has been shown to be exclusively hydrolyzed by these three peptidases, since enkephalin remains intact almost totally after it is incubated with either ileal or striatal membrane fractions of guinea-pig for 60 min at 37°C in the presence of three peptidase inhibitors. These three peptidases have been shown to inactivate not only [Met^5]-enkephalin but also many other endogenous opioid peptides. The relative importance of three enzymes in the inactivation has been found to be dependent on both the opioid peptide tested and the preparation employed. Finally, the relation of opioid peptides and opioid-receptor types has been examined in the presence of three peptidase inhibitors. Results show that β-endorphin, and [Met^5]- and [Leu^5]-enkephalin act as either δ- or μ-agonists, while adrenorphin, α- and β-neo-endorphin, dynorphin-(1-8) and -(1-17), rimorphin and leumorphin act as κ-agonists. And both [Met^5]-enkephalin-Arg^6-Phe^7 and [Met^5]-enkephalin-Arg^6-Gly^7-Leu^8 act as either δ-, μ- or κ-agonists although their potencies at κ-receptor sites are low.

JS4-4

THE EFFECT OF NEUROPEPTIDES ON EFFERENT NERVE ACTIVITY OF THE AUTONOMIC NERVE.
NIIJIMA, A. Dept. of Physiol. Niigata Univ. Sch. of Med., Niigata 951

Under anaesthesia (urethane 500-800 mg/kg and cholralose 40-70 mg/kg), effect of i.v. administration of pentagastrin, CCK-8, somatostatin and ANP on efferent activity of autonomic nerve was observed in rats.

An increase in activity was observed in gastric branch of vagus nerve following injection of pentagastrin, and that in pancreatic branch of vagus nerve after injection of CCK-8. A decrease in activity was observed in gastric, hepatic and pancreatic branch of vagus nerve following application of somatostatin or ANP. ANP application also caused a suppression in activity of adrenal and renal sympathetic efferents. The smallest effective dose of these substances was 100 pg.

In decerebrated preparations no change in efferent activity was observed after administrations of these substances.

The results indicate that neuropeptides such as pentagastrin, CCK-8, somatostation and ANP released into venous circulation modulate autonomic outflows through hypothlamic neuronal networks surrounding with insufficient blood-brain barrier.

JS4-5

STRESS AND VASOPRESSIN
YAGI, K. Dept. of Physiol., Jichi Med. Sch., Tochigi-ken 329-04.

Tail pinching and noxious heat stimuli to the paw in rats produce intense excitatory synaptic inputs to supraoptic vasopressin (VP)-secreting neurons and footshocks (FS) of 1 min-duration increase plasma VP to an extreme level. On the other hand FS of 2 s-duration intermittently applied at every 15 s were much less effective for increasing plasma VP than continuously applied FS were. Since rats exhibited 'freeze' behavior during intervals between intermittent FS, it is possible that VP secretion is potentiated by physical but suppressed by psychological stresses. Rats were trained by light and sound stimuli paired with FS. These stimuli suppressed the FS-induced VP secretion. Plasma ACTH and 'freeze' scores indicated a strong psychological stress to occur during testing session. Light and sound testing stimuli also decreased plasma VP in rats under hypertonic conditions. These conditioned VP responses disappeared in the rats which received unpaired light and sound stimuli during extinction session between training and testing. Physiological significance of differential VP responses to physical and psychological stresses were discussed.

JS4-6

STUDIES ON NEUROPEPTIDES IN THE BRAIN AND PITUITARY GLAND OF INHERITED HORMONE-DEFICIENT MOUSE.
NOGUCHI,T.,SUGISAKI,T. AND KANAMATSU,T. Dept. of Physiol. Toho Univ. Sch. of Med. Tokyo 143.

The adenohypophysis of Snell dwarf mice (dw) is composed largely of gonadotrophs; acidophils are absent and thyrotrophs are very scarce, so that GH, TSH, prolactin and ACTH are virtually absent. Isolated GH-deficient Little mice (lit) are deficient in GH and also decreased acidophils accompanied by a lack of GH-producing cells. Congenitally hypothyroid mice (hyt) have an undetectably blood concentration of T4 and an abnormally high level of TSH. Their pituitary gland features decreased acidophils and increased thyroidectomy cells. In previous studies, we established that both the dw and lit mice show strikingly reduced levels of spontaneous locomotion activity with indistinct diurnal periodicity, microcephalus, retarded growth of neurons in the cerebral cortex and in the suprachiasmatic nucleus (SCN), and cerebral hypomyelination. In contrast, the hyt mouse shows normal spontaneous locomotion activity with a distinct diurnal periodicity and normal development of neurons in the cerebral cortex and the SCN, although cerebral hypomyelination is present.

In continuation of these studies, we examined the neuropeptides, VIP and Met-Enk, and somatomedin C (IGF-1) in the brain and pituitary gland of these 3 types of inherited hormone-deficient mice, by radioimmunoassay and immunohistochemical techniques.

NARRATE ORALLY AND POSTER EXHIBITION

1

ON A FURTHER MODIFICATION OF THE MICROPHOTOELECTRIC PLETHYSMOGRAPHY FOR MEASURING BLOOD FLOW VELOCITY IN SINGLE MICRO VESSELS. OHKUBO, C. AND ASANO, M. Dept. of Physiol. Hyg., the Inst. of Public Health, Tokyo 108

We have modified the dual sensor method, microphotoelectric plethysmography(-gram;MPPG), in which two photosensors placed with a known distance on a single vascular image of the camera obscura. The flow velocity is determined photoelectrically by measuring the time required for markers such as red blood cells or plasma gaps to traverse the intersensor distance. As charateristic signal patterns of the markers on MPPGs obtained from upstream and downstream in the single vessel are generated by the trains of red blood cells and plasma gaps, the aperture between the two photosensors should be small. An improvement was carried out by using a small series dual element of CdS photoconductive cell(75CF, Moririca Co. Ltd., Japan) to obtain more acurate velocity profile. In stead of measuring the time delay by visual inspection of the two traces, these two signals were converted electrically into one signal by a summing amplifier and the time delay was measureed by a heart rate tachometer.

2

A MULTICHANNEL IMPLANTABLE ECG PREAMPLIFIER DEVELOPED FOR AWAKE CAT. NISHIURA,N., NINOMIYA,I., HONDA,T. AND YONEZAWA,Y* Dept. of Cardiac Physiology National Cardiovascular Center Research Institute, 5-7-1 Fujishiro-dai, Suita Osaka 565, and *Dept. of Electrical Enginnering Hiroshima Institute of Technology, Itukaichi, Hiroshima, 738 Japan

To analayze the electrical potential distribution of the heart in the freely moving cat, we developed a 24 channel implantable preamplifier. With body movements, artifacts in electrocardiogram (ECG) are induced from the lead cable between electrode and preamplifier, and therefore for reducing artefacts the cable length is shortened and the preamplifier is implanted in the body. Size and weight of the implantable preamplifier, consisted with hybrid IC chips and covered by waterproof material, is 10 cm^3(4 x 3.6 x 0.7 cm) and 55 grm, respectively. Power consumpsion is 1.1 mA with ±2.5 volts suplly. Gain and time constant of the preamplifier is 40 dB and one sec, respectively. The 24 output sigals of the preamplifier were converted into a pulse train by a pulse amplitude modulator, and was transmitted to a demodulator with single light weight lead cable. The demodulated 24 electrocardiograms can be measured simultaneously over one week after implantation surgery.

3

MODELS OF SIGNAL-DYNAMIC ENTROPY CODING: THEIR APPLICATIONS TO THE NEURONAL SPIKE ACTIVITY. AYA, K.[1], SHIMA, K.[1], YAMAMOTO, M.[1], FUJII, H.[2] and NAKAHAMA, H.[3]
[1]Div. Neurophysiol., Inst. Brain Diseases, Tohoku Univ. Sch. Med., Sendai 980
[2]Compt. Center, Shibaura Inst. Tech. Tokyo 108
[3]Dept. Physiol., Tokai Univ. Sch. Med., Isehara 259-11

We have developed a new coding theory of communication based on theories of thermodynamics and measurement, which we call "signal-dynamics". We are concerned with neural coding as transduction, sampling and mapping from one signal space to another. According to simple constant and integrate-and-fire models, we give a theoretical explanation to the frequency coding in the nervous system. Using the I-entropy and efficiency diagrams, we can make a comparison between the frequency and pattern codes for the amount of information transmission, as well as for the efficiency, in the nervous system. In order to identify a candidate code as a true neural code, we pinpoint a functional relation between a feature parameter of the receptor potential and that of the spike train: $\bar{V}=Af$, where $\bar{V}$ is the mean potential; A is the threshold; f is the mean rate. Both theoretical and experimental results strongly suggest that the mean value of neuronal signals is a real neurophysiologically utilized code, and that the 2nd order properties of signals are irrelevant to the neuronal measurement of stimulus and to the information transmission.

4

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., Gifu, [++]Dept. of Technol., Osaka City Univ., Osaka and [+++]Mitsubishi Heavy Industries, Kobe

The free flow electrophoresis are expected to execute support-free large scale separation or analytical electrophoresis of biological materials. We are trying to develop the aparatus for free flow electrophoresis. Because the system are made thin to minimize convection problem and to maintain stable temperature gradient, the sample fraction are gradually distorted due to both hydrodynamic and electroosmotic flow. The size of depth of electrophoretic cell exert the contradicted effects on the convection problem and electroosmotic flow. To estimate best available size and condition for the aparatus both on the earth and in the space, we analized the system theoretically.

For the calculation of electric field Poisson equation was first solved. From the calculated field strength the heat production term of thermal transport equation and forced term of electro-phorotic equation were calculated. The basic equation of flow and convection were consisted of Navier-Stokes equation, the equation of continuity and the thermal transport equation. These equations were coupled and solved numerically using three dimensional finite element method. For the time integration we used two step explicit method. The electroosmotic flow were calculated analytically from the theory of Nee and Hu (1979) and added to flow velocity field.

5

PITCH AND FORMANT ANALYSIS OF TE (TRACHEOESOPHAGEAL) SHUNTED LARYNGECTOMEES USING THE SIGNAL PROCESSOR. OKADA, Y., *KINISHI, M., *AMATSU, M. AND YAMAUCHI, R. Dept. Physiology and *Otorhinoloaryngology, Sch. Med., Kobe Univ., Kobe 650

Using signal processor 7T18 (NEC-Sanei), the pitch and formant analysis were performed in the normal and TE (tracheoesophageal) shunted laryngectomized adults. For the pitch analysis, the program of signal basic No.5 (NEC-Sanei) was modified for obtaining the interval histogram of each pitch from which the mean of pitch, the mean jitter (variation of consecutive pair of vocal period) and the jitter ratio (jitter/mean period x 1000) were calculated. The program of signal basic No.3 (NEC-Sanei) was modified for the analysis of the formant of each vowel sound. The pitch formation in the operated subjects developed distinctly without vocal cord. The fundamental speech freequency was 7.4 msec in normal subjects and 14.7 msec in the operated patients. The mean jitter and the jitter ratio were 0.08 msec and 11, respectively for normal subjects whereas those were 0.47 and 30 for the TE-shunted subjects. The formant formations of vowels did not differ with each other in the normal and laryngectomized subjects.

6

INSTANTANEOUS AND QUANTITATIVE AUTORADIOGRAPHY USING A MICROCHANNEL PLATE. Suzuki, H. and Tasaki, K. Dept of Physiol., Tohoku Univ. Sch. of Med., Sendai 980

In order to shorten the exposure time in autoradiography, we used an image intensifier with a microchannel plate. Instead of emulsion a sheet of plastic scintillater or a thin layer of liquid scintillater was put on a brain slice of the rat, in which 2.4 mCi of 18F-DG was injected intraperitoneally 1 hr before sacrifice. An image formed in the scintillater, reflecting the RI distribution within the slice, was focused on a photocathode of the image intensifier. The intensified image by almost a billion times was displayed on a monitor screen and/or stored in a frame memory. Quality of the displayed image after one second exposure was comparable to that of the autoradiogram obtained by using ordinary procedure. For quantitative studies blotting papers containing 14C-Met or 3H-DG were used. Effective surface densities were 148 Bq/mm^2 and 256 Bq/mm^2, respectively. Sixty seconds exposure for 14C-Met and 60 minutes for 3H-DG resulted in fine images. When the surface density of 3H-DG was lower than 0.4 Bq/mm^2, one hour exposure was not enough to obtain the image. Number of scintillation within the image and that of background were in proportion to the exposure time and to the RI concentration. We conclude that the system described above makes it possible to perform the electrophysiological, autoradiographic, and in situ biochemical experiments, simultaneously.

7

NEW METHOD FOR EVALUATION OF PURITY AND APPARENT STABILITY CONSTANT OF EGTA IN PHYSIOLOGICAL Ca-EGTA BUFFER SOLUTIONS. OIKI, S. AND OKADA, Y., Dept. Physiol., Fac. Med., Kyoto Univ., Kyoto 606

Calculations of the free Ca^{2+} concentration in the physiological EGTA buffer solutions require a set of values of the absolute stability constants or a value of the apparent stability constant (K') for Ca binding as well as the purity (q) of EGTA. This paper reports a simple method for simultaneous evaluation of the K' and q values by means of Ca^{2+} electrodes. When the value of log ([bound Ca]/(q[tatal EGTA]-[bound Ca])) is plotted against that of log [free Ca], the slope should be 1. On such a log-log plot, a best fitting q value was obtained by successive approximation procedures so as to attain the slope of 1. A K' value was directly evaluated from an intersect on the abscissa. The purity of four commercial brands thus estimated ranged from 99.04 to 95.89. The log K' value was found to be 7.06 at 0.1 M, pH 7.30 and 25°C.

8

LIQUID JUNCTION POTENTIALS OF VITELLIN MEMBRANE

OHSAWA, K., Dept. of Physiol., Fac. of Med., Univ. of Tokyo

When ionic solution is separated by ultrafiltered membrane; vitellin, egg shell, everted sac of small intestine and millipore filtered, the interfacial liquid junction is consisted of three compartments of liquid-porous-liquid. The interface is made up two ionic slopes in cation and anion and generated liquid junction potential; LJP. In two component electrolyte, a different concentration of ion was shown the size of LJP and the polar nature of LJP was made into a transport number of each ion. A variable equation of Nernst-Planck must alone apply to the two component ion in the interface of ionic slope. In three component ion of the same concentration, only the ionic transport number was decided both of the pole and LJP. The pole and isonic slope of an interfacial liquid junction were generated that an initial velocity of either cation or anion was dependent on ionic diffusion and associated with three factors of c, t and λ from Chanoz equation. The order of LJP in 1-1 electrolyte was embodied in the form of diffusion coefficient and Stokes radius of ionic circumference. LJP of multicomponent electrolytes without H^+ ion was not able to discriminate each ion at the size of potential difference and potential difference levels with calomel electrodes.

Capacitance of calomel electrode was 0.01- 0.05μF, impedance of IC input resistance; 1MΩ and time constant; 50- 100 msec was calculated from the value of C and R. LJP-measurement of the two component and a different concentration may be apppied to that of basement membrane.

9

STRUCTURE ANALYSIS OF MEMBRANE PROTEINS BY GAS CHROMATOGRAPHY-MASS SPECTROMETRY.

NISHIJIMA,T., SAKAMOTO,Y. AND UYEMURA,K.
Department of Physiology, Saitama Medical School, Saitama 350-04

Structure analysis of hydrophobic membrane proteins is quite difficult owing their insolubility. We developed a rapid and sensitive method for structure analysis of hydrophobic proteins using gas chromatography mass spectrometry (GC-MS). The PO and PASII glycoprotein were purified from bovine peripheral nerve myelin membrane. The purified protein was digested by trypsin and its peptides were fractionated by reverse phase liquid chromatography with Hitachi 3013-O resin. After partial hydrolysis of peptides with 5.7 N HCl for 15 - 30 min, peptides were N-acylated, permethylated and analysed by GC-MS with a Chrompack Sil 5 capillary column. By this method, 2-6 amino acid sequences of peptides, such as Lys-Val, Tyr-Val-Phe-Glu and Val-Val-Leu-Leu-Ala-Leu were determined. Fatty acids (palmitate,stearate and oleite) covalently linked to a hydrophobic peptide of PO protein were also determined by GC-MS. From these results, we suggested that the PO protein contained a single transmembrane segment [Tyr(125)-Ile(150)]. Probably these glycoproteins play important roles as adhesion molecules in molecular architechture of the myelin.

10

ON THE TRANSFORMATION FORMULA REPLACING BETA-DISTRIBUTION OF EULER INTO THE SCHRODINGER'S WAVE FUNCTION.
O'HATA,S., AIZAWA,K., KITAHARA,M., SAKAI,S., IMAGAWA,M., SAITO,H. AND YAMAO,M. Dept. of Physiol., Tokyo Medical college, Shinjuku-ku, Tokyo 160

We have reported the relationship between beta-distribution of Euler and the Schrödinger's wave function of a simple harmonic resonator, and referred to the exchange mechanism of Na and K in nerve membrane.
The transformation formula is given by $\xi=\tan^2\theta$, and the meaning of the transformation formula will be explained.

11

THE GROWTH OF THE MYELIN FIGURE
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Dept. of Physiology, Fac. of Hygienic Technology, Azabu Univ., Sagamihara, Kanagawa 229
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Myelin figures, which are composed of concentrically stacked multilamellae of lipid bilayers with a lot of water inside the tube, grow from lipid lamps in excess water at the phase transition temperature of the lipid. After the initial growth stage, tubes change to non spherical and spherical liposomes for a long time. That formation is very interesting as a model of a self organization in biological membranes.

We observed myelin figures of DPPC, DMPC, DSPC and DPPE by optical microscopy, a video recording system and a thermocontroller. We also investigated the effect of Na^+ on the myelin figures formation.

Results for the initial growth stage;

1. The shorter length of the hydrocarbon chains of lipid, the shorter the length of tubes grow up in lecithin.
2. The myelin tubes of DPPE are slender and longer than the DPPC. The myelin tubes of DPPC gradually saturate with growing their length, however the tubes of DPPE grow up linearly.
3. The growth of the myelin tubes are suppressed with increasing Na^+ concentration.

12

MONOCLONAL ANTIBODIES THAT RECOGNIZE DISCRETE STRUCTURES OF GUINEA-PIG CENTRAL NERVOUS SYSTEM.
AKAGAWA K., YOSHIMURA K., TANAKA S. AND UYEMURA K. SAITAMA MEDICAL SCHOOL, SAITAMA 350-04

We raised monoclonal antibodies against several discrete structures of adult guinea-pig CNS using subcellular fractions obtained from the brains as immunogen. Specificities of monoclonal antibodies were studied immunohistochemically. A monoclonal antibody S7D5 labeled neuronal fibers observed as pairs of parallel lines in the white matter. By an immunoblot study, this antibody was found to be against myelin basic protein. Immunoreactivity was also found in new born guinea-pig, demonstrating the presence of myelin structure at birth. An antibody N5F8 reacted with the cytoplasm in almost all neurons of both cerebrum and cerebellum. This antibody recognized a protein of which molecular weight was about 60K. An antibody 2F7 labeled nuclear membrane of all neurons in the brain whereas speckled labeling in neuronal nuclei was revealed by an antibody 5E5. 5E5 seemed to be reactive with a neuronal subpopulation in CNS.

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DETERMINANTS FOR MEMBRANE VISCOSITY AT THE MOLECULAR LEVEL. ARAISO, T. AND KOYAMA, T., Res. Inst. Appl. Elec. Hokkaido Univ. Sapporo, 060

Membrane viscosity has been measured by a time-resolved fluorescence depolarization method with a hydrocarbon probe, 1,6-diphenyl-1,3,5-hexatriene (DPH). This method offers the viscosity in the lipid layer as having almost the same meaning of that in normal liquid. There may be several determinants for the membrane viscosity at the molecular level. We examined the effect of following factors on the viscosity of the phospholipid bilayes.

a) The length of acyl carbon chain of phospholipids.
b) Existence of double bond on acyl chain of phospholipids.
c) Cholesterol. d) Fatty acids and diacylglycerols.

The decreasing of length of the acyl chain and existance of double bond(s) decreased the bilayer viscosity. When carbon number decreased from 16 to 12, viscosity varied from 2.6 to 0.28 poise at 37°C. Cholesterol increased the viscosity as reported previously. Fatty acids and diacylglycerol were of interest as degradation products of phospholipid with phospholipases A and C. Addition of these materials caused increase of the viscosity. These results indicate that these small components occupy free rooms in lipid bilayer and increase the viscosity.

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A study on the interaction between riboflavin binding protein and flavins. NISHINA, Y., USHIJIMA, H., AND SHIGA, K. Department of Physiology, Kumamoto University Medical School, Kumamoto, 860

We studied the effects of pH and ionic strength on the affinity of riboflavin binding protein (RBP) for flavins (riboflavin, FMN, and 3-carboxymethylriboflavin) in order to elucidate the binding mechanism. While the affinity for FMN or 3-carboxymethylriboflavin which has negative charge was increased upon the increase of ionic strength in the neutral pH region, the affinity for riboflavin which has no net charge was not. RBP is negatively charged in the pH region. Therefore the electrostatic interaction between the net charges can account for the present effect of ionic strength, i.e. the repulsion forces should be decreased by the increase of ionic strength. The pH profiles extrapolated to zero ionic strength were considerably different from each flavin. The affinity for riboflavin was stronger than the others. The pH profile for riboflavin was almost flat in the pH range 6 to 9, but those for FMN and 3-carboxymethylriboflavin had a slope in the pH region. The affinity for FMN in the dianionic form at the phosphate group was about 50 times weaker than in the monoanionic form. The present results indicate that the electrostatic repulsion force between the phosphate group of FMN and negative charge of RBP is mainly responsible for the weak affinity for FMN, rather than the steric effect of the phosphate group.

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EFFECT OF SALT ON HYDRATION OF FIBRINOGEN AND FIBRIN. TANAKA, Y., YOSHIOKA, Y., HASEGAWA, H., NAKAYA, S., KUROSAWA, N. & YAGI, S. 2nd Dept. of Physiol., Sch. Med., Iwate Med. Univ., Morioka 020.

Upon the preparation of fibrin gel (Gel) from fibrinogen (Fbg) solution, the resulting Gel was lost in the turbidity by increasing the concentrations of added NaCl and KCl, and then was examined on the NMR T_1 and T_2, comparing the effects of added NaCl and KCl. The Fbg solutions (10 mg/ml) were prepared with 0.2 M borate-borax buffer (pH = 7.75) containing the various concentrations of NaCl and KCl (0～0.5 M). Adding the thrombin to these Fbg solutions, the Gel samples were made in the cuvette (10 mm in light path) for measuring the turbidity electrophotometrically and also in the 5 mm NMR tube for measuring T_1 and T_2 of water protons. The higher the concentration of the added salts, the more transparent the resulting Gel. However, between these salts, the difference in the turbidity change was not seen. In these salt concentrations, T_1 of Fbg was 2.98 ± 0.12 sec and that of Gel 2.99 ± 0.08 sec. T_2 of Fbg was 1.38 ± 0.06 and that of Gel 0.76 ± 0.03 sec. Using these values, the hydrations of Fbg and Gel were calculated according to Kumosinski and Pessen (1982), as 0.2 and 0.4 g of water/g of protein, respectively.

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COMPARATIVE ^{1}H-NMR STUDIES ON THE WATER STRUCTURE IN MODIFIED BOVINE PLASMA ALBUMIN GEL (BPA*-GEL) AND HEPATIC TISSUE. ERA, S., KATO, K.+ KUWATA, K., SOGAMI, M., YOSHIDA, A.++ AND WATARI, H.+++ Dept. Physiol. and +Dept. Pathol., Sch. Med., Gifu Univ., Gifu 500, ++SANNO Inst. Busin. Adminst., Tokyo 158 and +++Dept. Mol. Physiol., Natl. Inst. Physiol. Sci., Okazaki 444

Partially hydrolyzed bovine plasma albumin (BPA*, M. W. 66K) has a tendency to form transparent gel (BPA*-gel) in D_2O around pD 4.0 above 8 % (Sogami et al, 1986). Cross-relaxation times (T_{IS}) between irradiated protein protons and HDO were obtained by f_2-irradiation at 7.13 or -2.45 p.p.m. from TSP at $\gamma H_2/2\pi$ of 39~107 Hz. Plots of $1/T_1$, $1/T_2$ or T_{IS} of BPA*-gel vs. protein concentration (W(%)) were far steeper than those of BPA solution. Plots of T_{IS} vs. W (%) showed significant difference between BPA*-gel and BPA solution, indicating the large amount of hydration of BPA* and the rapid exchange between bound and bulk water. Dependences of $1/T_1$ (H_2O) of normal hepatic tissues on dry weight were greater than those of hepatocellular tumor and regenerating rat liver. Dependences of $1/T_{IS}$ of normal rat liver, obtained by f_2-irradiation at 7.13 p.p.m. at $\gamma H_2/2\pi$ of 67 Hz on dry weight were far greater than those of hepatocellular tumor and regenerating rat liver, indicating the water structure of normal rat liver being more gel-like state than those of hepatocellular tumor and regenerating rat liver.

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^{1}H-NMR STUDIES ON THE CROSS-RELAXATION PHENOMENA IN BOVINE PLASMA ALBUMIN (BPA). SOGAMI, M., ERA, S., KUWATA, K. AND WATARI, H.+ Dept. Physiol., Sch. Med., Gifu Univ., Gifu 500 and +Dept. Mol. Physiol., Natl. Inst. Physiol. Sci., Okazaki 444

Intramolecular cross-relaxation phenomenon between irradiated and observed protons were studied on bovine mercaptalbumin (BMA) solution and modified BPA gel (BPA*-gel), using cross-relaxation times (T_{IS}) of Akasaka (1981, 1983). T_{IS} values were obtained by the saturation transfer (SAT.) and inversion recovery (INV.) methods with f_2-irradiation at 7.13, 0.40 or -2.45 p.p.m. from TSP at $\gamma H_2/2\pi$ of 39~107 Hz. T_{IS} values of BMA solution, obtained by the SAT. and INV. methods, were a single kind of T_{IS} for each side chain. T_{IS} values of BPA*-gel, obtained by the SAT. method indicated the presence of two kinds of T_{IS} values, that is, short and long T_{IS} values, for each side chain. However, T_{IS} values of BPA*-gel, obtained by the INV. method showed a single kind of T_{IS} for each side chain, corresponding to long T_{IS} obtained by the SAT. method. The short T_{IS} values of BPA*-gel, observed by the SAT. method, may be due to the aggregates of BPA*, resulting in an increase of rotational relaxation time. T_{IS} measurements by the SAT. and INV. methods might be useful to study the presence of two kinds of significantly different cross-relaxation processes.

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THE BOHR GROUPS OF HUMAN ADULT HEMOGLOBIN. IMAI, K., NISHIMOTO, S.*, OKADA, T.* AND TYUMA, I. Dept. of Physicochem. Physiol., Osaka Univ. Med. Sch., Nakanoshima, Osaka 530.

The ionizable groups responsible for the Bohr effect of human adult hemoglobin (Hb A) have been identified with the imidazole group of β146(HC3) His, the α-amino group of α1(NA1) Val, the imidazole group of α122(H5) His. Ohe & Kajita (Biochemistry 19, 4443-4450 (1980)) observed a large pK difference for α89(FG1) His imidazole group between deoxy-form (pK = 7.2) and carbonmonoxy-form (pK = 5.6) of Hb A by means of deuterium exchange reaction and proposed that α89 His is one of the major groups contributing to the Bohr effect of Hb A. They interpreted the pK change for α89 His in terms of a possible interaction between the imidazole group of the His and the ε-amino group of α139(HC1) Lys in liganded Hb A. Since no evidence for the contribution of α89 His to the Bohr effect was provided by other methods, we examined the validity of the proposal by Ohe & Kajita by accurate measurements of the Bohr effects of Hb Tokoname (α139 Lys → Thr) and canine Hb in which α89 His is replaced by Tyr. Hb Tokoname showed exactly the same Bohr effect as that for Hb A, indicating that the proposed interaction between α89 His and α139 Lys is unlikely to occur. Canine Hb showed a Bohr effect slightly differed from that of Hb A. However, that difference quite differed from that expected theoretically from the pK values obtained by Ohe & Kajita. The present study does not support the proposal by Ohe & Kajita described above. We thank Dr. T. Harano for Hb Tokoname sample.

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OXYGEN TRANSPORT IN HEMOGLOBIN SOLUTIONS STUDIED BY USING AN IMAGE-INPUT AND PROCESSING SYSTEM. HASHIMOTO, M., HATA, R., ISOMOTO, A., TYUMA, I., AND*UOZUMI, M. Dept. of Physico-chemical Physiol., Med. Sch., Osaka Univ., Osaka 530, and*Osaka Pref. Inst. of Pub. Health, Osaka 537.

We developed a method for estimating the oxygen saturation of hemoglobin in a position-sensitive manner by using an image-input and processing system. The system was composed of a microscope, a 3-tube video camera and a microcomputer-aided color image analyzer, which enabled us to measure the change of the oxygen saturation of hemoglobin microscopically. The experiments were done as the distribution changes of oxygen in hemoglobin solutions included in glass capillaries were monitored by using the system. The experimental results at various hemoglobin concentrations indicated that the transport was facilitated in proportion to the hemoglobin concentration, and the dynamic behavior led to an empirical formula $J = kY$, where J is the flux of oxygen at a point on the pass, Y is the oxygen saturation of hemoglobin there, and k is a constant.

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HIGH-PERFORMANCE LIQUID CHROMATOGRAPHIC (HPLC) STUDIES ON HUMAN SERUM ALBUMIN (HSA) OF THE ELDERLY. ERA, S., KUWATA, K., SOGAMI, M., KAWAI, K.+, SUZUKI,E., OKABE, H.++, NOMA, A.+++ AND UJI, Y.+++ Dept. Physiol. and +Dept. Ophthalmol., Sch. Med., Gifu Univ., Gifu 500, ++Dept. Lab. Med., Sch. Med., Kumamoto Univ., Kumamoto 860 and +++Tokyo Metropol. Geriatr. Hosp., Tokyo 173

HSA is the mixture of mercaptalbumin (HMA, reduced form) and nonmercaptalbumin (HNA, oxidized form). The present authors developed the convenient HPLC systems for the resolution of HMA and HNA [8 columns of Asahipak GS-520H (0.75 x 20 cm), 0.03 M sodium phosphate buffer, 0.15 M Na_2SO_4, pH 6.86 or Asahipak ES-502N (0.76 x 10 cm), linear gradient elution with increasing ethanol concentration from 0 to 10 % in 0.05 M sodium acetate, 0.40 M Na_2SO_4, pH 4.80]. Fractions of HMA, f(HMA), in sera of 20 patients with cataract (50~80 years) were 0.5~0.7. Major fraction of aqueous humor albumin of patients with cataract was found to be HNA. So, the present authors studied on human serum albumin of the healthy elderly. Mean value of f(HMA), $\bar{f}$(HMA), in sera of the elderly (60~90 years) was 0.47 ± 0.052 (n = 55). On the other hand, $\bar{f}$(HMA) of healthy male adults was 0.75 ± 0.028 (n = 28), indicating HSA of healthy male adults being more reduced state than that of the elderly.

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PATH INTEGRAL METHOD IN QUANTUM CHEMISTRY. YOKOTA, S. Dept. of Physicochem. Physiol., Osaka Univ. Med. Sch., Nakanoshima, Osaka 530.

Quantum chemistry has been developed in the framework of the Hartree-Fock (HF) self-concistency which is based on the variational principle in the Schrödinger picture. However, there is another scheme of quantum chemistry, that is, the quantum field-theoretical approach to many-body problems in the operator formalism. Expanding the field operators for a molecule in the linear combinations of atomic orbitals with the fermionic annihilation-operator coefficients and using Nambu-Gorkov formalism, the Hamiltonian is transformed into the Hückel-type one from which the one-particle Green's functions in the matrix form are constructed for the perturbative evaluation. In this scheme the HF self-consistency means one-loop corrections if the HF potential is once determined. Going to the anticommuting Grassmann world, the operator language is translated into the path integral formalism which requires the careful manipulations on the ordering problem. This difficulty is able to be resolved by returning to the symmetric definition of the path integral. In the field-theoretical context, direct application of quantum theory to the macromolecules is not only hopeless but also meaningless. It is desirable to construct the model fields coupled with the specific part of the macromolecule considered and to apply the non-perturbative methods which has been fully developed in the path integral framework.

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THEORETICAL APPROACHES TO THE REPULSIVE FORCES BY WATER MOLECULES IN A NARROW SPACE. YOSHIDA, A., GENERAL EDUCATION SANNO INSTI. 158 AND SOGAMI, M., AND ERA, S., MED., GIFU UNIV., GIFU 500

Hydrophilic radicals are considerably ordered on the surface of biological membranes. Since a water molecule has a dipole moment, the dipole moment of water molecules in the vicinity of the surface is directed toward the surface. If two membranes with hydrophilc radicals approach each other, the orderliness of the distribution of the dipole moment of water molecules will be disturbed at the middle of them. This decrease of the orderliness brings about an increase of the free energy of water molecules between two membranes. Consequentlv, it is considered that the increase of the free energy causes to happen a larger repulsive force between two membranes by bringing them closer.

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INTRAMOLECULAR SH, S-S EXCHANGE REACTION (MOLECULAR AGING) OF BOVINE MERCAPTALBUMIN (BMA). KUWATA, K., ERA, S., SOGAMI, M. AND WATARI, H.+ Dept. Physiol., Sch. Med., Gifu Univ., Gifu 500 and +Dept. Mol. Physiol., Natl. Inst. Physiol. Sci., Okazaki 444

In alkaline pH region, BMA isomerizes to the A-form by the intramolecular SH, S-S exchange reaction. The kinetics of the molecular aging reaction was analyzed, assuming the following equation, where N and A are the N (nonaged) - and A (aged)-forms, respectively. Values of k+/k-, Kapp at pH 8.6 at 20°, 25° or 30° in salt-free solution were almost unity. However, k+ and k- were greatly increased with an increase in temperature. Both k+ and k- were suppressed, with strong effects on k+, on increasing ionic strength from 0 to 0.10 M KCl and on decreasing pH from 8.6 to 7.0, resulting in the shift of equilibrium from the A- to N-forms. The global structural fluctuation for the aging reaction, corresponding to k+, was strongly affected by salt concentration and pH. ^{1}H-NMR spectra and cross-relaxation times between irradiated and observed protein protons were similar to those of the N-form. However, α-helical contents of the N- and A-forms were 70 and 62 %, respectively, at pH 8.6 in 0.10 M Na^+. A molecular volume of the A-form was 1.1 times of the N-form.

$$N \underset{k-}{\overset{k+}{\rightleftarrows}} A$$

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HIGH-PERFORMANCE LIQUID CHROMATOGRAPHIC (HPLC) STUDIES ON MODIFIED BOVINE PLASMA ALBUMIN FORMATION IN ACIDIC REGION. FUJII, H., KUWATA, K., ERA, S., SOGAMI, M. AND WATARI, H.+ Dept. Physiol., Sch. Med., Gifu Univ., Gifu 500 and +Dept. Mol. Physiol., Natl. Inst. Physiol. Sci., Okazaki 444

Bovine plasma albumin Fr. V (BPA) has known to contain small amount of proteolytic enzyme, which catalize a very limited and specific cleavage of BPA between Gln-392 and Cys-435 in one or two portions, when BPA exists in the F-form near pH 3.8. The primary and secondary proteolytic products, BPA* and BPA**, have molecular weights of 66K and 63K, respectively. Ion-exchange HPLC studies of the mixture of BPA, BPA* and BPA** on TSK SP-5PW at pH 5.0 showed clear resolution of three components, indicating BPA* or BPA** being more positive than BPA at pH 5.0. Kinetic studies on BPA* and BPA** formations were carried out at 3°, 25° and 35°. After 8 days incubation of BPA in 0.10 M NaCl at pH 3.80 at 35°, almost all of BPA was converted to BPA* and BPA**. Cross-relaxation times between irradiated and observed protein protons, obtained by f_2-irradiation at 7.13 p.p.m. at $\gamma H_2/2\pi$ of 39~69 Hz and pH-profile of CD-resolved secondary structure indicated that BPA* and BPA** have the F-like structure at isoionic pH.

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HIGH-PERFORMANCE LIQUID CHROMATOGRAPHIC (HPLC) STUDIES ON THE MERCAPT⇄NONMERCAPT CONVERSION OF HUMAN SERUM ALBUMIN IN ENDOCRINE AND METABOLIC DISEASES. SUZUKI, E., ERA, S.+, KUWATA, K.+, SOGAMI, M.+, TAKEDA, N., SAKATA, S., YASUDA, K., MIURA, K. AND IDO, T.++ 3rd Dept. Int. Med. and +Dept. Physiol., Sch. Med., Gifu Univ. and ++Gifu R. C. Hospt., Gifu 500

HPLC analysis of human serum albumin (HSA) on Asahipak GS-520 column (0.03 M sodium phosphate buffer, 0.15 M Na_2SO_4, pH 6.86) showed clear resolution of human mercaptalbumin (HMA) and nonmercaptalbumin (HNA). A mean value of [(HMA)/(HMA + HNA)], $\bar{f}$(HMA) for healthy male adults was 0.75 ± 0.028 (n = 28). In patients with various thyroid diseases, $\bar{f}$(HMA) values of Graves' disease, Hashimoto's thyroiditis and nontoxic goiter were 0.69 ± 0.047 (n = 74), 0.69 ± 0.054 (n = 26) and 0.71 ± 0.022 (n = 6), respectively. f(HMA) in patients with various thyroid diseases correlated with serum thyroid hormone concentration. In diabetic patients, $\bar{f}$(HMA) was 0.63 ± 0.067 (n = 47). f(HMA) in patients with diabetes mellitus correlated with plasma glucose concentration, but not with glycosylated HbA.

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^{1}H-NMR STUDIES ON THE WATER STRUCTURE IN SOFT CONTACT LENS. ERA, S., KUWATA, K., SUZUKI, E., SOGAMI, M., AMANO, H.+, KITAZAWA, Y.+ AND WATARI, H.++ Dept. Physiol. and +Dept. Ophthalmol., Sch. Med., Gifu Univ., Gifu 500 and ++Dept. Mol. Physiol., Natl. Inst. Physiol. Sci., Okazaki 444

As a model system for the water structure in biological systems, the water structure in soft contact lens (SCL, copolymers of 2-hydroxyethyl metacrylate, 2-alkyl-2'-hydroxyethyl metacrylate etc) was studied using ^{1}H-NMR spectra, spin-lattice relaxation times ($T_1(H_2O)$) and cross-relaxation times ($T_{1S}(H_2O)$) between irradiated polymer protons and water protons, obtained by f_2-irradiation at -4.00 p.p.m. from TSP at $\gamma H_2/2\pi$ of 69 Hz. Sharp and broad signals were observed at 4.72~4.74 p.p.m. and 4.47~4.65 p.p.m., respectively. The sharp and broad signals might correspond to surface and inside water phases, respectively, indicating the exchange rate between two phases being slow. Chemical shift, $T_1(H_2O)$ and $T_{1S}(H_2O)$ of the broad water signal decreased from 4.65 to 4.47 p.p.m., from 1.25 to 0.56 sec and from 2.38 to 0.37 sec, respectively, with decreasing water content from 68 to 29 %. Changes in $T_{1S}(H_2O)$ might indicate that the hydration of polymer matrix is strong and rapidly exchangeable with free water in SCL polymer matrix.

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AFFINITY OF HEMATOPORPHYRIN DERIVATIVE AND BLOOD COMPONENTS

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There has been increasing interest in the usage of porphyrins for tumor localization and therapy. Hematoporphyrin derivative (HpD) is a well-known tumor-specific photosensitizer. HpD has been used clinically as a photosensitizer in photodynamic therapy (PDT). PDT is performed after HpD is injected intravenously (i.v.). Therefore, we investigated the binding affinity of HpD to serum components. HpD was injected intravenously (i.v.) in a beagle dog at a dose of 5mg/kg dody weight. Blood was colected at 15min, 1hr and 3hr after injection. The serum components and the blood corpuscles was separated by centrifuge. The HpD fluorescence of blood corpuscles, serum and whole blood were measured by an eximer dye laser spectrophotometer and the fluorescence spectrophotometer. As a result, the fluorescence of HpD was not detected from blood corpuscles. However, that was detected in serum. Especially, large amounts of fluorescence were detected from the albumin fraction among serum components. The rate of fluorescence from albumin fraction decreased according for time after injection. Change of fluorescence from other components was hardly observed. These results suggested that HpD bound to albumin might be released and accumulate in tissues.

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HEMATOPORPHYLIN DERIVATIVE (HpD) UPTAKE BY ATHROMA DEMONSTRATED BY EXCIMER DYE LASER

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A new diagnostic and therapeutic endoscopical system consisting of an excimer pulse dye laser is presented. Using this equipment and hematoporphyrin derivative (HpD) which has been shown to have a high affinity for malignant tissue, we have diagnosed and treated malignant tumor.

This report demonstrates the accumulation of HpD in atheroma, as shown by the fluorescence of HpD. Atheroma was induced in the aorta of a WHHL (watanabe heritablehyperlipidemic) rabbits, and 5mg/kg HpD was injected intravenously and the rabbits were sacrified 24 hours laser. The aorta was dissected and the localization of HpDwas examined using the excimer pulse dye laser. Characteristic emission of HpD fluorescence, with peaks of 630 and 690 nm wavelength, was detected in the atheromatous lesions.

On the other hand, no fluorescence with peaks were detected in areas of aorta thatwere normal in appearance.The ratio of fluorescence intensity in atheroma, border zones and normal areas was 10.4:5.0:1.0. The above date suggests the possibility offuture applications of this equipment for diagnosis of atheroma.

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ABILITY OF PORPHYRINS TO BREAK DNA STRANDS BY PHOTORADIATION.

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There has been an increasing interest in the use of porphyrins for the detection of tumor localization and the therapy. Photodynamic therapy (PDT) involves low-energy irradiation by laser light to malignant tissue in which the photosensitizer porphyrin has accumulated. The photodynamic action is probably caused by generation of singlet oxygen by photoradiation. Gutter et al showed that the illumination of calf thymus DNA with visible light in the presence of hematoporphyrin resulted in the degradation of the guanin moiety. We compared the abilities of porphyrins to break the DNA strand. Fd form I DNA was used as DNA substrate and Mn, Zn, Sn, Ge were used as metals.

The ability of porphyrin to break DNA strand was seen to be affected by binding porphyrin with metal. The Mn and Zn complexes of porphyrin lost the ability to break DNA strands. But the Sn and Ge complexes had almost same ability as porphyrin without metals.

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THE LOCALIZATION PROPERTY OF NPe6

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The study of photodynamic therapy (PDT) has recently been given increasing attention, especially using hematoporphyrin derivative (HpD) which has a high affinity for malignant tissue. Recently, mono-L-asparthyl chlorin e6 (NPe6; Nippon Petrochemical Co.Ltd.) has been developed as a new photosensitizer for PDT. We studied the localization property of NPe6. NPe6 was intravenously injcted into tumor-bearing mice at a dose of 20mg/Kg weight. The relative intensity of fluorescence of NPe6 in both tumor and normal tissue was greatest at 3hrs after injection. Mice were illuminated at this time, and sacrificed later. At 24hrs after injection, the intensity from normal tissue decreased to 30% of that at 3hrs after injection. However, until 48hrs after injection, the fluorescence from the tumor showed the highest value. If mice were illuminated 24hrs after injection, skin damage was hardly observed. These results suggest NPe6 has good selective localization in tumor.

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SPECTRAL FEATURE OF MONO-L-ASPARTYL CHLORIN e6 (NPe6)

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It is known that HpD has a high affinity for cancer cells in vino and is therefore a useful material for PDT. Currently, vigorous research is being conducted throughout the world to discover a new material which can have greater cancer cell affinity than HpD and can be used effectively for PDT. Investigation has been conduced to determine the spectral feature and cancer cell affinity of NPe6, a recently developed material.

Structually, this chlorin (NPe6) differs from a porphyrin by reduced at the D-ring, thereby changing its spectral properties from that of HpD. This difference account for the strong absorption bands in wavelengths longer than those of HpD 630nm. Futhermore, NPe6 showed stronger absorption at 660nm in tumor than HpD shows at 630nm. Absorption by hemoglobin (Hb) in the blood occurs at wavelength of 500-600nm range, thereby lowering light transmittance. A compound which has a strong absorption band in wavelength longer than 600nm and consequently is not affected by Hb will naturally be activated by light at a greater depth in tissue than compounds which do not share this characteristic.

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Effects of CCK-8 and oxygen supply on redox state of mitochondrial cytochromes in exocrine pancreas. MATSUMOTO, T. AND KANNO, T. Dept. Physiol., Fac. Vet. Med., Hokkaido Univ., Sapporo 060.

Redox state of cytochrome $a+a_3$, b and $c+c_1$ were recorded simultaneously and continuously in the isolated rat pancreas arterially perfused at various flow rates. Under unstimulated conditions, varying the flow rate within the range 1.5-3.0 ml/min did not induce any change in redox state of the cytochromes, whereas decreasing the flow rate to 1.0 ml/min induced simultaneous reduction of the cytochromes. Coincided with secretory responses to CCK-8(30 pM, 100 pM and 1 nM) at the flow rate of 1.0 ml/min, almost a linear relation was obtained between the concentration of CCK-8 and reduction of each cytochrome. When the flow rate was increased to 1.5 ml/min, dose-dependent reduction of each cytochrome shifted to a higher concentration of CCK-8. Further increase in the flow rate to 2.0 and 3.0 ml/min, the reduction of all the cytochromes was almost nulified. These results suggest that CCK-8-induced reduction of respiratory chain components observed in the perfused pancreas reflects the occurrence of local hypoxia under limited oxygen supply.

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OUABAIN ABOLISHES PARALLEL REDUCTION OF CYTOCHROMES INDUCED BY HIGH POTASSIUM IN THE PYRIFORM CORTEX SLICE OF RAT BRAINS. SAITO,T.AND KANNO,T. Dept.of Physiol.,Fac. Vet. Med.,Hokkaido Univ.,Kita-ku, Sapporo 060

The redox state of cytochrome aa_3,b and $c+c_1$ in the pyriform cortex slice was measured with a scanning organ spectrophotometer. Rat brains were perfused with oxygenated HEPES-buffered Ringer solution containing 5% dextran-70 and heparin under ether anesthesia, and then removed after decaptation.Slices of the pyriform cortex containing lateral olfactory tract(LOT) were made by horizontal cut of the cortex(about 0.5 mm in thickness) and perifused with HEPES-buffered Ringer solution at a constant flow rate of 3ml/min at about 20°c,bubbled with 100%O_2. Parallel reduction of cytochromes was recorded by electrical stimulation of LOT, by perfusion with 60mM potassium solution or by hypoxia.Parallel reduction of cytochromes induced by 60mM potassium was abolished by perfusion with 1mM ouabain solution,but parallel reduction by hypoxia treatment was not nullified with the same dose of ouabain.Spontaneous electrical activity in the pyriform cortex was little influenced by perfusion with 60mM potassium or 1mM ouabain. These results suggest that cytochrome reduction by high potassium may correlate with activation of Na^+,K^+-ATPase in neurons and/or glia cells.

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COMPUTER ANALYSIS OF FLUORESCENT MICROSCOPIC IMAGES FOR INTRACELLULAR H^+ AND CA^{++} IN THE FROG PROXIMAL TUBULE. FUJIMOTO,M., KOTERA,K., KUBOTA,T., MATSUMURA,Y., KOIKE,T., AND YAMAGUCHI,J. 2nd Dept. of Physiol., Osaka Medical College, Takatsuki, Osaka 569

To study the ionic distribution of H^+ and Ca^{++} within the tubule cell of bullfrog kidney, we used a technique of computer-aided graphic analysis with Acridine Orange and Fura 2-AM as the fluorescent markers for kidney slice preparations perfused *in vitro*. Color signals of fluorescent dyes in the microscopic image were transferred to the input stage of a microcomputer (NEC-PC98XA) connected with a color analyzer (IFM/PC-512) and the color counts were displayed on a 512 X 512 dots screen. The conclusions obtained are as follows: 1) 10^{-5}M ionomycin, a Ca^{++} ionophore, 10^{-4}M produced an increase of cytosolic Ca^{++} in the proximal tubule. 2) 10^{-4}M dibutyryl cyclic AMP accelerated an accumulation of H^+ into the lysosomal vesicles, and elevated the cytosolic pH and Ca^{++} concentration with a decrease of cell Na^+, as demonstrated by ion-selective microelectrodes. 3) The above results indicated that the cellular ionic distribution is not uniform, and some vesicular transport must be taken into consideration for the regulation of cellular H^+ and Ca^{++}.

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METABOLISM OF NITROXIDE FREE RADICAL IN FROG MUSCLE. NISHIKAWA, H. Dept. Physiol. Kyoto Pref. Univ. Med., Kyoto 602

L-band electron spin resonance(L-band ESR) is a powerful tool to detect directly and nondestructively free radical in tissue containing a large quantity of water. But it is difficult to detect intrinsic free radical with very short life time or low concentration . In this paper we studied the metabolism of extrinsic stable nitroxide free radical in frog muscle by means of L-band ESR. ESR spectrum was obtained with a homemade L-band ESR system equipped with a single-loop coil(5mm i.d.). Observation frequency, field strength and field sweep range were 1.85GHz, 635gauss and $\pm$25gauss respectively. TEMPO, TEMPOL and 3-C-PROXYL were used as stable nitroxides. Ascorbic acid was used as a reducing agent of the nitroxides. Isolated frog muscle was placed in an isotonic solution with 1mM nitroxide for 1h. And then the ESR spectra of the muscle were obtained in time course at room temperature. The time constants of the reductions of TEMPO, TEMPOL and 3-C-PROXYL in a 2mM ascorbic acid solution were 6.1, 2.2 and 70.9min respectively. The time constants of the reductions of TEMPO, TEMPOL and 3-C-PROXYL in frog muscle were 7.6, 70.2 and $\gg$70.2min respectively. The differences between the time constants in a ascorbic acid solution and in frog muscle suggest that frog muscle may have other important reducing agents than ascorbic acid, for example cytochrome.

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INTRACELLULAR DISTRIBUTION OF DOPAMINE β-HYDROXYLASE IN ADRENOMEDULLARY CHROMAFFIN CELLS. MATSUMOTO,S., TANAKA,K., YAMAMOTO,A., NAKADA,H. UCHIDA,M. AND TASHIRO,Y. Dept. of Physiol. and Anesthesiol., Kansai Med. Univ. Moriguchi 570

Dopamine β-hydroxylase (DBH EC 1.14.2.1.) was purified from bovine adrenal medullae. Rabbit IgG raised against the DBH inhibited the enzyme activity by 80%. In the immunoblot analysis, the IgG specifically recognized two subunits of DBH (75kd and 72kd respectively). Chromogranin A (CGA) was also purified from bovine adrenal medullae. The rabbit IgG raised against CGA detected several chromogranins in the immunoblot analysis.

Intracellular distribution of DBH and CGA in the bovine chromaffin cells was examined quantitatively by immunoelectron microscopy using a post-embedding protein A-gold technique. DBH was observed both on the membranes and in the dense core contents of the chromaffin granules, whereas chromogranins were only in the latters.

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PERTURBATIONS OF THE HEPATIC ETHANOL METABOLISM UPON EXPOSURE TO LOW-FREQUENCY PULSED MAGNETIC FIELD. KOBAYASHI,S.,OMOTE,Y.,AND NAKAJIMA,S. Tateisi Inst. Life Sci.,Kyoto 616 & Dept.Surg.,Asahikawa Med.Col., Asahikawa 078-11

Electromagnetic interactions with the carbohydrate and respiratory metabolism 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_2-5%CO_2 saturated KHBB maintained at 37°C. PMF(N) generated from a solenoid (165ø,100T) was applied. The frequency was 200Hz and the intensity was 0.0055T. Scanning spectrophotometry and NADH fluorometry were performed on the liver surface. The effluent was monitored for pO_2 and analyzed for glucose, lactate, and pyruvate. [RESULTS] Exposure to PMF caused perturbations from ethanol-induced alterations —— reoxidation of NADH and re-activation of the inhibited glycogenolysis and glycolysis. Oxygen uptake was stimulated. The results suggest that those metabolic perturbations signify recovery which would come from the elevated level of ADP through electromagnetic stimulation.

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^{31}P- AND ^{1}H-NMR SPECTROSCOPIC ANALYSES OF CCL_4-INTOXICATED RAT LIVER.

NAKAJIMA, T.*, NAKASHIMA, T.*, [1]YOSHIZAKI, K. AND [1]NISHIKAWA, H. 3rd Department of Internal Medicine and [1]1st Department of Physiology, Kyoto Prefectural University of Medicine, Kyoto 602

The sequential changes in ^{31}P- and ^{1}H-NMR spectra of CCl_4-intoxicated rat liver were determined by using surface-coiled NMR spectroscopy (JEOL -SCM-200). In situ rat liver, fat signal increased significantly at 13 hrs after CCl_4 administration and thereafter ATP level decreased to be 85% of control at 24 hrs. In isolated perfused rat liver from CCl_4-treated rat, the ATP level was restored incompletely after an anoxic attack, as compared with the data from control. This suggests that mitochondrial oxidative phosphorylation system is damaged and fatty infiltration precedes the depletion of hepatic energy in CCl_4-intoxicated liver.

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TWO DIFFERENT TYPES OF POTASSIUM CHANNELS IN THE LUMINAL MEMBRANE OF AMPHIUMA DILUTING SEGMENTS.

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The luminal membrane of the Amphiuma diluting segment has a high potassium (K) permeability. This property is considered to be important for the recycling of K between the cell and lumen to supply K for the Na/K/2Cl co-transport system. We have used the patch-clamp technique to identify K channels in the luminal membrane. The diluting segment was isolated from a slice of the Amphiuma kidney. The lumen was opened by ripping off the tubular wall with fine forceps. The channels appear in clusters (3-6 channels per patch membrane) and are highly selective for K. The single channel conductance was 30 pS with 100 mM KCl in the pipette. They are mostly open at the resting potential (the open probability (Po) is about 0.8). Po decreased when membrane potential was hyperpolarized. The second channel does not open until membrane potential is raised above +40 mV. Po increased when membrane potentials were more positive. Po was also sensitive to Ca in the cytoplasmic side. The single channel conductance was about 200 pS.

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PROPERTIES OF MEMBRANE CURRENT INDUCED BY Na^+/AMINO ACID COTRANSPORT IN EPITHELIAL CELLS.

HOSHI,T., MARUYAMA,Y. AND NUNOKAWA,T. Dept. of Physiol., Faculty of Med., University of Tokyo, Tokyo 113

Although extensive studies have been made of kinetic properties of cation-coupled cotransport systems, mechanisms of translocation of the cotransported substances via the cotransporters are still largely unknown. Studies with conventional microelectrodes in intact epithelial cells suggest that the initial binding of a nonelectrolyte is followed by immediate opening of the pathway for the cation(e.g. Na^+) and the resultant flow of the cation couples with the flow of the substrate in some unknown way within the carrier. To see whether a cation/nonelectrolyte cotransporter behaves like an ion channel, i-v characteristics were studied in pancreatic acinar cells by using whole cell clamp techniques. It was found that application of 4mM L-alanine to only the outer medium caused an immediate inward current surge which was independent of membrane potential (pipette potential). The induced current revealed a high Q_{10} (3.6 between 20 and 30°C). When the pipette solution contained L-alanine, voltage-sensitivity appeared, but the equilibrium potential could not be determined. Thus, the cotransport current must be considered to be generated by a mechanism much different from that in ion channels.

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ROLE OF CYTOSOLIC Ca^{2+} IONS IN THE ACTIVATION OF ION CHANNELS DURING A REGULATORY VOLUME DECREASE IN CULTURED EPITHELIAL CELLS. HAZAMA, A., OIKI, S. AND OKADA, Y., Dept. Physiol., Fac. Med., Kyoto Univ., Kyoto 606

Upon exposure to hypotonic solutions, an epithelial cell line (Intestine 407) exhibits a regulatory volume decrease (RVD) after transient osmotic swelling. In the preceding meeting, we reported that independent activation of quinine-sensitive K^+ channels and SITS-sensitive Cl^- channels is responsible for the RVD process. In the present study, a role of intracellular Ca^{2+} ions in the operation of these channels was examined under low Cl^- conditions (6 mM in the bathing solution). Deprivation of extracellular Ca^{2+} ions inhibited hyperpolarizing responses (due to K^+ channel activation) to hypotonic challenge, but not subsequent depolarizing responses (due to Cl^- channel activation). Intracellular Ca^{2+} injections induced quinine-sensitive transient hyperpolarizations, but did not depolarizations. Using Ca^{2+}-selective microelectrodes, sizable increases in the cytoplasmic free Ca^{2+} concentration were observed to be coupled to hyperpolarizations, but not to subsequent depolarizations during the RVD process. Thus, it appears that the volume-regulatory K^+ channel is activated by an increase in the cytosolic free Ca^{2+} ions, but the Cl^- channel is not dependent on elevation of the cytosolic Ca^{2+} level.

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INTRACELLULAR CALCIUM RELEASE MEDIATED BY INOSITOL TRIPHOSPHATE IN HAMSTER EGGS. MIYAZAKI, S., Dep. Physiol., Jichi Med. Sch., Tochigi, 329-04.

The golden hamster egg at fertilization shows periodic increase in intracellular Ca ion concentration (Igusa & Miyazaki, 1986). Each Ca transient has the duration of 12-18 sec, and the interval between Ca rises is 40-120 sec. Analysis of the Ca increases has lead to the conclusion that each response is due to Ca release from intracellular stores. In the present study, the mechanism involved in the Ca release by sperm-egg interaction was analysed by microinjection of substances related to phospholipid metabolism in the plasma membrane. Injection of inositol 1,4,5-triphosphate (IP_3) into an unfertilized egg induced a Ca rise with the minimum concentration of 2-3 nM(calculated by the assumption that the injected substance distributes evenly in the cytoplasm). Injection of GTPγS, a hydrolysis-resistant analog of GTP, induced a Ca rise with a delay of 50-200 sec, when the concentration was lower than 50 μM. With higher concentrations, GTPγS produced periodic Ca rises like those induced by sperm. GDPβS, a hydrolysis-resistant analog of GDP, inhibited sperm-induced Ca rises as well as GTPγS-induced Ca rises. It is suggested that sperm-egg fusion activates phospholipase C by way of GTP-binding protein in the membrane, leading to hydrolysis of phosphatidylinositol 4,5-biphosphate to produce IP_3, which mobilizes Ca ions from intracellular stores.

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A PHYSIOLOGICAL ROLE OF CALMODULIN IN MITOCHONDRIA. HATASE, O., ITANO, T., MATSUI, H., DOI, A., ETOH, S. AND MINAMOTO, Y., Dept. of physiology, Kagawa Med. Sch., Kagawa, 761-07

We reported the existence and purification of calmodulin (CaM) in mitochondria (Mt) [B.B.R.C. (1985) 132,63-66]. We also identified several CaM binding proteins in Mt [Biochem. Internatl. (1986) 13,787-792]. In this report, we show a possible role of CaM in Mt which is closely related to the morphological changes.

The 90°light-scattering was measured at 540nm by a double beam fluorophotometer. Measurement of extra-Mt free Ca concentration was performed photometrically by arsenazo-III. The difference in optical density at 670nm-685nm was monitored by a double wavelength spectrophotometer. The amount of Ca which was accumulated in Mt was determined by an atomic flame spectrophotometer. Immunohistochemical localization of actin in Mt was proved by anti-actin sera and protein A-gold.

Two affinities of Ca to Mt swelling were revealed; high (2-5 μM) and low (more than 100 μM) systems. The high affinity change was inhibited by micromolar order of trifluoperazin and W-7 dose-dependently, but not by W-5 which is a less potent derivative of W-7. These drugs do not have any effects on the transport of Ca into Mt. Mt also have actin(like) protein(s) which was proved by the immunohistochemical studies. These data support that CaM has some important roles in the configurational changes in Mt.

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IMMUNOHISTOCHEMICAL STUDY OF CALCINEURIN IN THE RAT HIPPOCAMPUS USING A MONOCLONAL ANTIBODY. MATSUI, H., DOI, A., ITANO, T., ETOH., S., MINAMOTO, Y. AND HATASE, O. Dept. of Physiology Kagawa Med. Sch., Ikenobe, Miki, Kagawa, 761-07

Calcineurin is the major calmodulin-binding protein in the brain, which is composed of two subunits: A(61 kDa) and B(20 kDa). This protein is divalent metal ion dependent and calcium-calmodulin stimulated phosphatase, and is a metalloenzyme containing tightly bound zinc. But the physiological significance of the ions in calcineurin activity is not well established. Recently we developed a monoclonal antibody VD_3 which is specific for A subunit of calcineurin. This antibody enables us to study the immunohistochemical localization of calcineurin with much higher sensitivity and specificity than conventional polyclonal antibodies.

We report that calcineurin is rich in the hippocampus, striatum and thalamus in the rat brain. In the hippocampus, the enzyme is abundant in the stratum lucidum where giant synapses and high content of zinc are present.

Calcineurin phosphatase activity is strongly inhibited by zinc and is stimulated by Dithizone, a metal ion chelator which has high affinity for zinc. These data suggest that calcineurin associates with synaptic function and that physiological role of zinc is likely to control the enzyme activity in synapses.

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PROPERTIES OF POTASSIUM CURRENT IN CULTURED MACROPHAGE (P388D1) CELL MEMBRANE. MARUYAMA, T. Dept. of Applied Physiol., Tohoku Univ. Sch. of Med., Sendai 980.

The properties of potassium current of macrophage (P388D1) cell membrane was studied, using a whole cell mode of patch electrode voltage-clamp technique. Outward current were activated an exponential time course of several milliseconds time constant when the membrane potential was made more positive than -30 to -20 mV. The current voltage relation for the peak current was S-shaped, with a maximum was at about 50 mV. The reversal potential for the current relaxations changes with external K^+ concentration as predicted by the Nernst relation. The current was inhibited by quinine and 4-AP, but slightly affected by TEA. The amplitude of current decreases exponentially with time constants of several hundred milliseconds during the maintained voltage pulse. Mg^{2+}, Co^{2+} and low-Ca^{2+} suppressed the inactivation of current, but not amplitude of activated currents. The reversal potential for these current relaxations reversed at the potasium equibrium potential. These results indicates that the outward currents of macrophage (P388D1) cell membrane is predominently carried by K^+, and the inactivation of currents are controlled by Ca^{2+}.

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FACTORS MODULATING MITOGEN-REGULATED CALCIUM PERMEABLE CHANNEL IN T-LYMPHOCYTES. KUNO, M. & GARDNER, P.* Dept. of Physiology, Osaka city Univ. Med. Sch. & Stanford Univ. Sch. of Med.*

Recently, we have found Ca^{++} permeable channel in human T-lymphocytes using patch clamp technique. The channel was activated by mitogen and suggested to be involved in a rise of cytosolic free Ca^{++} during early stages of lymphocyte activation. Here, we studied the factors which regulated activity of the channel in human cloned helper T-lymphocytes and Jurkat cells (T-cell leukemia cell line). Gating of the channel did not appear to be affected by membrane potential. In inside-out patches, open probability of the channel was greatly decreased by 1uM and larger Ca^{++} on internal membrane surface and increased by lower concentrations (0.01 - 0.1 uM). In whole cell clamp, elevation of external Ca^{++} to 20mM was accompanied by a rapid decay of the larger inward current induced by phytohaemagglutinin (PHA). An application of inositol 1,4,5 triphosphate (IP_3, 2.5 - 10 uM) on internal membrane surface of inside-out patch increased open probability of the channel similar to PHA-induced activation in cell-attached patch. These results suggest that the Ca^{++} permeable channel is activated by IP_3 produced after mitogenic activation and inactivated by the resultant increased cytosolic Ca^{++}.

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EFFECTS OF INTRACELLULAR IONS AND ATP ON FUROSEMIDE-SENSITIVE ION COTRANSPORT IN HeLa CELLS. IKEHARA, T., YAMAGUCHI, H., HOSOKAWA, K. AND MIYAMOTO, H. Dept. Physiol., Sch. Med., Univ. Tokushima, Tokushima 770, Japan

Study of the effects of cellular levels of ions and ATP on ouabain-insensitive, furosemide-sensitive Rb influx (J_{Rb}) was made in HeLa cells. The cells were incubated at 37°C in normal medium but containing 10 μM ouabain. Then, the cellular Na content increased and the K content decreased with time. The contents of Na plus K and Cl were, however, maintained almost at the normal levels. The cells incubated for various periods in such medium had different contents of Na and K. These cells were used for assay of J_{Rb}. A significant positive correlation was demonstrated between J_{Rb} and the transmembrane gradient of chemical potential of Na ($\Delta\mu Na$), whereas there was a negative significant correlation between J_{Rb} and $\Delta\mu K$. The results suggest that Na is primary driving force for J_{Rb}, while cellular K increases J_{Rb} by stimulating K efflux through the diuretic-sensitive K/K exchange mechanism. We obtained the cells having various ATP levels by incubating them for 2 hours at 37°C in medium with 2 μM CCCP and varied concentrations of glucose. Hill coefficient of 1.49 was derived from Hill plot of J_{Rb} vs. the cellular ATP level, implying the presence of at least two ATP binding sites on the diuretic-sensitive ion cotransport system. However, further experiments are necessary to confirm this implication.

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Na/K PUMP ACTIVITY IN PLASMA MEMBRANE OF NEWT BLASTOMERES AT 2-CELL STAGE IS LOCALIZED IN THE NEW MEMBRANE. OHARA, A.[1], DOIDA, Y.[1], MURAYAMA, K.[2], IMAIZUMI, M.*[1] & KITASATO, H.[2] [1]Dept. Biol. and [2]Dept. Physiol., Shiga Univ. Med. Sci., Ohtsu 520-21.

Membrane potential of eggs of Japanese newt, Cynops pyrrhogaster, is hyperpolarized from about -10 to -80 ∿ -100 mV during the first cleavage (from 1- to 2-cell stage) and Na/K pump activity considerably contributes to the membrane potential at 2-cell stage (Ohara et al., 1984, 1985). The present study shows that the Na/K pump activity appears only in the new membrane formed at the first cleavage. (1) Na/K ATPase in the membrane of blastomeres at 2-cell stage was cytochemically stained for electron microscopic observation by Ernst's method (Ernst, 1972). The new membrane yielded abundant deposits of lead phosphate. But the old membrane did not produce reaction deposits. When eggs were incubated in a solution containing ouabain, reaction products were not found even in the new membrane. (2) The loose-patch clamp method was applied to blastomeres at 2-cell stage. Pipettes with diameters of 200 to 500 μm were used. Pipettes contained a bathing solution and their resistances were 50 to 80 KΩ. Patch membranes were held at the resting membrane potential of blastomere. On the new membrane, high seal resistances of 80 to 100 MΩ were obtained. Addition of ouabain to the solution of pipettes produced inward currents of 70 to 200 pA. On the old membrane, seal resistances were 2 to 10 MΩ. The addition of ouabain did not show the above effect.

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ROLE OF GUANINE NUCLEOTIDE REGULATORY PROTEIN IN HISTAMINE SECRETION FROM DIGITONIN-PERMEABILIZED RAT MAST CELLS. Sorimachi, M., Nishimura, S. and Yamagami, K. Dept. Physiol., Sch. Med., Kagoshima Univ., Kagoshima 890

The role of guanine nucleotide regulatory protein(N protein) in histamine secretion was investigated using rat mast cells permeabilized with digitonin. The addition of GTP, GTP analogue or NaF increased the sensitivity of secretion to Ca ions, and the simultaneous addition of GDP partially inhibited the stimulatory effect of GTPγS. The ^{35}S-GTPγS binding proteins were found in both the 100,000 g supernatant and pellet of the mast cells. However, the Ca dose-response curve with or without GTP analogue or NaF was not altered after 2 hr treatment of the cells with pertussis toxin,which is reported to inhibit the response to comp. 48/80 possibly by ADP-ribosylating one of N proteins. Release of ^{3}H-arachidonate from the prelabeled cells was siginificantly increased in response to Ca plus either GTPγS or NaF. The release of both arachidonate and histamine was reduced by the addition of p-Bromophenacyl Br or neomycin, which is an inhibitor of PLA_2 or PIP_2-PLC, respectively. However, none of products expected from these two reactions increased the sensitivity of secretion to Ca. These results suggest the existence in mast cells of a guanine nucleotide-dependent mechanism regulating the secretion of histamine, but its exact mechanism remains to be determined.

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ROLE OF PROTEIN KINASE C IN THE REGULATION OF AMYLASE RELEASE IN RAT PAROTID GLAND.
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Calcium ionophores (A23187 and ionomycin) or phorbol esters (PMA and phorbol dibutyrate(PDBu)) did not stimulate amylase release in the rat parotid slices, but the combination of both markedly augmented the amount of amylase release. The amylase release by α-adrenergic agonists (phenylephrine and methoxamine) or cholinergic agonists (carbamylcholine and oxotremorine) were significantly augmented by PDBu, but not by A23187, and the amount of amylase release by the combined addition of α-adrenergic or cholinergic agonist and PDBu was much higher than that by the agonist alone. We partially purified protein kinase C (C kinase) from the parotid gland using DE 52 cellulose chromatography and characterized its dependence on calcium, phosphatidylserine, diolein and PDBu. PDBu had a little effect on C kinase activity when added directly to the assay. Preincubation of the parotid slices with PDBu, but not with carbamylcholine and phenylephrine, decreased the activity of C kinase in cytosol fraction and increased it in membrane fraction. These results show that C kinase activation by phorbol esters acts synergistically with increased calcium to give an amplified amylase release. This mechanism, however, cannot completely explain the effect of α-adrenergic and cholinergic agonists.

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EFFECTS OF PROSTAGLANDIN A_1 AND 20-HYDROXY-PGA_1 ON SERUM INSULIN CONCENTRATION.
KAKU, M., SUZUKI, H. IMAMURA, Y. ** AND HORI, S. 1st Dept. of Physiol., *4th Int. Med. Hyogo Coll. of Med. **Kyowa Synth. Med. Lab. Nishinomiya

The effects of prostaglandin (PG)E_1, A_1 and 20-OH-PGA_1, the $\omega(20)$-hydroxylation product of PGA_1 by cytochrome P-450ia or P-450ca in intestinal mucosa, on concentrations of serum insulin, lipids and lipoproteins were studied in rabbits. Various doses of PGs were infused via vena continuously for 30min.

Low doses of PGs (2~4ng/kg/min) increased serum insulin immediately after infusion and then followed by a slow decrease. The maximum increment at 5 min for 20-OH-PGA_1 was 4.34 ± 0.24μU/ml (m±S.E., n=5). The order of effectiveness was 20-OH-PGA_1 > PGA_1 > PGE_1. On the contrary, high doses of PGs (100~200ng/kg/min) decreased serum insulin sharply within 5 min. After the fall, the rebound phenomenon followed on this and then serum insulin level reached at initial level slowly. The order of effectiveness was PGE_1>PGA_1 > 20-OH-PGA_1. The most decrement at 5 min by 20-OH-PGA_1 was 5.35± 0.25μU/ml(m±S.E.,n=5).The temporary decreases of free fatty acids (FFA), β-lipoproteins and low density lipoproteins were observed withih 10 min in cases of low doses of PGs. However high doses of PGs increased FFA gradually without initial fall. These changes in FFA might be induced by any factors caused by PGs as well as insulin.

It is interesing that the low and high doses of one and the same PG play an opposite role in control of plasma insulin and FFA.

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MESSENGERS IN THE MECHANISM OF GASTRIC ACID SECRETION.
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Histamine induces transient elevation of the intracellular cAMP level, triggering acid secretion. Histamine H_2 receptor antagonists such as cimetidine, ranitidine, famotidine inhibit the acid secretion. In this study we report that reduced glutathione content in rabbit gastric glands was very high and the presence of 2-cyclohexene-1-one (2-CHX-1) reduced the glutathione content. The reduction of glutathione content in glands triggered acid secretion in the absence of secretagogues such as histamine, Ach, cAMP. Next in frogs (bullfrogs and Xenopus), the addition of ranitidine arrested acid secretion in the presence of cAMP or/plus theophylline. This finding is impossible to explain from the histamine →cAMP mediator theory. After the arrest, the addition of 1 mM 2-CHX-1 completely recovered the acid secretion. But in the presence of colchicine, the effect of 2-CHX-1 disapperaed. These results suggest that H_2 antagonist induced an unknown "stop" signal which was not related with cAMP and that the decrease in the level of intracellular glutathione could pass or execute the stop signal.

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DIELECTRIC ANALYSIS OF HUMAN RED CELL GHOSTS, SPHEROCYTES AND ECHINOCYTES IN THE 10 kHz - 500 MHz RANGE.

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In an attempt to standardize the procedure for a noninvasive dielectric analysis of living cells we analyzed the dielectric behavior of spherical erythrocytes (i.e., ghosts and spherocytes) and echinocytes. Dielectric dispersions of the spherical ghosts and spherocytes were almost ideally of the Debye type with Cole-Cole's β parameters of $\sim$0.97, while dispersions of the echinocytes were broader than the former and were of the Cole-Cole type having a β-value of 0.90. Discocytes in physiological saline showed an apparent deviation from typical circular loci, which was most probably due to their nonspherical shape. On the basis of Hanai's theory for concentrated suspensions, we proposed a procedure for point-by-point analyses of dispersion data — a sort of 'dielectric peeling' of surface membrane to expose the cell interior. Application of this new procedure revealed that: (1) both the ghosts and spherocytes shared a common membrane capaity (C_m) of 0.6 $\mu F/cm^2$ which compares favorably with the C_m of artificial lipid bilayer membranes, (2) the intracellular permittivity for both specimens centered around 67, a value lower by 15% than the medium permittivity, and (3) the internal-to-external conductivity ratios were 0.61 for spherocytes and 0.43 for echinocytes.

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MODULATION OF EPIDERMAL GROWTH FACTOR BINDING TO A431 CELLS BY EXTRACELLULAR ATP

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Incubation of A431 epidermoidal carcinoma cells with 0.1 to 10 mM ATP reduces the number of high affinity EGF binding sites on these cells to less than half the number on control cells. The effect is detectable after 5 min of incubation, and is maximal after 15 - 30 min of incubation at 37°C, but not at 2°C, over a pH range of 6 to 8.5. UTP, GTP and ADP, but not CTP or AMP have effects on EGF binding similar to that of ATP, but are less effective than ATP. The incubation of the same cells with ATP under opitimal condition also stimulated the phosphorylation of EGF receptors suggesting the possibility that extracellular ATP, either directly or indirectly, activates a protein kinase which phosphorylates the receptor proteins followed by changes of the receptor affinity for EGF.

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ANALYSIS OF SECRETION MECHANISM OF TISSUE-TYPE PLASMINOGEN ACTIVATOR IN A HUMAN MELANOMA CELL LINE (BOWES).

SAKAI, T., OKADA, K., BANDO, H., KIKUCHI, H., UESHIMA, S., TANAKA, N. and MATSUO, O. Dept. Physiol. Kinki Univ. Sch. Med., Sayama, Osaka 589.

A human melanoma cell line (Bowes) secretes tissue-type plasminogen activator (t-PA) into culture medium. As previously reported, monensin, an ionophore for monovalent cations, depressed secretion of t-PA. In the present study, secretion and intracellular distribution of t-PA were investigated under normal and monensin-treated conditions. Plasminogen activator (PA) activity or t-PA antigenicity in the cell organelles measured by the discontinuous sucrose density gradient ultracentrifuge method, was not uniformly distributed, but rather localized to the fractions where cell organelles were rich. ^{35}S-methionine or ^{3}H-mannose labeled t-PA antigens also showed localized distribution similar to that of PA activity after a long term labeling (4 h). Pulse labeling with ^{35}S-methionine (3 min) showed that intracellular labeled t-PA antigen was produced in about 10 min, reached to maximum in 30 min, and decreased after 40 min. Radioactivity of secreted t-PA antigen was observed in 30 min and increased linearly at least following 20 min. Enzymography revealed that there were a major intracellular PA activity at 72 kDa and a minor one at 50 kDa. Monensin treatment caused intracellular accumulation of 72 kDa component which was immunologically homologous to secreted t-PA.

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SEX DIFFERENCE OF PROTEINASE F IN THE THREE MAJOR SALIVARY GLANDS OF INBRED MICE Murai,T., Atsumi,T., Hosoi,K. and Ueha,T., Dept. of Oral Physiol., Josai Dental Univ., Sakado, Saitama 350-02

Using the radioimmunoassay technique, we determined the contents of proteinase F (pro F) in the three major salivary glands of five inbred strains (ICR, BALB/CA, C3H/HeN, C57BL/10N and DBA/2N) of mice. We found that both the parotid gland (PG) and sublingual gland (SLG) contain appreciable amounts of pro F, though they were about 100 times less than those in SMG. In DBA/2N, there observed no sex difference in the enzyme content but in other strains, the male glands (SMG, PG and SLG) generally contained more pro F than female glands except those in ICR SMG and C3H/HeN SLG in which the contents were high in females and low in males. In females and castrated males, the injection of the androgen decreased the pro F contents in SMG (ICR) and SLG (C3H/HeN) but it increased the enzyme in the PG and SLG (ICR), and in SMG and PG (C3H/HeN). Thus the contradictory of the sex differences seen in ICR SMG and C3H/HeN SLG also depends on androgen though the direction of the hormone response is opposite.

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ELECTRON MICROSCOPIC STUDY ON MAST CELL DEGRANULATION.
OKADA,T., SAKAI,J., NAKASHIMA,A., NAKAMURA,Y., YAMANOUCHI,H. and SUGIE,I.
Dept. of Physiol., Aichi Med. Univ., Nagakute. Aichi, 480-11

Dynamic records of cytological changes with a time-lapse cinematography revealed the process of degranulation of mast cells caused by various stimuli. Sensitized rat mast cells were purified with a modified coil planet centrifuge and challenged with antigen (DNP-As). Ultrastructural changes were studied with transmission or scanning electron microscope. Mast cells are packed with electron dense granules which cause hemispherical elevations when observed with SEM. Granules extrude from degranulation pores and labyrinthic cavities containing altered granules are formed beneath the cytoplasmic membrane. Granules except for those in the cavity remain intact even 3 hours after antigenic challenge. Degranulated cells become smaller in size and the numbers of surface microvilli or ruffles decrease. These characteristics of exocytosis are quite different from those observed in spontaneously damaged cells.

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CHANGES IN ORGANIZATION OF ACTIN FILAMENTS, FIBRONECTIN RECEPTOR AND GAP JUNCTIONAL COMMUNICATION BY PROLIFERATION AND DIFFERENTIATION OF 3T3-L1 CELLS. SHIBA, Y., SASAKI, Y. AND KANNO, Y. Dept. of Physiol., Hiroshima Univ. Sch. of Dent., Hiroshima 734.

Modulation of cell-cell and cell-substratum interactions by growth enhancement and adipocyte conversion was studied in an attempt to clarify their role in control of proliferation and differentiation. The ability to form cell-cell contacts and permeability of gap junctional communication were measured by microinjection of Luciffer Yellow CH. Distribution of fibronectin receptor was observed by using latex beads coated with plasma fibronectin. The latex beads coated with fibronectin did not bind to quiescent 3T3-L1 cells, but addition of serum and fibroblast growth factor enhanced binding of beads to cells. Disappearance of actin filaments and decrease in the permeability of gap junctional communication were observed in the cells with bound beads. Adipocyte conversion also induced the similar changes. These results indicate that growth enhancement and adipocyte conversion are accompanied with the modulation of cell-cell and cell-substratum interactions and with reorganization of cytoskeleton.

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CELL-TO-CELL COMMUNICATION OF RAT BROWN AND WHITE ADIPOCYTES IN PRIMARY CULTURE. SASAKI, Y., SHIBA, Y. AND KANNO, Y. Dept. of Physiol. Hiroshima Univ. Sch. of Dent., Hiroshima, 734.

Gap junctional cell-to-cell communication competence was measured by microinjection of Lucifer Yellow CH (M.W. 457.3) during adipocytes differentiation of preadipocytes from rat interscapular adipose tissue (BAT) and epididymal white adipose tissue (WAT). Numbers of dye recipient cells of preadipocytes from BAT and WAT were 52.9+3.7 (mean+S.E., n=20) and 55.4+3.2 (n=20), respectively. Numbers of dye recipient cells of the adipocytes were decreased to 1.8+1.4 (20) and 1.2+0.5 (20), respectively. Treatment with noradrenalin (100 uM) and isoproterenol (100 uM) for 24 hr significantly enhanced cell-to-cell communication of the preadipocytes and the adipocytes.

These results indicate that cell-to-cell communication competence is suppressed during the adipocytes differentiation and is enhanced with noradrenalin. This work was supported by Grant-in-Aid for Encouragement of Young Scientist (No. 61770074).

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STUDY ON INSULIN BINDING OF THYMOCYTES IN STREPTOZOTOCIN-INDUCED DIABETIC RATS. OKIMOTO, T., HATO, F., OSHITANI, N., TOYOKAWA, T., KIMURA, S. AND KINOSHITA, Y., Dept. of Physiol., Sch. Med., Osaka City Univ., Osaka 545

We previously documented that the disorder of differentiation and maturation of thymus lymphoid cells was observed in the streptozotocin(STZ)-induced diabetic rats. In order to study on the relationship between the disorder and STZ-induced hypoinsulinemia, the insulin binding of the cells was scrutinized. From the result presented by Scatchard plots, a significant reduction in the number of insulin receptors on the surface of thymocytes was found with aging in the STZ-nontreated control, but in the diabetic rats, the reduction was not significant. It was assumed that the receptor number in the STZ-diabetic rats was relatively increased as compared with the control, however, the receptor affinity seemed to be reduced in the STZ -induced diabetic rats. Then, the cell size of the thymocytes was analyzed by the size distribution analyzer. The increase in the constitutive ratio of large lymphocytes was observed in the STZ-diabetic rats. On the other hand, the insulin receptors were hardly detected after removal of the large lymphocytes by the adhesion column treatment in both groups. It was speculated that the increase in the receptor number in the diabetic rat thymocytes would be caused in general by an enhancement of the constitutive ratio of the large lymphocytes in the thymus.

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SEPARATION OF THE BIOLOGICALLY ACTIVE POLYPEPTIDES FROM CULTURE SUPERNATANT OF RAT THYMUS EPITHELIAL CELL LINE (IT-45R1). TANIYAMA, T., HATO, F., MORIOKA, K., KIN, T., TOHJI, Y., TOYOKAWA, T., KIMURA, S., KINOSHITA, Y. Dept. of Physiol., Sch. Med., Osaka City Univ., Osaka 545

It has been considered that the thymic hormones secreted from thymus epithelial cells play critical roles in the differentiation and maturation of T cell series. Then, we separated several thymic polypeptide fractions from culture supernatant of IT-45R1, thymus epithelial cell line derived from Wistar strain rats, by high-performance liquid chromatography equipped with gel-filtration column. It was found that C fraction had an activity to endow non-rosette forming cells, possibly precursor T cells, with rosette forming capacity and that molecular weight of the fraction (about 3,000) approximated to that of thymosin α_1, one of active thymic hormones. The biological activity was significantly suppressed by pretreatment of the fraction with anti-thymosin α_1 antiserum. It was, therefore, assumed that the polypeptide molecule which possessed the same antigenic determinant as thymosin α_1 might exist in C fraction. We further purified the fraction by reversed phase column and found that the activity exsisted in major two subfractions in the separated polypeptide subfractions.

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DNA-MEDIATED GENE TRANSFER INTO MYELOMA CELLS BY ELECTROPORATION USING A NOVEL TYPE OF RECTANGULAR-PULSE GENERATOR. OKADA, Y., *HIRAYOSHI, K.*, NISHIKAWA, S.* AND KATSURA, Y.*, Dept. Physiol. and *Chest Dis. Res. Inst., Fac. Med., Kyoto Univ., Kyoto 606.

To generate square wave pulses of high electric fields (up to 3kV) between electrodes interposed with physiological electrolyte solutions, a new type of machine with a low output impedance (about 40 ohms) was constructed by combining a capacity discharge circuit and a pulse-transformation circuit. Duration of rectangular pulses can quantitatively be varied between 10 and 300 μs. Plural pulses can be applied at short intervals (within 1 s) without bringing about reduction of the amplitude. Using this pulse generator, transfection of the plasmid DNA was performed in mouse myeloma J558L cells. It was found that not only pSV2-neo (5.6 kb) but also pSV-Vμ1 (20 kb) can be introduced with high transformation frequency (up to 2 x 10^{-4}) by applying 2 pulses of 3 kV/cm (duration 150 μs). The radioimmunoassay for anti-NP antibody and the Western blot analysis indicated that introduced genes are intactly functioning within the cell.

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EFFECT OF MACROPHAGE-CONDITIONED MEDIUM ON SURVIVAL AND DNA SYNTHESIS OF ADULT RAT HEPATOCYTES IN PRIMARY CULTURE. KAORU HASEGAWA, KAZUTO WATANABE AND MUTUYOSI KOGA, Dept. Physiol., Dokkyo Univ. Sch. Med., Mibu, Tochigi 321-02.

We have previously reported the induction of proliferation of adult rat hepatocytes in primary culture. Post-mitotic hepatocytes, however, gradually degenerated after one week of culture. To study regulatory mechanism of proliferation as well as differentiation, long-term culture of post-mitotic hepatocytes is necessary. For this purpose, we cultured macrophages, and examined the effect of the conditioned medium on hepatocytes. Rat peritoneal macrophages were obtained 3 days after intraperitoneal injection of liquid paraffin, and cultured in a MEM alpha medium supplemented with insulin (100ng/ml) and Trasylol (2 U/ml). After medium refreshment at 1 hr later, endotoxin (5 μg/ml) and adjuvant peptide (1 μg/ml) were added. Macrophage-conditioned medium (CM) was collected 20-24 hrs after plating. When CM was supplemented at pre-replicative period, DNA synthesis was inhibited dose-dependently. Maximum inhibition was observed at 10% of CM. On the other hand, when CM was added to post-mitotic confluent culture of hepatocytes, survival time of hepatocytes was prolonged to 4 weeks as compared with 1-2 weeks in control culture. These results indicate that macrophages synthesize and release factor (s) that promotes survival time and inhibits DNA synthesis of hepatocytes in primary culture. Now we are purifying this factor(s) in CM.

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STIMULATION OF GROWTH OF MOUSE MAMMARY TUMOR CELLS BY CONDITIONED MEDIA OF VARIOUS FIBROBLASTS. ENAMI, J. AND KOGA, M. Dept. Physiol., Dokkyo Univ. Sch. Med., Mibu, Tochigi 321-02

We have previously reported that mammary fibroblast-conditioned medium (CM) contained a growth factor(s) for normal and neoplastic mammary epithelial cells of the mouse (Gann 74, 845, '83). We have also reported partial purification and characterization of the factor (in "Growth and Differentiation of Mammary Epithelial Cells in Culture", Japan Scientific Societies Press, '87). In this study, we have examined whether fibroblasts from other organs also produce growth factors for mammary tumor cells in culture. Among varieties of fibroblast-CM tested, adult vaginal, prostate, salivary fibroblasts and embryonic mammary, salivary mesenchymes stimulated the growth of mammary tumor cells. Thus, it was shown that stromal fibroblastic cells of various organs produce a growth factor(s) for mammary tumor cells. The similarities of these factors to mammary fibroblast-derived factor remain unknown. These factors may act not only to mammary tumor cells but to epithelial cells of their own origin.

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ANTINEOPLASTIC EFFECTS OF CARNOSINE(CAR) AND HOMOCARNOSINE(HCAR).

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Antineoplastic effects of carnosine(CAR) and homocarnosine(HCAR) were examined in vivo using ddY mice implanted with the solid tumor Sarcoma-180. The tumor cells were treated with tripsin and implanted (10^5 cells) subcutaneously in the back of the animals, then the test agents were administered subcutaneously 2 cm from the implantation site starting on the next day. The animals treated with CAR or HCAR alone showed prolongation of survival with T/C values (%) of 123-180%, and the growth of the tumor was inhibited. Regression of the tumor was observed in the animals treated with either of the agents. The effects of these agents were enhanced when administered in combination with the non-specific active immuno-enhancing agent, OK-432. Those treated with CAR or HCAR and OK-432 showed a prolongation of survival to a T/C value of >218, 181%. Inhibition of tumor growth and prolongation of survival (T/C = 177%) were also observed in the animals treated with γ-irradiation in combination with the administration of HCAR. We further point out that the conventional theory of immunity has ignored tissue repair function of the interstitial tissue and is, therefore, not consistent with the defense mechanisms of the body, and discuss the significance of the interstitial tissue in antineoplastic action.

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Effects of various agents on the breakdown of glycogen in rat submandibular gland.

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The breakdown of glycogen was increased by pilocarpine, adrenaline, or NaF in a dose-dependent manner. Glucagon slightly stimulated the breakdown of glycogen, but insulin did not. The response to adrenaline was inhibited by phentolamine and/or propranolol, while that to NaF was not. The effect of NaF was not influenced in the presence of 1 mM caffeine. The breakdown of glycogen was stimulated by DBcAMP or DBcGMP. The breakdown of glycogen by adrenaline was inhibited by Ca antagonist such as La, diltiazem, and verapamil. On the other hand, the response to NaF was significantly inhibited by La, but was not inhibited by diltiazem or verapamil. Chlorpromazine, trifluoperazine and W-7, calmodulin antagonists, did not inhibit the breakdown of glycogen induced by adrenaline or NaF. These results suggest that the effect of adrenaline on the breakdown of glycogen depended on the increase in Ca influx as compared with the case of NaF and that calmodulin was not involved in the process of the glycogen breakdown induced by adrenaline or NaF.

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IONIC CHANNELS IN SYNOVIAL CELLS FROM THE KNEE JOINT OF RHEUMATOID SYNOVITIS.

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We studied ionic channels in the cells from human lining layer using the patch-clamp technique. In the lining layer, two cell types (A- and S-cell) have been identified by EM (Barland & Novikoff, 1962). A-cell is called a macrophage-like cell, having phagocytotic vesicles. S-cell is called a fibroblast-like cell, having secretory granules. We obtained synovial cells from the knee joint of rheumatoid synovitis at operations and cultured them in MEM with 20% FBS. In culture, A-cell changed its appearance from a macrophage-like to a bipolar cell. S-cell was primarily a large round cell, becoming a fibroblast-like one after several days. Addition of cyclic AMP to the medium changed the S-cell into a stellate appearance. The resting membrane potential recorded in the whole-cell current-clamp mode was ca. -45 mV in the large round cell and ca. -26mV in the bipolar cell (with a pipette solution (in mM) : 125 KCl, 30 KOH, 4 $MgCl_2$, 2 $CaCl_2$, 10 EGTA, 5 HEPES, pH=7.2 and normal bathing medium). From cell-attached single-channel recordings (with a pipette solution (in mM) : 145 KCl, 1 $CaCl_2$, 3 HEPES, pH=7.4), we found 33-pS (presumably) Cl^--channel in the large round cell and 29-pS (presumably) non-specific (Na^+/K^+)-channel in the bipolar cell. We also recorded K^+-channels in the stellate cell which were activated by the mechanical stimulation.

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CHANGES IN CYTOPLASMIC FREE Ca^{2+} CONCENTRATION AND DOPAMINE SECRETION IN BRADYKININ-STIMULATED PC12 CELLS. OGURA, T., WARASHINA, A., FUJIWARA, N. AND SHIMOJI, K. Dept. Physiol. and Anesthesiol., Niigata Univ. sch. of Med., Niigata, Japan.

Effect of bradykinin (BK) stimulation on dopamine (DA) secretion from PC12 cells was investigated. For this purpose, the cells were mounted on a filter paper and perfused with test solutions. DA output in perfusates was analyzed by HPLC-ECD method. The DA secretion with 200 nM BK was increased by a 3.2-fold from the basal level. This increase was suppressed in Ca-free (EGTA added) ringer but not affected by the addition of a voltage-dependent Ca channel blocker, D600, to the normal ringer. D600, however, completely inhibited an increase of DA secretion caused by a high K^+ solution. The intracellular free calcium ion, $(Ca^{2+})i$, level during the BK stimulation was monitored in fura-2 loaded PC12 cells. The resting $(Ca^{2+})i$ level around 200 nM was transiently elevated to about 800 nM at the peak response to BK. This BK response was abolished in the absence of extracellular calcium ion, but not affected by D600. These results indicate that BK causes the increase of $(Ca^{2+})i$ in PC12 cells, which in turn evokes DA secretion. Although the BK-induced increase in $(Ca^{2+})i$ depended on the presence of extracellular calcium ion, Ca entry through voltage-dependent Ca channels is not responsible for the process. The existence of BK receptor-mediated Ca channels is suggested.

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WHOLE CELL AND SINGLE CHANNEL CURRENTS IN CULTURED MAMMARY EPITHELITAL CELLS. FURUYA, K., ENOMOTO, K.[1], EDWARDS, C.*[2] AND OKA, T.*[2] Nat. Inst. Physiol. Sci., Okazaki 444, [1] Shimane Med. Univ., Izumo 693, [2]NIH; NIDDK, Bethesda, MD 20892, USA

Patch clamp methods were applied to mammary epithelial cells of lactating mice in primary culture, and some (at least 5) types of channels were detected in these cells. In the whole cell recordings, spontaneous inward and/or outward membrane current fluctuations were observed in some cells. In the cell-attached recordings, the channels of ~130 pS, ~90 pS and ~60 pS were observed frequently using the pipette containing 150 mM KCl. In many cases, these channels showed inward rectification. In some cases, the activity of the channel of ~90 pS fluctuated spontaneously and the channel events appeared intermittently with the period of ~10 s. These current fluctuations of the whole cell and single channel correspond to the fluctuations of membrane potential which were first observed by Enomoto et al. using microelectrode method and were thought to play a crucial role in hormonal control of the cell proliferation and differentiation (Proc. Natl. Acad. Sci. 83, 4754, 1986). Inside-out patch experiments revealed the existence of the Cl channel (62 pS and 36 pS for outward and inward direction respectively using 150 mM Cl in both side) and the K channel (20 pS and 42 pS for outward and inward direction using 150 mM KCl in both side). There also exist another type of K channel which run down rapidly during the inside-out experiments.

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HISTOLOGICAL ANALYSIS OF SPLEEN IN EXPERIMENTAL HEMOLYTIC ANEMIA IMAGAWA, M., SAITO, H., KITAHARA, M. AND O'HATA, S.
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Using phenylhydrazine hydrochloride, an experimenral hemolytic anemia was produced for histological properties of spleen. The anemia was produced in rabbits by the method of R. H. DeBellis et al (J. Clin. Invest., 43, 1329. 1964). On Hematoxylin-Eosin stain of spleen, numerous erythrocytes were present in the sprenic sinus, and it pressured sprenic cords. In red pulp and follicullar marginal zone of spleen, reticular cells contained enough ferric iron to give a positive Berlin blue stain, and yet the cells contained ferrous iron to give positive Turnbull blue stain. On the other hand, both Lipid stain and Melanin stain were negative. These results revealed that the reticular cells had hemosiderin, and that its ionic state was ferric and ferrous iron.

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EFFECTS OF OSMOTIC PERTURBATION ON MORPHOLOGICAL AND PASSIVE ELECTRICAL PROPERTIES OF CULTURED RAT BASOPHIL LEUKEMIA CELLS. SUZAKI, T., ICHINOWATARI, T., WATANABE, M. AND IRIMAJIRI, A. Department of Physiology, Kochi Medical School, Nankoku, Kochi 781-51

In order to correlate properly the dielectric behavior of cultured rat basophil leukemia (RBL-1) cells with cell structure, various morphological parameters were determined as a function of medium osmolality (140-400 mOsmolal). Morphometric analysis of ultra-thin sections revealed that sub-cellular volume fractions of nucleus, mitochondria, and other small vesicles remained almost unaffected (24-28%, 2.3-3.7%, >0.8%, respectively) by the osmotically induced changes in total cell volume. We have recently reported that RBL-1 cells showed a characteristic "two-step" frequency dependence, and proportion of the subdispersion at higher frequencies increased with increasing osmolality (Irimajiri et al., B.B.A., 896: 214-223, 1987). Taking those morphological parameters into consideration, this increase could possibly be interpreted as a result of increase in conductivities of the internal phases of small organelles such as mitochondria and small vesicles.

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IMPEDANCE ANALYSIS OF ERYTHROCYTES SUSPENSION TRAETED WITH OXIDANT.
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It is known that the oxidant hemolysis is dependent on the quantity of vitamine E in erythrocyte membrane. Two species of oxidants were used. One is hypoxantine-xantine oxidase (HX-XOD) reaction which generates superoxide anion and the other is 2,2'-azobis (2-amidinopropane) hydrochloride (AAPH) which generates carbone peroxide radical .And two kinds of erythrocytes were used. One is vitamine E sufficient rat erythrocytes (E+) and the other is vitamine E deficient rat erythrocytes (E-). The change of relative permittivity is larger than that of the conductivity in erythrocytes with effects of both oxidants. Especially HX-XOD reaction system cause the increment of relative permittivity in (E+)-erythrocytes along the time course, but AAPH reaction cause the decrement of relative permittivity in (E+)-erythrocyte. Using Pauly-Schwan's theory, membrane parameters, C_m (membrane capacity), κ_i (the inside conductivity of the erythrocyte) and ϕ (volume fraction of erythrocytes) are determined. Consequently, C_m is 1μ F/cm ,and C_m seems to be almost const, and ϕ is decreased and κ_i is increased along the time course of membrane oxidation.

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LIVER-SPECIFIC FUNCTIONS IN PROLIFERATING HEPATOCYTES DURING PRIMARY CULTURE. WATANABE,K., HASEGAWA, K. AND KOGA, M. Dept. Physiol., Dokkyo Univ. Sch. Med., Mibu, Tochigi 321-02

Liver-specific functions in proliferating adult rat hepatocytes in primary culture were examined. 1) Hepatocytes retained ornithine carbamoyltransferase activity and produced arginine. They also retained arginase activity and secreted urea to the medium. The presence of phenylalanine monooxygenase activity was indicated by the fact that hepatocytes secreted tyrosine to the medium when cultured in Koga's HEM, which is tyrosine-free. Tyrosine aminotransferase activity in the hepatocytes were retained. When dexamethasone (1 μM) was added to at any time during 0- to 4-days of culture, the enzyme activity increased 4 or 7 times at 12 hr after dexamethasone addition. 2) SDS-polyacrylamide gel electrophoretic analysis of the media collected from 1- to 4-day culture of hepatocytes showed that the hepatocytes secreted various serum proteins including alubumin and transferrin. The electrophoretic patterns of the media were almost the same as that of rat serum. These results indicated that hepatocytes in culture retained liver functions even during the phase of proliferation.

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PROPERTIES OF A SPERM-ACTIVATING PEPTIDE(S) FROM HERRING EGGS. OHTAKE, H.[1], MORISAWA, M.*[2], TANIMOTO, S.*[3], and KOGA, M.[1], [1]Dept. of Physiol., Dokkyo Univ. Sch. Med., Mibu, Tochigi 321-02, [2]Lab. of Physiol., Ocean Res. Inst., Tokyo Univ., Nakano, Tokyo 164, [3]Dept. of Biol., Fac. of Sci., Toho Univ., Narashino, Chiba 274

Spermatozoa of herring (*Clupea pallasii*) are not active at the time they are discharged in sea water, but become highly activated when they come to contact with the egg surface, especially in the vicinity of the micropyle. This suggests the possibility that in the micropyle area there is a specific sperm-activating factor which is essential for normal fertilization of the egg. When herring eggs were suspended in sea water for about 1 hr, the sperm-activating activity was found in the supernatant of the egg suspension (egg water). However, only low activity was detectable in the egg water when eggs are suspended in deionized water. This sperm-activating factor affected slowly moving spermatozoa to swim rapidly, but it had no effect on motionless spermatozoa. This factor was readily destroyed by treatment with trypsin or pronase, suggesting that this factor has a peptide nature. This factor was readily precipitated in a saturated solution of ammonium sulfate and it was not dialyzable against sea water. To purify this sperm-activating factor, we have tried to examine the availability of hydrophobic chromatography and gel-permeation chromatography in the presence of a high concentration of salts.

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SUBCELLULAR DISTRIBUTION OF PROTEIN DISULFIDE ISOMERASE IN RAT HEPATOCYTES AND EXOCRINE PANCREATIC CELLS. AKAGI,S*, YAMAMOTO,A., YOSHIMORI,T., MASAKI,R., TASHIRO,Y., Dep. of Physiol. and Orthopedic Surgery.* Kansai Medical Univ. Moriguchi, 570.

We investigated quantitatively the distribution of protein disulfide isomerase(PDI) in rat hepatocytes and exocrine pancreatic cells by immunoelectron microscopy using post-embedding protein A-gold technique. In hepatocytes, PDI exists mainly on the cisternal surface of rough and smooth endoplasmic reticulum(ER) and nuclear envelope, and only few on the plasma membranes. In the exocrine pancreatic cells, PDI abunduntly exists not only on the ER but also on the plasma membranes and on the secretory granules. Density of PDI on the plasma membranes of the exocrine pancreatic cells was about 20 times higher than that of hepatocytes. PDI on the ER may play a role in the formation of disulfide bonds of nascent polypeptides, whereas that on the plasma membranes may have a different function.

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THE UPTAKE MECHANISM OF [^{3}H]LEUCINE IN GLUCAGON-PRODUCING TUMOR CELLS (ITC-1). SAKAI, S., HASHIGUCHI, M., TASAKA, J., TOSAKA, T. AND O'HATA, S. Dept. of Physiol., Tokyo Med. Coll., Shinjuku-ku, Tokyo 160

Leucine is a constituent of glucagon, which consists of a single-chain peptide containing 29 amino acid residues. [^{3}H]Leucine uptake in the cultured ITC-1 cells was examined within the concentration range of 4 nM to 50 μM leucine. The uptake systems of [^{3}H]leucine could be divided into three components: (1) Na-independent i) Non-saturable component (Kd=0.0025 min^{-1}) ii) Saturable component conforming to Michaelis-Menten kinetics (L system ?) (2) Na-dependent, saturable component conforming to Michaelis-Menten kinetics (A system ?). The Hill number of 1.7 for Na-dependent component suggests that two is the minimum number of sodium ions involved in the transport of one leucine molecule. The low concentrations of external Cl^- substituted with isethionate, propionate or thiocyanate decreased [^{3}H]leucine uptake, although removal of external Ca^{++} had no effect. Radioactive glucagon in ITC-1 cells reached to the maximum level at 1 hr after an incorporation of [^{3}H]leucine and it was then released for 3 hr to the medium.

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The generation of field potentials from the guinea pig olfactory cortical slice which are resistant to hypoxia and the effect of adrenaline on them. Fujii, T. Kyoto Municipal Jr. College of Nursing, Higasi-takada, Mibu, Nakagyo, Kyoto 604

The amplitude of field potentials evoked by electrical stimulation of lateral olfacory tract in guinea pig olfactory cortical slice (ca 400 μm thick) maintained in vitro at 37°C, disappeared several min after the replacement of 95% O_2 + 5% CO_2 gas mixture with 95% N_2 + 5% CO_2. The slice was repetitively incubated under the cycles of hypoxia-normoxia. During the 3rd and the 4th hypoxic period, the potentials augmented in amplitude and at the same time the slice showed an increase in the rate of ^{14}C-deoxy-glucose incorporation, and also the administration of 5×10^{-5}M adrenaline to the slice brought about an increase in the potential amplitude. It would be considered that the potentials augmented because the glycolytic function of producing energy in neuronal tissues was facilitated after the repetitive alternation of hypoxia and normoxia, while the redox-state of cytochromes in mitochondria was kept at similar reductive levels, which reflected the function of oxidative phosphorylation. These results indicated that the repetitive incubation of the slice under the hypoxic condition increased the glycolytic function of promoting the production of energy. We concluded that this functional change induced the generation of potential resistant to hypoxia.

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QUANTITATIVE FLOW CYTOMETRY ON BINDING OF OKT3, OKT4 AND OKT8 TO HUMAN T CELLS. Tadahiro Oonishi[1], Kanako Sakashita[2] and Nobuhiro Uyesaka[3] [1]Dept. of Pathol., [2]Medical Information Institute, The Kanto Teishin Hosp., Higashi-Gotanda, Shinagawa-ku, Tokyo, [3]Dept. of Physiol., Nippon Medical School, Sendagi, Bunkyo-ku, Tokyo

Binding of monoclonal antibody (OKT3, OKT4 and OKT8) with human T cells was investigated on flow cytometry at various temperature. A flow cytometer was calibrated by a standard fluorescence microsphere as previously described[1)], which made it possible to determine the amount of bound antibody molecules. The maximum binding varied with temperature. Kinetic analysis according to the Hill equation revealed that the value of Hill coefficient for OKT3 changed from 1.8 to 1.0 when the temperature was raised from 12°C to 36°C, whereas those for OKT4 and OKT8 did not vary with temperature. It is likely that T3 to which OKT3 binds may alter in its molecular environments with temperature. Thermodynamic parameters obtained from the van't Hoff plot indicated that the binding of OKT3 was exothermic (ΔH° = -1.83 Kcal·mol^{-1}), and those of OKT4 (ΔH° = +3.20 Kcal·mol^{-1}) and OKT8 (ΔH° = +4.10 Kcal·mol^{-1}) were endothermic. The molecules that OKT3, OKT4 and OKT8 recognize on the T cell surface play a crucial role in an appropriate interaction between T cells and target cells. Possible meanings of the present results in the T cell interaction with target cells were discussed.

1) Oonishi,T. and N.Uyesaka, J.Immnol.Methods 84, 143, 1985

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CALMODULIN-DEPENDENT PHOSPHATASE IN BOVINE PAROTID GLAND. YOKOYAMA, N. AND FURUYAMA, S., Dept. Physiol., Nihon Univ. Sch. Dent., Matsudo, Chiba 271

Calcineurin, a calmodulin(CaM)-binding protein, was originally discovered in brain. Recently it was shown that calcineurin possesses a phosphoprotein phosphatase activity which is stimulated by CaM in the presence of Ca^{2+}.

Now, CaM-dependent phosphatase activity has been found in the supernatant fraction from bovine parotid gland. This phosphatase activity was determined using p-nitrophenyl phosphate or 4-methylumbelliferyl phosphate as a substrate.

This CaM-dependent phosphatase activity was blocked by W-7 or trifluoroperagine. The activity of the phosphatase in parotid gland as well as in brain was increased significantly by Ni^{2+}, Mn^{2+} and Mg^{2+}. The addition of Ni^{2+} quenched the fluorescence due to the tryptophan residues in both cases. These data suggest that CaM-dependent phosphatase exists in the parotid gland.

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SYNERGISMS BETWEEN α-ADRENERGIC OR CHOLINERGIC AGONISTS AND ISOPROTERENOL IN RAT SUBMANDIBULAR KALLIKREIN RELEASE.

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Carbamylcholine (CCh) induces kallikrein release in rat submandibular slices as phenylephrine (Phe) dose, and isoproterenol (Isop) acts synergistically both with CCh and Phe (J. Physiol. Soc. Japan 48: 157, 1986). The maximum amount of kallikrein release by combined addition of Phe or CCh and Isop was higher than that of Phe or CCh alone and was comparable to that of norepinephrine or epinephrine. Similar results were observed by other cholinergic agonists (acetylcholine and methacholine) and α-adrenergic agonist (methoxamine). Oxotremorine and pilocarpine did not stimulate the kallikrein release with or without Isop. The kallikrein release by α-adrenergic- or cholinergic-agonists and the augmentation by Isop were almost abolished by omission of calcium in the medium. Since similar synergisms was observed between dibutyryl cyclic AMP or IBMX and α-adrenergic agonists, the effect of Isop may be mediated by cyclic AMP. Dibutyryl cyclic AMP, however, did not augment the effect of CCh, which fact could not understood in present stage.

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ELECTRICAL STIMULATION EFFECTS ON PARTICLE MOVEMENTS IN CAULERPA

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The effects of an electric field on particle movement in Caulerpa lentillifera were observed by video-enhanced microscopy. Caulerpa is a coenocytic marine green alga containing large bundles of microtubules in the cytoplasm and is, therefore, a good model for microtubule-associated particle movement. Cytoplasmic particles -mitochondria,amyloplasts,chloroplasts,etc.- move bidirectionally along the bundle of microtubules in a steady stream. The rate of particle movement is about 3 um/sec. Electric stimulation consisting of 2 msec pulses was applied with 2 platinum electrodes. Particle movement was stopped or slowed by the electric pulses. Particles could be divided into 2 groups according the change in velocity. In one group velocity reached its minimum 5 sec after application of a pulse, and in the other 10 sec after the pulse. The decrease rate of the velocity depended on the intensity of the pulse. After reaching minimum velocity the particle movement returned to its original speed. The same phenomenon was also observed in some neurons of mice and rats.

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PERMEABILITY IN RAT SUBMANDIBULAR GLAND UNDER SYMPATHETIC AND PARASYMPATHETIC STIMULATIONS.

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The effect of autonomic nervous system stimulation on the permeability of tight junctions in the rat submandibular gland was investigated. Using large(lactoperoxidase, MW=93,000), moderate(Horseradish peroxidase, 40,000), and small-sized(microperoxidase, 1,800) tracers, we examined the permeability of the tight junction to these molecules from blood to saliva in submandibular glands of male Wistar rats under sympathetic(S), parasympathetic(P), or combined stimulation. A taste stimulus(10% citric acid) also used. P stimulation, superimposed on S, increased the output of all the tracers in the saliva, although stimulation of either system alone did not increase it. Cytochemical observation showed that molecules of MW lower than 40,000 entered the lumen via tight junctions following combined P and S. Increased permeability was also noted by stimulation of taste buds. Thus the combined stimulation of S and P systems, as well as taste stimulation, increased permeability of tight junctions.

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PROLIFERATION AND Ca CONCENTRATION IN THE PRIMARY CULTURE OF EPITHELIAL CELLS FROM ORAL MUCOSA. KASAI, S., IKESHIMA, K., OKADA, H., AND TERASAWA, T., Dept. of Physiol., Tohoku Dent. Univ., Kohriyama-shi, 963.

Optimal concentration of Ca and Ca^{2+} for the growth of oral epithelial cells from rabbit was investigated in the primary culture using MCDB 152 (152M) containing various contents of Ca and normal or chelated serum.

The results were as following. 1). Ca^{2+} in the normal serum(containing 126.7ppm Ca) hold 45.6% to 40.6% of total Ca content in Ca-free 152M containing 1.25% to 20% serum, respectively. Conversely, in the chelated serum (7.78ppm Ca) Ca^{2+} decreased from 3.5%-15.2% in Ca-free 152M as elevation of the serum content from 3.6% to 28%. This discrepancy and other results suggested that substnces in the chelated serum and 152M bind with Ca^{2+} at various degrees. 2) Cell proliferation which indicated as colony number was dependent on Ca^{2+} concentration rather than total Ca content in culture media, that is, optimal Ca^{2+} was 12-27μg/ml (0.3-0.68mM) in the normal serum containing media, and 4-20μg/ml (0.1-0.5mM) in the chelated one. 3). Colony number increased about 3 folds in the media containing chelated serum than that of normal serum at the same protein content and under the optimal Ca^{2+} concentration.

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SIMILARITIES AND DISSIMILARITIES IN STIMULATING MECHANISMS OF ELECTROGENIC Na-K PUMP ACTIVITY BY ACh BETWEEN SALIVARY AND LACRIMAL ACINAR CELLS. *HAYASHI, H., TAKAHASHI, H., NISHIYAMA, A. and **KATOH, K. Dept. of Physiol., Sch. of Med., *Col. of Med. Sci., **Dept. of Animal Physiol., Faculty of Agriculture, Tohoku Univ., Sendai 980

Microelectrode recordings were made from segments of mouse submandibular and lacrimal glands. In submandibular acinar cells ionophoretic application of ACh evoked a potential change consisting of initial hyperpolarization followed by ouabain-sensitive delayed hyperpolarization. The delayed hyperpolarization was abolished in absence of external Na or Cl, or in presence of furosemide. However, it was little affected by amiloride. In the lacrimal acinar cells ACh stimulation for 4 min evoked a ouabain-sensitive delayed hyperpolarization. The delayed hyperpolarization was severely reduced in a low-Na or K-free solution. It was fairly reduced in presence of amiloride, but slightly reduced in absence of external Cl or in presence of diuretics. It was markedly reduced but not abolished in presence of amiloride in the Cl-free or diuretics-containing solution. From these results followings were proposed. In both gland acinar cells ACh may secondarily stimulate Na-K-pump activity through an increase in $[Na]_i$. However in salivary acinar cells the increase in $[Na]_i$ may result from activation of Na-K-Cl cotransport, while in lacrimal cells it may result from activations of multiple types of Na transporter (Na-H, Na-K-Cl and others).

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IMPEDANCE MEASUREMENT IN SALIVARY GLAND

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The secreting salivary gland lost its conductivity. We reported that the drop of the conductivity was due to the ECF decrease. In present study, the salivary secretion and ECF changes in the secreting gland were studied. The salivary secretion consist of two phases. The first was the initial secretory phase, the second the steady secretory phase. The steady secretory phase depends on the glandular blood flow. When the interlobular fluid, which was observed histologically was diminished on the condition of stimulation after circulatory arrest, the circulation was re-opened and stimulation was performed. In this condition the initial secretory phase was diminished. Coincidence of the marked decrease in interlobular fluid and diminish of the initial secretory phase suggest that the initial secretory phase depends on the ECF, especially interlobular fluid. On the other hand, The relative permittivity change was measured, when the conductivity change was minimize in perfused gland. The relative permittivity decreased. The change was small but reproducible. The relative permittivity change suggests that in the acinar cell membrane of the secreting salivary gland.

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REGULATION OF INTRACELLULAR pH OF THE MOUSE LACRIMAL GLAND ACINAR CELLS. SAITO, Y., OZAWA, T., SUZUKI, S. and NISHIYAMA, A. Dept. of Physiol., Tohoku Univ. Sch. of Med., Sendai 980

The mechanism of intracellular pH (pH_i) regulation in the isolated lacrimal gland acinar cells has been studied using H^+ ion-selective microelectrodes. In a physiological saline solution (HEPES/TRIS buffer, pH 7.4), pH_i was about 7.2, being about 0.5 unit higher than the equilibrium level. Changes in the extracellular pH by ±0.4 unit caused a shift of pH_i of ±0.08 unit. The intracellular buffering power estimated by an addition of NH_4^+ or CO_2 gas was about 30mM/pH. Application of secretagogue ACh (1μM) or A23187 (10μM) caused an increase in pH_i preceded by a small transient decrease in pH_i. Removal of ACh resulted in a further increase in pH_i and then a slow return to the non-stimulated level. In the presence of amiloride (0.1mM) or the absence of Na^+ in the bathing solution, addition of ACh decreased pH_i by 0.2–0.3 unit. The presence of a stilbene derivative DIDS (0.2mM) enhanced the increase in pH_i evoked by ACh. We have concluded that 1. pH_i is regulated in a narrow range by active extrusion of H^+ ion, 2. stimulation with secretagogue increases the rate of H^+ production as well as H^+ extrusion, and 3. Na^+/H^+ and OH^-/Cl^- exchange transport processes are involved in the regulation of pH_i.

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THE EFFECT OF EXTRACELLULAR CALCIUM AND SODIUM ON SECRETAGOGUE-INDUCED INCREASE IN THE CYTOSOLIC CALCIUM CONCENTRATION OF THE MOUSE LACRIMOCYTES. OZAWA, T., TAKAHASHI, H., SUZUKI, S., SAITO, Y. and NISHIYAMA, A. Dept. of Physiol., Tohoku Univ. Sch. of Med., Sendai 980

The effects of cholinergic stimulation, and removal of extracellular Ca and Na on cytosolic Ca (Ca_i) were studied by Ca-selective microelectrode and fluorescence spectroscopy methods. In a physiological saline solution, Ca_i determined with Ca-electrodes was 0.6μM. Addition of 1μM ACh caused two-tenfold increase in Ca_i with concomitant hyperpolarization of the membrane potential (V_m). In a Ca-free solution V_m was depolarized, Ca_i was decreased and ACh-induced increase in Ca_i became smaller. In a Na-free solution, V_m was hyperpolarized and response in Ca_i to ACh was reduced. Return to the control solution from Na-free or Ca-free solution increased Ca_i to the normal level. Fluorimetry on the dispersed, Quin2 loaded acinar cells prepared by enzymatic digestion of the gland showed that Ca_i of the non-stimulated condition was 0.1–0.2μM, addition of 0.1mM CCh increased Ca_i to about 0.5μM, and removal of Ca or Na from the solution reduced the response in Ca_i to CCh. The present results showed that cholinergic stimulation of the acinar cells causes a significant stimulation of Ca influx from the sorrounding medium in addition to Ca mobilization from the cellular pool. Extracellular Na may be required for supporting the agonist-induced Ca influx.

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EFFECT OF MONENSIN ON THE STIMULATION OF Na/K TRANSPORT BY INSULIN. KITASATO,H., KANBE,M., AND SUGIMOTO,Y. Dept. Physiol., Shiga Univ. of Med. Sci., Ohtsu Shiga 520-21

It has been reported that insulin stimulates ^{22}Na efflux in frog skeletal muscle. This stimulating effect of insulin was blocked by monensin ($5x10^{-7}M$), although ouabain-resistant basal ^{22}Na efflux increased on addition of monensin into the bathing solution. In parallel to the change of the basal ^{22}Na efflux, basal [^3H]ouabain binding also increased. The preincubation with monensin caused a rise of the intracellular Na concentration. The parallelism between increases of the basal ^{22}Na efflux and the basal [^3H]ouabain binding may be accounted for by an increase of the intracellular Na ions. Insulin (250mU/ml) increased [^3H]ouabain binding by about two fold. The intracellular Na concentration went down on addition of insulin. In the presence of monensin ($1x10^{-7}M$), the stimulating effect of insulin on [^3H]ouabain binding was slightly suppressed.

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INCREASE OF Na/K-PUMPING UNITS IN MUSCLE PLASMA MEMBRANE BY INSULIN. KANBE, M. and KITASATO, H. Dept. Physiol., Shiga Univ. Med. Sci. Ohtsu 520-21

Insulin-induced increase in Na/K-transport activity in skeletal muscles was analyzed by examining the effect of insulin on Na,K-ATPase activity in leaky membrane vesicles. Plasma membrane fractions were prepared from frog skeletal muscles (*Rana catesbeiana*). On adding saponin to the membrane suspension the Na,K-ATPase activity increased depending on the concentration of the detergent. The maximum activity was about two times of the control value at 0.33mg saponin/mg protein. Addition of insulin to saponin-treated membrane suspension had no effect on the Na,K-ATPase activity, whereas the maximum activity of Na,K-ATPase in whole muscles was stimulated by exposing to insulin. Insulin also induced changes in the dependencies on the substrates concentrations. At any concentration of substrates examined, the Na,K-ATPase activity was always higher in preparations derived from insulin-treated muscles than those derived from control muscles. The results support the view that the stimulation of the Na,K-ATPase activity by insulin is due to an increase in the capacity of Na,K-ATPase in the plasma membrane fractions and that the Na/K-transport units responsible for the newly developed Na,K-ATPase by insulin are slightly different in structure from those have been already functing before insulin exerts its effect on Na,K-transport.

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THE EFFECTS OF INSULIN ON BLOOD COMPONENTS AND RETINAL ACTIVITIES IN AMPHIBIA. KATAYAMA, Y. Dept. Phisiol., Tokyo Women's Med. College, Shinjuku, Tokyo 162

The effects of the injection of a porcine insulin or glucose on plasma glucose, plasma K and plasma insulin were studied in pithed bullfrogs. The control mean plasma glucose levels, plasma K and plasma insulin were 14.4±3.9 mg/dl, 2.4±0.5 mEq/l, and 6.7±1.3 μU/ml respectively. Plasma glucose levels elevated over 120 min after the injection of insulin 10 IU and 20 IU in frogs with and without glucose 10 mg injection and attained to the maximum value of about 64 mg/dl. Whereas 20-30 % decrease in plasma K level was caused. This rise in glucose level was almost abolished by pancreatomy or adrenalectomy. In the retinal activity, the suppression of the a-wave amplitude of ERG induced by ouabain was prevented by the insulin pretreatment, the effect was dependent on the insulin dose above 0.01 IU. These results suggest that insulin increases the activity of Na-K pump in cell membranes and results in a decrease in $[K]_o$, and suppresses the inhibitory effect of ouabain on Na-K pump. An important role of endogenous insulin in amphibia may be the modulation of Na,K-ATPase activity.

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EFFECT OF AGE, SEX AND GENETIC PREDISPOSITION OF HYPERTENSION TO THE CATION TRANSPORT SYSTEM OF THE RED CELL MEMBRANE IN JAPANESE NORMOTENSIVES. SAITO, T., MIZOKAMI, K., KAI, N., KOSHIBU, Y., YAMAMOTO, K., IWATA, J., TONOOKA, M. AND INAGAKI, Y. THE 3rd Dept. of Int. Med., Chiba Univ., Sch. of Med., Chiba 280

We studied the effect of sex, age and genetic predisposition of hypertension to the monovalent cation transport systems(Na-K cotransport Na-K COT, Li-Na countertransport Li-Na CT and Na-K pump activity) of the red cell membrane in 163 Japanese healthy normotensive subjects. In the results, (1)The intraerythrocytic Na content and Na/K ratio had a tendency to increase in older subjects. Increased Na and Na/K ratio in red cell revealed in person with family history of hypertension(FHH(+)) than without family history(FHH(-)). (2)Male donors had significantly greater Na-K COT and Li-Na CT than did female donors. And also these parameters showed higher value in FHH(+) than in FHH(-). (3)Na-K pump activity showed no significant difference in age and sex, but was higher in FHH(+) than in FHH(-). It was concluded that the intracellular electrolytes, and cell membrane cation transport systems of normotensives were different in age, sex and genetic predisposition of hypertension.

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STUDY ON THE PERMEABILITY OF SODIUM ION IN SHR RAT ERYTHROCYTES BY ^{23}Na-NMR. KWAN, C. Y., SEO, Y.*, MURAKAMI, M.*, AND WATARI, H.*, Dept. Neurosci., McMaster Univ., Hamilton, Ontario 18N 3Z5, Canada. *Natl. Inst. Physiol. Sci., Okazaki 444, Japan.

The Na^+ contents of KWY and SHR rat erythrocytes were measured by ^{23}Na-NMR, using a nonpermeant chemical shift reagent, dysprosium triethylenetetramine hexaacetic acid, $Dy(TTHA)^{3-}$. The intracellular Na^+ concentration in freshly isolated and washed erythrocytes in both rats was very low (5 mM) and prograssively increased with prolonged incubation at 37 C. Incubation with 1 mM ouabain resulted in elevated intracellular sodium concentration and substantially retarded expenditure of ATP measured by ^{31}P-NMR. The increase of intracellular Na^+ signals was linearly correlated with the decrease of extracellular Na^+ signals with a slope of unity suggesting all intracellular Na^+ signals were NMR visible releative to the extracellular Na^+ signals.

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STUDY ON ATP-DEPENDENT Ca^{2+} UPTAKE BY RAT RENAL BASOLATERAL MEMBRANE VESICLE (BLMV). TSUKAMOTO, Y., TAMURA, T. AND MARUMO, F., Dept. of Med., Kitasato Univ. Sch. of Med., Kanagawa 228

BLMV was separated from renal cortex homogenate of male Spraque-Dawley rats by the Percoll gradient method. $^{45}Ca^{2+}$ uptake by BLMV was measured by Millipore rapid filtration method in the presence or absence of 2 mM ATP-Mg_2. The assay mixture usually contains 50 mM KOH and its pH was adjusted by various buffers without any other inorganic anion (300 mOsm/L). Free Ca^{2+} concentration was controlled by 0.1 mM EGTA. ATP-$^{45}Ca^{2+}$ uptake was stimulated by acid internal pH down to 6.8 and was not influenced by external pH (pH_{in} = 6.8, 7.4, 8.0; 1.52, 1.27, 0.9 nmole Ca^{2+}/30 sec/mg prot., respectively). ATP-Ca^{2+} uptake has negative cooperativity with respect to internal $[H^+]$ ($K_{0.5} = pH_{in}$ 7.25, n_{app}=0.56 ± 0.02). Valinomycin did not affect ATP-Ca^{2+} uptake in the presence of equilibrated K^+ or inwardly or outwardly K^+ gradient. Free-flow dialysis method revealed ^{14}C-DMO uptake by BLMV driven by ATP-Ca^{2+} influx, suggesting the alkarinization of internal pH. These results strongly suggest that an electroneutral ATP- driven Ca^{2+}/H^+ antiport exists in the basolateral membrane of rat renal proximal tubule.

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INTERRELATIONSHIPS BETWEEN CELL Ca AND CELL pH IN THE BULLFROG PROXIMAL TUBULES. MATSUMURA,Y., FUJIMOTO,M., KOTERA,K., AND MORIMOTO,Y.Department of Physiology, Osaka Medical College, Takatsuki city, Osaka, 569.

By means of double-barreled Ca or H ion selective microelectrodes, we measured both cellular ion concentrations in paired samples under the following conditions: 1. Control (1.5%CO_2, 15mM HCO_3^-) 2. Respiratory acidosis (1.5% → 5%CO_2) 3. Metabolic acidosis (15mM→ 2mM HCO_3^-) 3. 30mM K Ringer solution. The kidney was doubly-perfused. The solutions were changed peritubularly. 1. In control, cell Ca activity (p(Ca); γ_{Ca}=0.32) was 7.02 ± 0.17 SE (N=28). Cell pH was 7.33 ± 0.03 (N=7). The membrane Pd (V_{bl}) was 53.8 ± 1.5 mV(N=7). 2. In respiratory acidosis, cell Ca was not changed (Δp(Ca)=0.14 ± 0.15,N=9,p>0.4). Cell pH was decreased from 7.37 ± 0.03 to 7.25 ± 0.04 (N=7, p<0.01) with depolarization of 4.3 mV. 3. In metabolic acidosis, cell Ca was decreased (Δp(Ca)=0.43 ± 0.12, N=12, p<0.01). Cell pH was decreased from 7.37 ± 0.02 to 7.22 ± 0.04 (N=5,p<0.005) with depolarization of 17.3 mV. 4. In 30 mM K Ringer solutions, cell Ca was decreased (Δp(Ca)=0.72 ± 0.19, N=10, p<0.01). Cell pH was increased from 7.23 ± 0.04 to 7.47 ± 0.02 (N=6,p<0.005) with depolarization of 33.4 mV. It is suggested that, in bullfrog proximal tubules, cell Ca does not have any significant predictable relationship with cell pH, and that depolarization would be associated with a decrease in cell Ca.

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K ION TRANSPORT IN THE MALPIGHIAN TUBULE OF RHODNIUS. KOTERA, K., FUJIMOTO, M., MATSUMURA, Y., SASAKI, S., NAKAGAKI, I. AND WHITTEMBURY, G.* Dept. of Physiol., Osaka Med. College, Takatsuki, Osaka 569. * Venezuelan Institute of Scientific Investigations.

An insect, Rhodnius prolixus has a couple of Malpighian tubules known to secrete K ion rich fluid. Using double-barrelled K ion selective microelectrodes for the isolated tubule soaked in Maddrell's media, we measured intracellular and luminal K activities (Ki and Ku) and membrane potential (Em) after serotonin (5-HT) stimulation. In resting tubules, mean values of Em, Ki, and K ion equilibrium potential (Ek) were -46 mV, 85 mM, and -61 mV, respectively. After 5-HT stimulation (10^{-4} M), Em hyperpolarized to -53 mV within 12 min with a gradual recovery to the resting value in 50 min. Ki rapidly decreased to 50 mM within 6 min, and then increased to 67 mM at 12 min while fluid secretion was maintained. Ku was 32 mM at 16 min after stimulation, and decreased to 10 mM within 50 min with a marked hyperpolarization of luminal membrane from -25 mV to -44 mV.

These data indicate that hyperpolarization of Em was caused by increased K permeability of the cell membranes, Em approaching Ek. Rapid decrease of Ki with stimulation may suggest an activation of K extrusion mechanism (= common cation pump) at the luminal membrane. The biphasic change of Ki shows a sequence of events : an initiation of luminal K secretion, followed by a salt and water transport across the basal membrane.

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ION CHANNELS IN THE BASOLATERAL MEMBRANE OF THE RABBIT PARIETAL CELL RECORDED BY THE PATCH CLAMP TECHNIQUE. SAKAI, H., OKADA, Y.°, MORII, M.*, AND TAKEGUCHI, N. Lab. Biophysical Chemistry, Faculty of Pharmaceu. Sci., Toyama Med. & Pharmaceu. Univ., Toyama 930-01, °Dept. Physiol., Faculty of Med., Kyoto Univ., Kyoto 606

We have applied the patch clamp technique to study ion channels in the basolateral membrane of the rabbit parietal cell in gastric glands. In the whole cell configulation, zero-current potential was not shifted systematically by change in $[K^+]_o$, suggesting that membrane potential at zero-current did not depend only on K channels. Furthermore, both outward and inward rectifications of current were found. Outward rectification was blocked by $[Cs^+]_o$ or $[TEA]_o$, while $[Ba^{2+}]_o$was not effective Inward rectification could be completely abolished by $[Ba^{2+}]_o$. The conductance of inward rectifier was proportional to the square root of $[K^+]_o$, similar to the anomalous rectifier of other tissues. Corresponding to these rectifying events, we have found two types of rectifying single channel currents in inside-out membrane patches. The inward rectified K^+ channel (230pS) was sensitive to $[TEA]_i$, and insensitive to change in $[Ca^{2+}]_i$. We also have found non-selective, non-rectifying cation channel (25pS), which was independent of change in $[Ca^{2+}]_i$. Kinetics of these channels were studied. Single channel events were observed rarely.

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SINGLE Cl^- CHANNEL CURRENTS IN THE LUMINAL MEMBRANE OF RAT PARIETAL CELLS IN PRIMARY CULTURE. UEDA, S.[2], KOTERA, T.[2]* AND OKADA, Y.[1], [1]Dept. Physiol., and [2]Dept. Intern. Med., Fac. Med., Kyoto Univ., Kyoto 606

Using monolayer rat parietal cells in the primary culture system (Okada & Ueda, J. Physiol. 354, 109, 1984), single channel recordings on the luminal membrane were carried out under cell-attached and inside-out configurations. Location of tight junctions and microvilli observed under electron microscopy showed that the upper membrane in contact with a culture medium can be defined as the luminal membrane. Before stimulation with acid secretagogues, the cells often exhibited activities of non-selective cation channels with a unitary conductance of about 40 pS, but not of anion channels. After stimulation with histamine, carbachol and high K^+ conditions, another type of channels with a conductance of about 30 pS became observable. The single channel current and the reversal potential were not affected by the cationic concentration gradient. The channels were found to be much more permeable to chloride ions than sulphate ions. Since this activity appeared only after stimulation, it is likely that the Cl^- channel on the luminal membrane plays a role in HCl secretion by the parietal cells.

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SYNERGISTIC ACTION OF cAMP- AND CALCIUM-MEDIATED CHLORIDE SECRETION IN DISTAL COLON OF GUINEA-PIG. YAJIMA, T., SETOYAMA, H., *KANEKO, K AND *SUZUKI, Y. Yakult Central Institute, Physiol. Group, Kunitachi, Tokyo 186, *Dep. Physiol. Yamagata Univ. Sch. Med., Yamagata 990-23

Synergistic effects of VIP, PGE_2 or 8-Br-cAMP and bethanechol (BCh) or A23187 on electrolyte transport across the guinea-pig distal colon were studied in vitro using an Ussing-chamber technique. The epithelial preparations consisted of mucosa and muscularis mucosae were used in the presence of indomethacin (10^{-6}M) and TTX (10^{-7}M) to prevent synthesis of endogeneous PGEs and activity of mucosal nerves, respectively. VIP (10^{-8}M), PGE_2 ($2x10^{-7}$M) or 8-Br-cAMP (10^{-3}M) produced a spike-like or a little increase in short-circuit current (Isc) and then a susteinable decrease in the Isc. BCh (10^{-5}-10^{-3}M) or A23187 ($5x10^{-6}$M) produced a little increase in Isc. The Isc-response to BCh was drastically potentiated by the presence of either VIP, PGE_2 or 8-Br-cAMP by 6-7 folds. The Isc-response to A23187 was also augmented by the presence of 8-Br-cAMP by 7-8 folds. These responses were inhibited by bumetanide ($5x10^{-5}$M) but not by amiloride (10^{-4}M). Unidirectional Na^+ and Cl^- flux measurements indicated that the increase in Isc produced by both presence of BCh and 8-Br-cAMP was due to net Cl^- secretion. The results suggest that an interaction of intracellular cAMP and Ca^{2+} synergistically produced net Cl^- secretion accompanying increase in Isc.

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INFLUENCE OF ENTERIC NEURONS ON ION TRANSPORT IN GUINEA PIG COLON.
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To determine whether or not enteric neurons influence ion transport across the mucosal epithelium, the effects of electrical field stimulation (EFS) on short-circuit current (Isc and ^{36}Cl fluxes were determined in the isolated guinea pig colon stripped of its muscularis propria. Rectangular, bipolar stimulus pulses (0.5 msec each, 1-5 mA, 5-10 Hz) were applied through aluminum foil electrodes placed on the submucosal surface of the colon. EFS evoked increases in Isc and ^{36}Cl flux from serosa to mucosa. These responses were completely abolished by the pretreatment with 3×10^{-7} M tetrodotoxin. The increase in Isc induced by EFS was reduced to an approximately half in the presence of 5×10^{-6} M atropine. Cholinesterase inhibitor, physostigmine (10^{-6} M), enhanced the EFS-induced increase in Isc significantly. These results suggest that EFS increases Cl secretion by activating enteric neurons. This effect is mediated at least in part by a release of acetylcholine which acts on muscarinic cholinergic receptor.

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WATER TRANSPORT AND AMINO ACID METABOLISM IN THE EEL INTESTINE.
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The net water flux across the seawater eel intestine was increased by L- and D-alanine, L-glutamine or L-glutamate, but not by other amino acids. The enhanced water flux by L-alanine was inhibited by aminooxyacetate, an inhibitor of aminotransferase which catalyzes the conversion of alanine into pyruvate. In the presence of aminooxyacetate pyruvate enhanced the net water flux. The effect of pyruvate was inhibited by oxythiamine, an antagonist of thiamine which acts as a coenzyme for decarboxylase. These results indicate that alanine stimulates the water transport through TCA cycle. The enhancement of the water flux by glutamine or glutamate was not inhibited by aminooxyacetate, but inhibited by 2,4-dinitrophenol or oxythiamine, suggesting that the metabolisms of these amino acids are also involved in regalating water transport. On the other hand, in fresh-water eel intestine the net water flux was not stimulated by alanine, but the alanine-sensitivity was augmented after administration of cortisol. From these results a possible model for regulating water transport is proposed.

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EFFECT OF PROLACTIN ON THE ACTIVE Na TRANSPORT ACROSS THE FROG SKIN.
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The long-term effect of prolactin (PRL) on the active Na transport across the skin of larval Rana catesbeiana during metamorphosis was investigated. The potential difference (PD), the short circuit current (SCC), the resistance to the active Na current (R_{Na}), and the electromotive force of the active Na current (E_{Na}) were low at stage XXI animals. PD, SCC, and E_{Na} were gradually increased, while R_{Na} maintained low value, as stage advanced. Injection of PRL (20 μg/g body weight every other day for 2 weeks) into stage XXI animals maintained PD, SCC, E_{Na}, and R_{Na} at values of stage XXI. On the other hand, application of PRL of same dose at stage XXV (young adult) animals induced increase in R_{Na} but not E_{Na}, resulting decrease in PD and SCC. The long-term application of PRL at stage XXI seems to inhibit the differentiation of Na pump, and once Na pump and Na entry mechanism were differentiated, PRL may inhibit only the latter.

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THE SHORT CIRCUIT CURRENT OF FROG SKIN IN THE NON-STEADY STATE CONDITION.
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The short circuit current was measured in ouabain treated frog whole skin and split skin in the non-steady state. We prepared the isolated frog skin incubated with ouabain-high K and low Na Ringer solution for 90 minutes. When we changed solutions in the both chambers to the normal Ringer solution with ouabain, we observed the positive transient short circuit current. Next, we prepared the split frog skin incubated with the normal Ringer solution with ouabain for 60 minutes. When we changed solutions in the both chambers to to the ouabain-high K and Na free Ringer solution, we observed the negative transient short circuit current. These transient short circuit currents reflected the passive cation fluxes via epithelial cells. We showed the short circuit current in the non-steady condition meant not only actively transported Na fluxes, but also diffusionaly transported cation fluxes.

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REGULATION OF EXOGENOUS GM_1-GANGLIOSIDE ON AMINO ACID UPTAKE AND MEMBRANE TRANSPORT ENZYME ACTIVITY IN PERIPHERAL GANGLIA EXCISED FROM RATS.
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Effect of GM_1-ganglioside on active uptake of non-metabolizable α-aminoisobutyric acid (AIB) and Na^+,K^+-ATPase activity in superior cervical sympathetic ganglia (SCG) and nodose ganglia (NG) excised from adult rat were examined during aerobic incubation at 37°C for 2 h. In SCG, AIB uptake was apparently inhibited (-27%) with slight decrease in Na^+,K^+-ATPase activity by the addition of GM_1 (5 nM). In NG, on the other hand, the amino acid uptake was greatly accelerated with the addition of GM_1 (+85%) with strong stimulation of Na^+,K^+-ATPase activity (+180%). A kinetic study of active AIB uptake showed that GM_1 produced an increase in Km without the change in Vmax in the SCG, whereas it caused a decrease in Km with slight increase in Vmax in the NG. These results suggest that exogenous GM_1-ganglioside may modulate membrane transport of amino acid by a process with affecting the activity of a transport enzyme, Na^+,K^+-ATPase.
Acknowledgment: We are grateful to Drs. T.Taketomi and A.Hara of Shinshu University for their kind supply of pure GM_1-ganglioside.

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IMMUNOELECTRON MICROSCOPIC DEMONSTRATION OF (Na^+-K^+)ATPase ON THE CILIARY EPITHELIAL CELLS.
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Rat eyes were fixed by perfusion with 4% paraformaldehyde containing 0.1% gultaraldehyde, and embedded in Lowicryl K4M. The ultrathin section were incubated with antibody against holo(Na^+-K^+)ATPase purified from the rat kidney, and subsequentry with protein A gold complex then observed under an electron microscope. Immunoblot analysis showed that the antibody bound exclusively with α-subunit of (Na^+-K^+)ATPase in the ciliary body. Both in the pigmented epithelial cell (PE) and nonpigmented epithelial cell (NPE), gold particles were found mainly on the basolateral surface, but much less on the apical and ciliary channel surfaces. Labelling density was higher on the PE than NPE. The basolateral surface of PE and NPE are markedly infolded. This means almost of all (Na^+-K^+)ATPase are located on the basolateral surface. We suggest that not only the (Na^+-K^+)ATPase on NPE but also on PE plays an important role in aqueous humor secretion.

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IMMUNOCHEMICAL STUDY OF Na^+,K^+-ATPase ISOZYMES

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We prepared the α and $\alpha(+)$ catalytic subunits of Na^+,K^+-ATPases from microsomes of the rat kidney and brain, and raised antisera against these subunits in rabbits. Using the antisera and Western blot technique, isoforms of α subunits in microsomes of various tissues were examined. α isoform was found in all tissues examined, whereas $\alpha(+)$ isoform, in nervous and muscle tissues alone. A new isoform of α subunit was found in the submandibular gland (SMG); it had a molecular weight slightly less than the α isoform, and strongly cross-reacted with anti kidney α antiserum. The α subunits in kidney or brain microsomes were not cleaved by incubating these microsomes with SMG homogenates or extracts. The newly found α subunit did not disappear when the SMG microsome was prepared in the presence of various proteinase inhibitors. These results suggest that the unidentified α isoform is not an artifactual product formed during the preparation process. By autoradiography, the new immunoreactive α subunit was demonstrated to be labeled with $[\gamma\text{-}^{32}P]$-ATP in the presence of ouabain but not, in the presence of K^+.

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NUCLEOTIDE SEQUENCE OF RAT BRAIN $[NA^+,K^+]$ATPASE β SUBUNIT CDNA AND *IN VITRO* INSERTION OF ITS ENCODED POLYPEPTIDE INTO MICROSOMAL MEMBRANES.

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We cloned and sequenced a cDNA(2299bp) which contained complete coding sequence of rat brain $[Na^+,K^+]$ATPase β subunit. To analyze the orientation of the β subunit on microsomal membranes, the cloned cDNA and the cDNA fragment(~750bp) which lacked a half portion of the coding region(C-terminal site) were inserted into an expression plasmid vector PTZ 18. Transcription of the resulting recombinant plasmids with T7 RNA polymerase yielded synthetic mRNAs and these mRNAs were used for wheat germ cell-free translation system in the presence or absence of microsomal membranes. Protease digestion experiments of the translated products showed that only N-terminal portion of the β subunit(~30 amino acids) was exposed to the cytoplasmic surface of microsomal membranes.

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MEASUREMENT OF ELECTRO-OSMOTIC EFFECT AND DETERMINATION OF THERMODYNAMICAL PARAMETERS.

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Transmembrane potential acts as water driving force, when there is some difference of reflection coefficients between cation and anion. A duct of rat submaxillary gland was cannulated and connected to a vertical tube (1 m long) containing isotonic NaCl or Na_2SO_4 solution. Pressure decay and its relation to flow were investigated, monitoring by a pressre transducer. Pressure decay of Na_2SO_4 solution was slower than that of NaCl solution, because the former deepened intraductal negative potential. We also showed pure electro-osmosis in a frog skin and gastric mucosa. Thermodynamical parameters were decided in comparison with osmotic driving force. The values of $Lp(cm/sec/atm/cm2)\sigma_{Cl}-\sigma_{Na}$ were $4*10-7,0.14(\sigma_{Na}=0.82,\sigma_{Cl}=0.96)$ for skin, $9*10-7,-0.11$ for gastric mucosa.

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^{31}P NMR STUDY ON ENERGETIC RECOVERY FROM HYPOTHERMIC PRESERVATION IN THE RAT LIVER.

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Functoinal recovery of the preserved organ depends on the recovery of energy metabolism. To assess this recovery, the high energy phosphorus compounds and intracellular pH were measured by ^{31}P nuclear magnetic resonance, oxygen consumption and bile flow rate were also measured in the preserved liver, before and after preservation. A right lobe of a liver was isolated and preserved at 0°C. The ATP signal decreased to noise level during hypothermic preservation. After 6 or 24 hr preservation, the liver was reperfused with Krebs-Henseleit solution at 37°C. The ATP levels of the 6 and 24 hr preserved liver recovered to 92 % and 76 % of the pre-preservation level, respectively. The intracellular pH recovered to the prepreservation level after both 6 and 24 hr storage. The oxygen consumption of the 24 hr preserved liver was higher than that of the fresh liver. Bile flow rate recovered to 85 % of the control even after 24 hr preservation. These findings as increase in mitochondrial respiration and low ATP level, support the idea that the efficiecy of oxidative phosphorylation decreases by 24 hr hypothermic preservation, but still remains the possibility of increase in ATP hydrolysis by other process than bile secretion.

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^{31}P NMR STUDY ON HIGH ENERGY PHOSPHORUS COMPOUNDS DURING INITIAL SECRETION BY SALIVARY GLAND.

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The kinetics of creatine phosphate (PCr), inorganic phosphate (Pi) and NTP (ATP+GTP) during initial stage of secretion was studied by phosphorus nuclear magnetic resonance (^{31}P NMR) spectroscopy. Time resolution of the NMR measurement was increased up to 30 sec by accumulating spectra from 8-12 serieses of experiments on the isolated perfused mandibular gland. The onset of decrease in PCr and increase in Pi started at 2 min from the start of stimulation by acetylcholine (ACh; 1 μM) and reached their plateau levels with 3-5 min of time constant. NTP was unchanged during stimulation, suggesting that ATP consumption was compensated immediately by rapid supply of ATP. By withdrawal of ACh, PCr and Pi recovered to their resting levels quickly (time const.;30 s-1 min). The high dose (1 mM) of ACh caused a 2-step decrease in PCr (an undershoot and a gradual decrease), suggesting two PCr pools in the salivary gland.

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INTRACELLULAR Na AND K IN PERFUSED RAT SALIVARY GLAND STUDIED BY ^{23}Na AND ^{39}K NMR.

SEO, Y., MURAKAKMI, M., NISHIKAWA, H. & WATARI, H. Natl. Inst. Physiol. Sci., Okazaki, 444 and Dept. Physiol., Kyoto Pref. Univ. Med., Kyoto, 602

The present study was carried out by sodium- and potassium- nuclear magnetic resonance (^{23}Na and ^{39}K NMR) to measure Na and K in the isolated perfused mandibular gland of rat (24°C). The intra- and extra-cellular electrolytes were discriminated using a chemical shift reagent, dysprosium triethylenetetramine-N,N,N',N",N"',N"'-hexaacetic acid. During control perfusion, the intracellular Na (Na_{in}) and K (K_{in}) was estimated as 10 and 135 mmol/l ICF, respectively. During secretion by ACh (1 μM), Na_{in} increased by 9 mmol/l ICF. During perfusion with ouabain (1 mM) and ACh (1 μM), Na_{in} increased by 44 mmol/l ICF and K_{in} decreased to around 100 mmol/l ICF.

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THE EFFECT OF CYCLIC NUCLEOTIDE ON THE MEMBRANE POTENTIAL DIFFERENCE.
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We used double-barrel K^+, Na^+, H^+ ion selective microelectrodes to study the effect of dibutyryl-cyclic AMP (dbcAMP) on the membrane potential difference and ion transport mechanism in doubly-perfused bullfrog proximal tubules. The peritubular membrane potential difference (E_M) and intracellular K^+, Na^+ activities ($(K)_i$, $(Na)_i$) and intracellular pH were monitored continuously after peritubular application of dbcAMP (10^{-3}-10^{-4} M). Results: 1) dbcAMP hyperpolarized E_M by 6-15 mV with an increase of $(K)_i$ by 5-7 mEq/L; 2) the peritubular application of high K^+ (50 mM) solution depolarized E_M by about 40 mV. On the addition of high K^+ to the dbcAMP administration, E_M was hyperpolarized by about 5 mV followed by a depolarization to the same level as control; 3) dbcAMP caused a decrease of $(Na)_i$ by 5-10 mEq/L and $(H)_i$ by about 0.16 pH. Conclusions: 1) the increase of K^+ permeability in the peritubular membrane was caused by dbcAMP; 2) intracellular alkalinization by dbcAMP would be due to the increase of H^+ transport from cell cytosol to vesicle; 3) the above findings support the concept that dbcAMP inhibits directly Na^+-H^+ countertransport in the luminal membrane.

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EFFECTS OF FUROSEMIDE AND OUABAIN ON THE ION DISTRIBUTION IN PIG PANCREATIC ACINAR CELLS.
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Electron probe X-ray microanalysis of freshly freeze-dried thin sections of pig pancreatic acinar cells showed that the Na, Cl and Ca concentrations increased and K concentration decreased in the cytoplasm, while the Na, Cl and K concentrations increased in both the secretory granules and the lumen, with CCK stimulation.

After ouabain (10^{-4} M) exposure to the bath solution the Na and Cl concentrations increased, but K concentration decreased in the cytoplasm, and in the luminal space there were slightly increase in Na and Cl concentrations.

Addition of furosemide at final concentration of 10^{-5} M to the bath solution produced significant changes in ionic concentrations in acinar cells. There was an increase in K concentration and decrease in Na and Cl concentrations in the cytoplasm, and the Cl decrease in luminal space. Possible localization of pump, carrier and channel were discussed.

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THE EFFECTS OF PUMP AND CARRIER INHIBITORS ON ION TRANSPORTS IN SILK GLAND CELLS.
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It has been proposed that there exist a K-pump and a Cl-K-Na cotransport carrier on the luminal and basal plasma membrane, respectively (J. Exp. Biol., 1987, in the press). We studied the effects of H^+,K^+-ATPase inhibitor, omeprazole and $2Cl^-$,$1Na^+$,$1K^+$cotransport inhibitor, furosemide on the ion transport in the posterior silk gland cells, using electrophysiological and electron microprobe techniques.

By the treatment with omeprazole, the membrane potential of posterior silk gland cells hyperpolarized and the cytoplasmic K concentration decreased, whereas the luminal K and Cl concentrations did not change. By the treatment with furosemide, the membrane potential of the gland cells depolarized and immediately after that, hyperpolarized. The cytoplasmic K concentration increased and luminal Cl concentration decreased, simultaneously.

From these data, it is suggested that a omeprazole sensitive K-pump and a furosemide sensitive Cl-K-Na cotransport carrier are localized on the luminal and/or baso-lateral plasma membrane of the gland cells.

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NETWORK SIMULATION OF MEMBRANE TRANSPORT. IMAI,Y., MIYAMOTO,S., SOHMA,Y.
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Both theoretical and experimental investigations have been required for understanding the highly organized biological system. For the mechanisms of biomembrane transport, we attempt to synthesize the circuit model with the improved method of network thermodynamics.

Using the network representation of epithelial transport system inluding the Na-K pump, we studied theoretically the effeciency of active transport. The pump effeciency was expressed by the ratio of power required with pump and power supplied with ATP reaction. It was shown that the effeciency was representated by the function of electro-chemical potential differences of active transported iones and affinity of ATP reaction. On the frog skin, the effeciency of Na-K pump located at the basolateral cell membrane was caliculated about 65% in the normal condition.

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Cl SUBSTITUTION AND pHi CHANGES IN CHICKEN ENTEROCYTE SUSPENSION: INVOLVEMENT OF ANIONIC MECHANISMS. KINOSHITA,Y. and IRIMAJIRI,A.
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Substitution of Cl by SO_4 or gluconate in the medium suspending chicken enterocytes induced intracellular alkalinization as measured by the acridine orange method. The substitution-induced increase in intracellular pH (pHi) was not due to metabolic inhibition by the substituted anion. Rather, they appeared to involve anion exchange mechanisms. When cells suspended in Cl-medium were diluted into Cl- or SO_4-medium, pretreatment with DIDS (50 μM) reduced the pHi difference between the two media to less than half that otherwise observed. Diphenylamine-2-carboxylate (0.1 mM), a blocker of the Cl conductive pathway, induced small pHi increases in both cells suspended in Cl- and SO_4-media, suggesting the presence of a Cl conductivity and that the blockade of Cl exit would result in an augmentation of electroneutral Cl/OH(HCO_3) exchange in favor of OH or HCO_3 entry. These results suggest that the anion substitution-induced pHi increase involves influxes of base equivalents, driven by an outwardly-directed Cl gradient, by the electroneutral Cl/OH(HCO_3) exchange and electrophoretical coupling, the former probably dominating. Because, although nominally HCO_3-free media were used here, intracellular acidity was shown to stem mainly from the TCA cycle, the decisive anion species (OH or HCO_3) involved in the pHi increase remains to be determined.

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BICARBONATE TRANSPORT IN GUINEA PIG CECUM. KANEKO, K. AND SUZUKI, Y.
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Transepithelial HCO_3 transport in the guinea pig cecal mucosa was studied in vitro in Ussing chambers under short-circuit conditions. One side of tissues was bathed with the HCO_3-CO_2-containing solution while the other side was bathed with the buffer-free solution. Absorptive (Jms) and secretory (Jsm) HCO_3 fluxes, determined by use of the pH-stat technique, were 1.24 ± 0.18 and 1.91 ± 0.21 $\mu mol \cdot cm^{-2} \cdot h^{-1}$, respectively. These rates were stable at least within 90 min. Anoxia or 10^{-4} M 2,4-dinitrophenol added to the mucosal side reduced both Jms and Jsm by 55-70 %. Serosal ouabain (10^{-4} M) reduced Jsm but had no effect on Jms. We conclude that active HCO_3 transport of both absorptive and secretory directions are present in the cecum and that the secretory process is dependent on the Na pump in the basolateral membrane.

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THE MECHANISM OF BASAL FLUID SECRETION IN HYPERTROPHIED PANCREAS OF THE RAT. ISHIKAWA,T AND KANNO,T. Dept.Physiol.Fac.Vet.Med.,Hokkaido Univ., Kita-ku Sapporo 060

A synthetic protease inhibitor (FOY-305) was administered orally once a day for 21 days. This procedure caused hypertrophy of rat pancreas. Basal level of fluid secretion in isolated perfused preparation of the hypertrophied pancreas showed a value seven times greater than that of normal pancreas. Na concentration of basal pancreatic juice of normal and hypertrophied pancreas was about 150 mM. Basal level of fluid secretion from the hypertrophied pancreas was reduced by lowering Na or K concentration in perfusing solution and by ouabain(1 mM) or amiloride (0.1 , 1 mM). On these results, we proposed that activities of ouabain-sensitive Na,K-pump and amiloride -sensitive Na-H antiport are responsible for maintaining basal level of fluid secretion in hypertrophied pancreas of the rat.

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STABLE PHOSPHOLIPID MEMBRANE SUPPORTED ON A POROUS FILTER PAPER KUMAZAWA, N., TSUJIMOTO, T., Dept. of Physiol., Wakayama Med. College, 9-banchou, Wakayama 640

Uniform lipid membrane had constructed on porous filter-paper(FM22) by application of the Langmuir-Blodgett method. The electrical conductance of the membrane which was immersed in water solution, was 10^{-8} - 10^{-7} moh cm^{-2}. This value was equal to that of the black lipid membrane(BLM). The capacitance of the membrane was also corresponded to that of the value of BLM. The conductance of the membrane increased in the presence of protonophore(SF6847) or the ionophore(gramicidin) in water solution. The electron microscopic observations of the surface of the constructed filter-paper showed that membrane existed on one side of the paper. These results show that the structure of the membrane is the bilayer structure. The membrane formed in this method is quite stable in aqueous solution and in air. In addition, this membrane has large areas. These good manipulability may serve as a useful experimental tool in the studies of biomembranes and artificial membranes.

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A COMPUTER ANALYSIS OF KINETIC CONSTANTS FOR TRANSPORT SYSTEM CONSISTING OF TWO COMPONENTS CARRYING SAME SUBSTRATE. HASHIGUCHI, T., TOSAKA, T., TASAKA, J., AND SAKAI, S., Dept. of Physiol., Tokyo Medical College, Shinjuku, Tokyo 160

A method which can estimate the Michaelis-Menten constants for two transport systems carrying the same substrate has been proposed by Spears et al. (1971). According to their algorithm, we have devised a computer program adopting a non-linear least square approximation in place of a linear regression method. Thus transformation of the Michaelis-Menten equation to a linear form was avoided. We have carried out a simulation experiment using three representative models consisting of two components and confirmed the correctness of the program in each case. In particular, the correct constants were derived for the model 2, in which a simple graphic derivation was not applicable. The sensitivity of the method to experimental errors was also studied in detail. The goodness of fit, introduced in the present experiment, was found to be a practical measure to assess the accuracy of the derived constants.

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ELECTROPHYSIOLOGICAL PROPERTIES OF NEURONES IN RABBIT VESICAL PELVIC GANGLIA.

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Resting and active properties of neuronal membrane in vesical pelvic ganglia (VPG) were examined with intracellular recording techniques in vitro. The resting membrane potential was 56.9 ± 0.7 mV (mean ± SE, n=86). The input resistance and the time constant were 82.6 ± 6.0 MΩ (n=42) and 7.3 ± 0.8 msec, respectively. The threshold was 20.3 ± 0.8 mV (n=47). The amplitude of the spike was 73.5 ± 1.3 mV. The amplitude of the spike after-hyperpolarization (AHP) was 13.8 ± 0.7 mV. The duration of the AHP was 3.93 ± 0.67 sec. The action potential was composed with two components, the TTX sensitive, probably Na^+ spike and TTX resistant Ca^{2+} spike components. The spontaneous hyperpolarization (SH) was recorded from 50 % of neurones with either KCl or K-acetate microelectrode in the Krebs solution. Both the slow AHP and the SH might be generated by an activation of g_{KCa}, since they were blocked by lowering external Ca^{2+}. Three types of VPG neurones were identified by the voltage-current relationship. In 50 % neurones, membrane possesses a prominent inward rectification at a potential more negative than -90 mV. In some neurones (30 %), membrane showed an inward rectification near the resting membrane potential. Remaining 20 % neurones have no noticeable time-dependent inward rectification.

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EFFECTS OF VINCAMINE AND BROVINCAMINE ON MEMBRANE CURRENTS OF GIANT NEURONES OF AN AFRICAN GIANT SNAIL (ACHATINA FULICA FÉRUSSAC).

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Effects of a vinca alkaloid, vincamine, and its bromoderivative, brovincamine, on membrane currents of identifiable Achatina giant neurones were studied, in comparison with those of verapamil. The three drugs blocked the calcium current; the effects of brovincamine was the strongest. The concentrations to produce the 50 % inhibition were: 0.02mM for brovincamine, 0.2mM for vincamine and 0.3mM for verapamil. The three drugs at 0.1 mM did not affect the sodium current. The outward currents, measured in the physiological solution, were reduced by the two vinca drugs. However, fast outward current and delayed outward current, measured in the calcium-free solution, were not affected by the two drugs. It suggests that the reduction of outward currents, measured in the physiological solution, is due to the disppearence of calcium-activated potassium current, in consequence of the entry block of calcium caused by the two vinca drugs.

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IONIC CURRENTS OF THE ISOLATED CHICK COCHLEAR GANGLION NEURON.

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Cochlear ganglion neurons of chick embryos were primarily cultured and the excitability of membrane was studied by voltage clamp technique. Na-, Ca- and some K-channel conductances were observed. Properties of Na-channel (22°C): $V_{1/2}$ of the I-V curve (-26mV), the steady state inactivation (V_h=-59mV, slope factor=6.5mV), half peak time of activation (0.47ms at 0mV) and τ of inactivation (0.48ms at 0mV). TTX(10^{-6}M) blocked Na channel. Ca-current showed two types of kinetics; non-inactivating and inactivating. Non-inactivating current was analyzed by fitting H-H m^2 kinetics: τ_m was 1.5ms (0mV, $[Ca]_o$=2.5mM), the steady state open-probability estimated from the tail current amplitude was about 70% at the peak-inward current potential. $V_{1/2}$ was shifted to positive direction as a function of divalent cation concentration of the bath, indicating screening effects on the surface charge. Ca showed larger shift (10 mV at 2.5mM) than Ba and Sr. This resulted in a slower kinetics of Ca-current than Ba- and Sr-current at membrane potentials (between -10 and 5 mV).

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NA- AND K-CURRENTS IN CALCITONIN-SECRETING CELLS OF THE CHICK STUDIED WITH PATCH-ELECTRODES. KAWA, K. Dept. of Pharmacol. Sch. Med., Gunma Univ., Maebashi 371

Calcitonin-secreting cells were isolated from ultimobrachial gland of the chick embryos (18 days after incubation). When the membrane potential was depolarized from holding potential (-83∿-103mV), transient inward current was produced which was followed by slowly developing outward current. The inward current was identified as Na^+ carried current since (1) the amplitude strongly depended on the holding potential and (2) replacement of external Na^+ with choline$^+$ or external application of tetrodotoxin (1μM) abolished the current reversibly. In the presence of external tetraethylammonium (1∿10mM) or 4-aminopyridine (1mM), the outward current was selectively reduced which indicated that this outward current was membrane potential dependent K current. These cells were positively stained with anti-calcitonin antibody (#7701R1) raised in the rabbit. Some cells showed no measurable inward currents and were stained faint or negligible with the antibody. These cells may represent non-secreting cells or supporting cells in the gland.

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IONIC CHANNELS RESPONSIBLE FOR ACTIVITY OF THE MOUSE PANCREATIC B-CELL. MURAYAMA, K., OHARA, A.† AND KITASATO, H. Dept. Physiol. and †Dept. Biol., Shiga Univ. Med. Sci., Ohtsu 520-21

It has been reported that stimulation of the efferent vagus nerve and also the direct application of acetylcholine (ACh) to the pancrease cause an increase in insuline release from pancreatic B-cells. To elucidate the membrane mechanism of this effect, we studied the direct effect of ACh (1-5 μM) on the membrane potential and also on single-channel currents in the mouse pancreatic B-cell using the patch-clamp technique. The resting membrane potential recorded in the whole-cell current-clamp mode was about -65 mV (with a pipette solution containing 3 mM ATP and 0.06 μM Ca^{2+}). Bath application of ACh caused an transient depolarization of 30-35 mV lasting about 2 min with spike-like potential fluctuations, occasionally followed by subsequent depolarizations with an interval of less than 1 min. Single-channel recordings on the outside-out patch showed that ACh applied to the outer surface of the membrane transiently suppressed the opening of large-conductance Cl^--channels (340-435 pS). Little effect was observed on the ATP-, Ca^{2+}- and voltage-insensitive K^+-channel (130 pS). Although ionic mechanisms for the depolarization produced by ACh still remained unsolved, the present results strongly suggest that ACh exerts direct effects on the B-cell to modify its ionic permeability and thereby the release of insulin.

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Two components of Ca^{++} channels in human GH-producing pituitary tumor cells. Yamashita N. Matsunaga H. and Ogata E*. 4th Dept. Int. Med. Sch. Med. Univ. Tokyo. Tokyo 112

Ca^{++} channel currents were examined in five dissociated human pituitary adenoma cells that secrete growth hormone. For electrophysiological study, whole cell variation of the patch electrode voltage clamp technique was employed. The dissociated pituitary cells were identified as GH-producing cells by using reversed hemolytic plaque assay in two adenomas. About 90% of the cells formed hemolytic plaque, indicating most cells using in the present study are GH-producing cells.

In 20 mM Ba^{++} Na-free medium, inward current with activation and inactivation kinetics (T-type) was observed. In addition, steady inward current (L-type) was also observed. Both currents were blocked by adding 0.5 mM La^{+++} or 5 mM Co^{++} to the external medium. T-type Ca^{++} channels were inactivated when the holding potential was depolarized to -50 mV from -80 mV, while L-type showed little change. Deactivation time constant of T-type was slower than that of L-type. Nitrendipine (1 uM) inhibited L-type Ca^{++} channels and Bay K8644 (1 uM) mainly enhanced L-type. Hormone secretion was inhibited by nitrendipine and enhanced Bay K8644. Thus hormone secretion was correlated to the change of Ca^{++} channels by these agents.

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EFFECTS OF JELLYFISH VENOM ON FROG MUSCLE. ANRAKU, M.,[1]KIHARA, H.,[2]OHNO, M. and[1]HASHIMURA, S. Lab. of Physiol., Sch. of Allied Med. Sci., and [1]Dept. of Physiol., Fac. of Med., Kagoshima Univ., Kagoshima 890 and[2]Fac. of Sci., Kyushu Univ., Fukuoka 812.

Effects of the venom from jellyfish collected around the Truk Islands were studied on frog muscle. The venom caused a significant depolarization and rising of the resting tension of the muscle. Depolarization of muscle was dependent on the venom(6-300μg/ml) and also Na concentration. Membrane potential and resting tension of the venom treated muscle did not return to normal after washing. However, when NaCl was replaced by choline-Cl, repolarization and relaxation occured. The addition of TTX or La^{3+} showed no effect on depolarization. The addition of La^{3+} or the removal of Ca^{2+} showed a decrease of the rised resting tention.The venom decreased muscle membrane resistance in normal Ringer. In choline-Ringer membrane resistance did not change during the application of the venom. From these results, depolarization by the venom was interpreted as being the result of increased permeability of muscle membrane to Na^{+}. Rising of resting tension was speculated to be due to Ca-influx resulted from muscle depolarization induced by the venom.

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INHIBITION OF THE Na CHANNEL INACTIVATION BY SEA ANEMONE TOXINS.
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The effect of toxin III (ATX III) and IV (ATX IV) isolated from the sea anenome, Anemonia sulcata on the membrane current of the crayfish giant axon was studied. Like other sea anemone toxins, ATX III and IV slowed selectively the Na inactivation to exhibit a maintained Na current during depolarizing voltage pulse. ATX III was about five times as potent as ATX IV in terms of the toxin association rate. The action of both ATX III and IV was markedly suppressed at depolarized membrane potentials. Using the intensity of the maintained current as a measure of the fraction of toxin binding to Na channels, we could clarify that the suppression of ATX III (as well as ATX IV) binding during depolarization was mainly caused by an increase in the dissociation rate. The sharpest change in the dissociation rate occurred in a potential rage where the Na channel inactivation (and also activation) took place. The detailed characteristics of the voltage-dependent association and dissociation for ATX III were very similar to those for ATX IV despite the difference in the net charge distributions of the two toxins. These results suggest that the alteration of the toxin binding kinetics with the membrane potential is derived not from a simple electrostatic interaction between toxin molecules and the membrane potential but from a change involving in the gating process of Na channel.

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EFFECTS OF SYNTHETIC ω-CONOTOXIN ON THE TWO TYPES OF Ca CHANNELS AND INTRACELLULAR ELEVATION OF Ca IN CLONAL GH3 CELLS.
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The effect of synthetic ω-conotoxin on two types of Ca channels in clonal rat pituitary cells (GH3) was studied using the whole-cell variant of the patch-clamp technique. Low concentration of the toxin was found to block a long-lasting Ca channel current but a much higher concentration had little effect on a transient type of Ca channel current, which was activated at relatively more negative voltages and showed marked inactivation. The toxin was utilized to test the contribution of long-lasting type of Ca channel current to the elevation of intracellular Ca concentration when stimulated thyrotropin-releasing hormone. The stimulation-inducing intracellular Ca elevation, however, was not suppressed even in the presence of higher concentration of the toxin, suggesting that the elevation of intracellular Ca after stimulation was ascribed mainly to Ca released from the internal store, not to Ca current through a long-lasting type of Ca channel.

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EFFECT OF INTRACELLULARLY ADDED OR DEPLETED Ca IONS ON ANION PERMEABILITY OF NERVE MEMBRANE IN SQUID GIANT AXONS.
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Dept. Cell Physiol., National Inst. for Physiol. Sci., Myodaiji Okazaki 444.

Effects of intracellular Ca concentrations ranging 10^{-2}M to 10^{-11}M on the membrane permeabilities of Cl and other anions were examined using intracellularly perfused squid giant axons. The axon immersed in atrificial sea water (ASW) was internally perfused with a K-salt (KCl, KF, or K-glutamate) solution. In normal condition, the membrane potential hyperpolarized by about 18 mV for 10 fold increase in K-salt solutions, showing a property of K ion selective.

When a high concentration of Ca ion (>10^{-3}M) was applied intracellularly, the resting membrane hyperpolarized with the increase in Ca concentration. The membrane showed a Ca ion selective property. In addition to that, during the Ca ion perfusion, a Cl ion permeability gradually increased.

When the axon was previously perfused with a very low Ca solution buffered with EGTA for 10 minutes, the membrane changed its ion selective property prominently. Namely, by the internal perfusion of the KCl, K-glutamate, or KF solution, the membrane potential depolarized by 25-30 mV for 10 fold increase in the K-salt concentration. This showed that the membrane changed to highly anion selective.

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MEASUREMENT OF INTRACELLULAR CA CONCENTRATION IN THE BULLFROG SYMPATHETIC GANGLION CELL.
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The intracellular free Ca concentration ($[Ca^{2+}]_i$) of single sympathetic ganglion cells of the bullfrog was measured with fura-2 fluorescence under the resting and electrically or chemically stimulated conditions and compared with changes in membrane potential or current using an intracellular electrode. The resting $[Ca^{2+}]_i$ was 94 nM. The Ca entry through voltage-dependent Ca channels was observed by raising the extracellular K^+ concentration to 50 mM. The onset of rise in $[Ca^{2+}]_i$ was delayed for several tens of seconds after the membrane depolarization. Periodic increases of $[Ca^{2+}]_i$ by Ca^{2+} release from intracellular Ca reservoirs were observed by appling 1 mM caffeine and their time courses were paralleled with rhythmic membrane hyperpolarizations. Repetitive stimulation of both pre- and post-ganglionic nerves raised $[Ca^{2+}]_i$, although the increment of $[Ca^{2+}]_i$ by a single action potential was not detectable. ACh 100 uM, applied in the presence of atropine 50 nM, produced a rise in $[Ca^{2+}]_i$ whose time course coincided with that of the inward membrane current, indicating the entry of Ca^{2+} through the nicotinic ACh-receptor channel. However, the definite evidence for the Ca^{2+} entry through muscarine-activated cation channels was not obtained.

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ACh-INDUCED CHANGES IN MEMBRANE POTENTIAL CHANGES AND INTRACELLULAR Ca^{2+} CONCENTRATIONS IN RAT HIPPOCAMPAL NEURONS.
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ACh-induced membrane potential changes and intracellular Ca^{2+} concentration ($[Ca^{2+}]_i$) changes in cultured hippocampal neurons (CA_1) were studied with the whole-cell patch clamp and the Ca^{2+} sensitive dye, Fura-2. The typical patterns of those signals were the membrane depolarizations accompanied with the membrane conductance decreases (M channel closure) and the increases in $[Ca^{2+}]_i$ resulting from the openings of voltage-dependent Ca^{2+} channels. However, some neurons showed the membrane hyperpolarizations and the increases in $[Ca^{2+}]_i$. In the cases, no inward current was observed under the voltage clamp. Then, Ca^{2+} may come from some intracellular Ca^{2+} store site as e.r.. This process may be mediated by some second messengor, e.g. IP_3. Actually, the IP_3 injected through a patch pipette caused the increases in $[Ca^{2+}]_i$ and the outward K^+ current. Besides the responses, ACh sometimes decreased the $[Ca^{2+}]_i$. Heterogeneity of the electrical responses to ACh in cultured CA_1 neurons may be, in part, explained by the variety of $[Ca^{2+}]_i$ changes which activate or inactivate the ionic channels in the neuron membrane.

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EFFECT OF A SCHWANN CELL LAYER RESISTANCE ON THE NERVE EXCITATION. KUKITA, F., Lab. Membrane Biol. Natl. Inst. Physiol. Sci., Okazaki 444.

A resistance of Schwann cell layers of the squid giant axon was changed by the osmotic water flow across these Schwann cells and an axolemma. The change in this resistance in series with the axonal membrane capacitance (C_m) (a series resistance) could be observed in the decay time constant of the capacitative surge under the voltage clamp. When the outward water flow was applied, the series resistance decrease and the removal of K^+-accumulation in the periaxonal space were observed at the same time. Under these condition, the increases in the inward Na current and in the conduction velocity of the action potential were observed also and could be partly explained by the descrease in the series resistance. These results clearly showed that a contribution of the Schwann cell layer resistance was significantly large at a normal nerve conduction.

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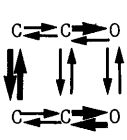
THE INITIATION OF THE SPIKE POTENTIALS ON THE MULTIPLE SPOTS ALONG THE AXON OF APLYSIA NEURON. KOIKE, H., UMITSU, Y. AND MATSUMOTO, H., Department of Neurophysiology, Tokyo Metropolitan Institute for Neurosciences, 2-6 Musashidai, Fuchu City, Tokyo

Action potentials conducting along the axon of neurons of Aplysia were recorded by paired extra-cellular electrodes placed on the nerves with an aid of spike triggered averagings. The time difference between the action potentials recorded from the cell body and those from the axon of the neuron was significantly smaller than the conduction time of the antidromic spike. The time difference was not constant but greatly varied according to the conditions of the initiation of the spike potentials. In the spontaneously occurring spikes the time difference became smaller with time for several minutes after the penetration of the intracellular electrode. Usually it was much smaller when the spikes were initiated by passing depolarizing current through the electrode. It was the smallest when the spikes were spontaneously initiated in Ca-free bathing solution. Since the conduction velocity of the spikes was constant under these conditions, the results indicate that the spikes were not initiated at a fixed trigger zone on the proximal axon close to the cell body, but at some multiple spots along the axon of the neurons of Aplysia.

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SWITCHING BETWEEN TWO TYPES OF BURSTING ACTIVITY OF SINGLE Ca^{2+}-ACTIVATED K^+ CHANNELS. YAMAMOTO, D. Neurophysiol. Lab., Mitsubishi-Kasei Inst. Life Sci., Tokyo 194.

The two open states of the Ca^{2+}-activated K^+ channels of dissociated adult cockroach neurones, unlike those of other preparations, are quite distinct from each other, i.e. in a "long-open burst", the channels does not close for 3.5 to 12.5 ms (depending on membrane potentials) on average, whereas in a "flickering burst" rapid transitions between closed and open states take place and the mean duration of the brief openings is of the order of 0.5 ms. These two classes of bursting activity are readily visible by inspection of patch clamp records, and we have detected direct transitions between these two types of burst. Previously proposed kinetic schemes for the Ca^{2+}-activated K^+ channels cannot account for the present observations. I propose the following "parallel scheme" to explain our results:



In this scheme thick arrows represent rapid transitions. Two types of bursts are produced by two C-O (closed-open) transitions in the right-hand side of the scheme. The incorporation of a rapid C-C transition ensures the equal frequency of occurrence of two types of bursts. The O-O transition is postulated to account for the switching between the long-open burst and flickering burst.

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TRANDITION BETWEEN BEATING AND BURSTING ACTIVITIES IN MOLLUSCAN NEURON.
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Onchidium pacemaker neuron without polarizing current beats regularly. The beating rhythm depends on injecting current through an intracellular electorode. When the cell is hyperpolarized, regular bursts are generated. The bursts are unstable in the regions between the beating and the bursting activities. The interspike interval of the irregular burst gradually becomes long and then comes back to a shorter one through an interburst interval. When the cell is further hyperpolarized, the bursts are suppressed.

Three kinds of spontaneous discharge of the pacemaker neuron, that is, the beating, the irregular bursting, and the regular bursting activities were analysed by means of a one-dimensional map of interspike intervals and a Poincare return map obtained from a cross-section of an attractor embeded in a three-dimensional phase space. The maps of irregular bursts reveal an apparent single-valued function. This indicates that the fluctuations in interval and membrane potential are chaos which is subject to a deterministic law.

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EFFECT OF TRIGEMINAL STIMULATION ON THE VAGAL ANBIGEUS NUCLEUS IN CATS
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We previously demonstrated the close relationship between firing patterns of neurons in the solitarius nucleus as well as the dorsal nucleus of the vagal nerve and trigeminal stimulation. To elucidate the relationship between trigeminal stimulation and vagal ambiguous nucleus, effects of trigeminal simulation on the changes in firing pattern of neurons in the ambiguous nucleus were examined.

Unit discharges from the ambiguous nucleus were recorded using a glass micropipette containing fast green FCF, and the microelectrode position was assertained histologically after the experiment. The analysis of unit discharges was performed with an ATAC-450 microcomputer.

There were three types of neurons in the ambiguous nucleus from the view-point of effect of trigeminal stimulation: neurons for which firing was accelerated by trigeminal stimulation, neurons for which firing was decreased by trigeminal stimulation and neurons indifferent to trigeminal stimulation.

These findings suggest that trigeminal stimulation modifies the neuronal firing pattern and consequently causes changes in vagal outflow, finally evoking the Reilly phenomenon in oral medicine.

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PERMEANT IONS IMPEDE CLOSING OF A SARCOPLASMIC RETICULUM K CHANNEL.
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Dept. Physiol., Nagoya Univ. Sch. Med., Nagoya 466

Effect of K^+ on the voltage dependent K channel from rabbit skeletal sarcoplasmic reticulum(SR) was examined at various K^+ concentration (100 to 500mM) on either side of the channel. K channels in SR were incorporated into planar lipid bilayers by a fusion of SR vesicles with the bilayers and single channel K currents were measured under a voltage clamp condition. The open time of individual channels incresed linearly with the concentration of K^+ on the trans side (inner side of SR), while the closed time of them unchanged. K ions on the opposite side(the cis side) had no significant effect. The voltage sensitivity of the open and closed time was unchanged with K^+ concentration. This means that , at constant voltages, the activation energy for channel closing is increased with K^+ concentration through lowering of the free energy of the open state. Na^+, which binds more tightly in the channel, had stronger effect than K^+ suggesting that the presence of permeant ions in the ion conducting pathway inhibits the closing of the gate of SR-K channel as has been suggested for delayed rectifier in squid axons.

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A HIGH MEMBRANE RESISTANCE OF THE AXON TERMINAL OF RETINAL HORIZONTAL CELLS AND ITS IMPLICATION TO SIGNAL CONDUCTION. YAGI, T. AND KANEKO, A. Natl. Inst. Physiol. Sci., Okazaki, 444.

The horizontal cell of the fish retina consists of a soma and an axon terminal (AT; about 400 μm long and 7 μm thick) connected by a slender axon (about 500 μm long and less than 1 μm thick). Both the soma and AT respond to a diffuse light with graded potential changes of almost the same amplitude and time course. Since AT has no synaptic contact with photoreceptors, the electrotonic conduction from the soma is the sole input to AT. However, a cable model suggests that the electrotonic conduction is possible only if the membrane resistance is much higher than the value generally accepted for neuronal membranes (1 $k\Omega \cdot cm^2$). Membrane properties of AT were studied on preparations enzymatically dissociated from the goldfish under the voltage-clamp, and compared with the soma. Membrane properties of soma and AT were qualitatively the same: both had a K current through the anomalous rectifier and a voltage-gated Ca current. Quantitatively however, the membrane current of AT was only 1/20 of the current of the soma. Thus, the specific membrane resistance of AT was as large as 200 $k\Omega \cdot cm^2$ in the physiologically operating range. The present data fulfil the condition which makes the electrotonic interaction between the soma and AT possible.

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HOLDING POTENTIAL-EFFECTS ON GABA-INDUCED Cl^- CURRENTS IN FROG SENSORY NEURONS. MARUHASHI,J.(1), INOUE,M.(2), AKAIKE,N.(2) and OOMURA,Y.(2). (1)Dept. Biol., Daiichi College of Pharm. Sci., Fukuoka 815 and (2)Dept. Physiol., Fac. Med., Kyushu Univ., Fukuoka 812.

GABA-induced clamp currents (Cl^-) were measured at different holding potentials of membrane voltage clamped condition by "suction pipette method" in single sensory neurons of the frog, under Cl^--ions only permeable through cell membrane with $[Cl^-]_{inside}$ and $[Cl^-]_{outside}$ are the same concentration of 120 mM.

GABA-induced Cl^--currents increased linear with membrane holding potentials from negative to positive during -20 mV to +20 mV, which reversal potential was about + 4 mV. Holding potentials over ±20 mV, increasing rates of GABA-induced currents became small. Plateaus of their responses increased with holding potential raised, both in negative and positive. Attenuation rates in GABA-induce Cl^- currents were independent with every holding potential. At their plateaus, the square root of calculated binding energies per receptor between GABA and their bound receptors increased linear with their holding potential raised [5-6 x $(10^{-15}\text{watts})^{\frac{1}{2}}$ at ±50 mV and almost zero at +4 mV of holding pot.].

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PATCH CLAMP ANALYSIS OF NEURONAL DIFFERENTIATION IN A TERATOCARCINOMA CELL LINE. KUBO, Y. Dept. Neurobiol., Inst. of Brain Res., Sch. Med., Univ. of Tokyo, Tokyo 113

Teratocarcinoma stem cell is known to have pluripotency and differentiate to various types of cells under certain conditions. The process of neuronal development was studied by Neurofilament (NF) staining and whole cell clamp method at various stages of differentiation. PCC4 Azal EC-A2 stem cells were NF negative and had only slight outward K current. They were induced to differentiate by applying Retinoic Acid (RA) or by reducing Fetal Calf Serum in the medium. In both cases NF positive round cells with long processes appeared on the sheet of flat endoderm like cells. It was showed that some round cells before extending processes already expressed NF at 48h after RA treatment. These cells were inferred to be at an initial stage of neuronal development, and were compared electrophysiologically with cells having processes which first appeared at 72h. The former showed Na, fast inactivating Ca, but little slow inactivating Ca inward current. In contrast, the latter showed larger Na, slow Ca, but fast Ca was smaller or lost. Both showed outward K current. The fast Ca observed was resistant to 50 µM Cd but the slow Ca was almost blocked by 50 µM Cd and enhanced by 1 µM Bay K8644. Neurons with processes obtained by serum reduction showed the fast Ca in addition to Na, the slow Ca, and K current, and can be considered to be less mature than those obtained by RA treatment.

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SELF-DIFFERENTIATION AND INDUCTIVE DIFFERENTIATION IN THE CLEAVAGE-ARRESTED BLASTOMERES ISOLATED FROM AN ASCIDIAN EMBRYO. OKADO, H. AND TAKAHASHI, K. Dept. Neurobiol., Institute of Brain Res., Sch. Med., Univ. of Tokyo, Tokyo 113

To analyse the developmental process in multicellular organisms, the following two kinds of experiments were performed by using Halocynthia rorentzi. Firstly, the self-differentiation in the cleavage-arrested blastomeres isolated from the 8-cell was studied. Secondly the differentiation under the interaction with neighboring cells was studied by contacting two types of the blastomere during development. The anterior a42 and posterior b42 ectodermal blastomeres of the 8-cell evoked a long-lasting Ca action potential and antiepidermal monoclonal antibody 2C5 was bound to their cytoplasm, suggesting the epidermal type differentiation when they were cultured in isolated condition. In contrast, the a42's produced Na spikes in 70% of all examined cases when they were cultured under close contact with the A41 blastomere. In this situation the 2C5 was not bound to the cytoplasm, suggesting the differentiation other than the epidermal type. Considering that, in the case of the vertebrate, the axial mesoderm, the presumptive notochordal region, can induce the neural plate from the ectoderm, in this protochordate, an ancestral form of the vertebrate, the a42, presumptive brain vesicle region, was inferred to be induced by the A41, the presumptive notochordal region, and to differentiate into neural type.

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PROPERTIES AND INACTIVATION MECHANISMS OF EGG-TYPE AND NEURAL-TYPE Na CHANNELS IN ASCIDIANS. SHIDARA, M. AND OKAMURA, Y. Dept. Neurobiol., Inst. Brain Res., Sch. Med., Univ. of Tokyo, Tokyo 113

The previous study showed that the reopenings of a single Na channel at the later phase of the voltage step were more frequently observed in the neural-type blastomere than in the egg cell, which explained the larger slowly inactivating component in the macroscopic Na current of the neural-type blastomere. In the present study we tried to further clarify the reopening mechanisms at the single channel level. The mean open time histograms of the neural-type channel were fitted by single exponential curves as those of the egg type and showed no difference between the earlier and the later parts of the voltage step, indicating that two open state model was unlikely. We adopted the two inactivation state model, H0 <--> H1 <--> H2 (H0 : open state) and calculated four rate constants from the macroscopic Na currrents. The three out of four showed almost the same values in both types, while the rate constant of the transition from H1 to H0 was much larger in the neural-type, which was reflected in the closed time histograms of single Na channels that showed more frequent long closures in the neural-type. These results led us to conclude that the difference of slow components between the two types of macroscopic Na currents is derived from the different probability of the return from the inactivation state to the open state.

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THE DISTRIBUTION OF INHIBITORY AMINO ACID RESPONSES IN THE MOUSE BRAIN MEASURED BY mRNA TRANSLATION SYSTEM. HORIKOSHI, T., ASANUMA, A. AND YANAGISAWA, K. Dept. of Physiol., Tsurumi Univ., Sch. of Dent. Med., Tsurumi-ku, Yokohama 230

In order to study the distribution of the neurotransmitter receptors in the central nervous system (CNS), three strategies, electrophysiology, immunohistochemistry and autoradiography, are widely used. In this study, we use another strategy, utilizing the Xenopus oocytes translation system of mRNA, to examine the distribution of inhibitory amino acid responses. From an adult mouse, the CNS was cut out, and separated into 4 parts; cerebrum, cerebellum, brain stem and spinal cord. $Poly(A)^+$-RNA from each of the 4 regions of the CNS was injected into oocytes (stage IV or V). Two to three days after the injection of mRNA, current responses to GABA, glycine, taurine and β-alanine were obtained under ordinary voltage clamp conditions at holding potential of -60 mV. The mean peak amplitudes of current responses to four amino acids in each regional mRNA injected oocytes were following order; cerebrum or cerebellum, GABA $>$ β-alanine $>$ taurine $\fallingdotseq$ glycine; brain stem, glycine $>$ β-alanine $>$ GABA $>$ taurine. Oocytes injected with spinal cord mRNA scarcely responded to these amino acids, the value obtained being almost too small to read. These differences in the regional distribution of relative responses may reflect the distribution of these amino acids receptors in the CNS.

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THE CHANGE OF THE CONDENSER WITH THE PARALLEL RESISTANS AND SERIES RESISTANS IN SQUIDE GIANT AXON BY THE AMPLITUDE OF APPLYING FINITE ALTERNATING POTENTIAL. SAITO, T. Dept. Phsiolog. Nippon Dental College, Tokyo.

The auther settled that the model of the living body is the condenser c with the series resistance R and the parallel resistance r and messured them with the finite alternating potential $E_m \sin\omega t$ using the next formulae,

$$\tan\phi = \frac{\omega r^2 c}{R+r+\omega^2 R r^2 c^2} \qquad i = \frac{E_m\sqrt{1+\omega^2 r^2 c^2}}{\sqrt{(R+r)^2+(\omega Rrc)^2}} \sin\phi$$

Here ϕ is the deviated phase angle of the appluing potential and the passing through the squid giant axon and i is the amplitude of the passing potential at the time which the finite alternating potential is zero in the constant condition of the passing potential. They are meassured in varias angle frequencies and the amplitudes of the applying potential are changed.
By this experimental results the change of the seris resistance is 10% decrease, the parallel resistance 90% decrease and the capacitance 5 times increase according to the applying electricity increase.

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EFFECTS OF OSMOTIC CHANGES ON CELL MEMBRANE EXPANSION AND EXCITABILITY OF TISSUE CULTURED NEURONS. HORIE,H., TAKENAKA,T. AND ITO,S.
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Diameters of neurons dissected from 3 age groups of mice (fetal, 3-month-old, 27-month-old) were measured by a super imposed scaler on a television monitor screen (Hamamatsu C-1966 Microscope system) connected to the Zeiss inverted Axiomat microscope. When external medium was changed to low osmotic medium (x1/2), the diameters rapidly increased and became 1.1 times larger than those before the change and then gradually decreased to the original sizes. The rate of membrane expansion decreased with aging. During this membrane expansion action potentials scarecely changed. This result suggests that the mechanism of the cell membrane expansion caused by low osmotic solution might be different from that by the treatment of 2-decenoic acid which inhibited action potentials.

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THE EFFECTS OF FATTY ACIDS ON THE MEMBRANE PERMEABILITY IN PERFUSED SQUID GIANT AXON. HORI,H., HORIE,H., KAWAKAMI,T. AND TAKENAKA,T.
Dept.Physiol.,Sch.Med.,Yokohama City Univ.,Fukuura,Yokohama 236.

The effects of fatty acids on the membrane permeability was studied by using radio isotope tracer in internally perfused squid giant axon. The permeability of caprylic acid, capric acid and lauric acid are 2.6 x 10^{-5}, 1.4 x 10^{-5}, 1.4 x 10^{-5} cm/sec respectively. These values are 10 times larger than that of sucrose. Perfusion of a fatty acid accelerates the membrane permeability of the other fatty acids. When 1mM 2-decenoic acid was perfused, the permeability of capric acid increased the value of 6.0 x 10^{-5} cm/sec while that of sucrose stays in the same value. The acceleration effect of 2-decenoic acid was completely reversible. The electrical excitation does not effect on the membrane permeability of fatty acids.

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IDENTIFICATION OF THE OPTICAL SIGNALS OF NERVE RECORDED WITH THE PHOTOELASTIC MODULATOR.
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An apparatus was assembled to detect changes of optical properties when the nerve is excited. The apparatus consisted of a light source, optical filters, a polarizer, a photoelastic modulator (PEM), an analyzer, a photodetector, and a lock-in amplifier. The nerve was dissected from a walking leg of a lobster and placed between the PEM and the analyzer. When the nerve was excited by electrical stimulation the lock-in output was transiently changed. The signal (the R-signal) was made of two components, A and I. The A-component was influenced by slight change of nerve azimuth. This was therefore the result of changes in linear birefringence and/or linear dichroism. They could be recorded separately without using PEM. It was found that the linear birefringence change was more than ten times larger than the linear dichroism change. The I-component was insensitive to the slight rotation of the nerve. This was therefore the result of changes in circular birefringence and/or circular dichroism. The theory predics that the circular dichroism signal be reversed on rotating the nerve by 90° but not the circular birefringence signal, and that the circular birefringence signal be reversed on rotating the analyzer by 90° but not the circular dichroism signal. Experiments identified that the I-component shows properties of the circular birefringence change.

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PROPERTIES OF H-CURRENT (I_h) IN CEREBELLAR PURKINJE NEURONS IN CULTURE. Kasai, H. Dept. of Physiology, Faculty of Medicine, University of Tokyo, Bunkyo-ku, Tokyo 113

Properties of the neuronal I_h were studied using the whole-cell recording configuration of the patch-clamp method in cultured cerebellar Purkinje cells. Cerebella from 16 to 18 days old fetal mice were sieved through 200 um nylon mesh and cultured for more than 15-day. The neurons which were characterized by their thick dendrites were labeled with an antibody against calbindin, a marker protein for the Purkinje neurons. These cultured Purkinje neurons always showed anomalous rectifying inward currents (I_h) in the voltage-clamp experiments; 1) the current was activated by hyperpolarization of the membrane negative to -55 mV; 2) the current was eliminated by 2.5 mM Cs^+ applied externally, but not blocked by 0.5 mM Ba^{2+}; 3) the current was carried by both Na and K ions. The neuronal I_h seemed to be modulated by both Ca^{2+} and cAMP in the cytoplasm. 1) The I_h was markedly reduced by the preceding membrane depolarization to 0 mV for 1 s. This reduction was not detected in the absence of external Ca^{2+}, suggesting that the Ca^{2+}-influx via the voltage-dependent Ca-channels is one of the essential factors for the modulation. 2) Forskolin (a specific and direct activator for the adenylate-cyclase) reversibly augmented the I_h. Since the I_h is continuously active at the resting potential of the neurons (-60 mV), the modulation of I_h may underly the changes in excitabilities of the Purkinje neurons in vivo.

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GLUTAMATE-INDUCED CELL DEATH AND CYTOSOLIC CALCIUM IN CULTURED HIPPOCAMPAL NEURONS. OGURA, A., MIYAMOTO, M.*, AMANO, T. AND KUDO, Y., Mitsubishi-Kasei Institute of Life Sciences, Machida-shi, Tokyo 194

Hippocampal pyramidal neurons are labile to ischemic hypoxia. An excessive release of glutamate from the input nerve terminal followed by an anomalous accumulation of calcium in the postsynaptic cytoplasm is a hypothesized cause of the neuronal death. Hippocampal neurons under dissociated cell culture conditions, if the glutamate-induced cell death is reproducible, should be an appopriate material for analysis of subcellular mechanisms of the cell necrosis. The hippocampal neurons were enzymatically isolated from embryonic (day 18) rat cerebra and plated on a astroglial monolayer. Various (4-14) days after the isolation, the cells were exposed to L-glutamate (10^{-5}-10^{-3} M) for a limited period (1-15 min). The cells underwent breakdown of neurites followed by apparent disintegration of cell bodies in 12-48 hours. Quantitative analyses revealed that the death rate depended on concentration of applied glutamate, concentration of external Ca^{2+}, duration of glutamate-exposure, day of culture. Among the known glutamate agonists, kainate and quisqualate were significantly more potent than glutamate. Magnesium and nitrendipine, but not tetrododoxin and aminophosphonovalerate, were effective in reducing the glutamate-toxicity. We applied a video-assisted Ca^{2+} microfluorometry system on a single-cell basis, recently established by us, to the hippocampal neurons under identical conditions. The slowness of recovery of the resting cytosolic Ca^{2+} concentration, rather than the amplitude of Ca^{2+} elevation itself, paralleled with the glutamate toxicity. That is, high glutamate concentration, high environmental Ca^{2+}, long duration of glutamate exposure and increased days of culture slowed the cytosolic Ca^{2+} recovery.

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THE SITE OF ACTION OF GRAYANOTOXIN IS LOCATED IN THE INTRACELLULAR SIDE OF AXONAL MEMBRANE OF THE SQUID. SEYAMA, I. AND KATO, R. Dept. Physiol., Sch. Med., Hiroshima Univ., Kasumi 1-2-3, Hiroshima 734

When grayanotoxin (GTX), batrachotoxin, veratridine and aconitine were applied externally, depolarization in the perfused axon occurred at much less extent than that in the non-perfused axon, suggesting that these toxins open the Na channel from inside the nerve membrane. It has been shown that tritium-labelled GTX (^{3}H-GTX) can permeate through the cell membrane. Although administration of 1μM tetrodotoxin suppressed the membrane depolarization caused by externally applied ^{3}H-GTX, count in the effluent from the perfused axon monotonically increased, indicating that permeation of GTX does not occur through the Na channel. A finding that when ^{3}H-GTX applied externally, count in the effluent did not change irrespective of excessive administration of cold GTX in either external or internal phase also precludes the possibility of the involvement of carrier-mediated sysyem in the permeation of GTX. Because there was a parallel relationship between the concentration of ^{3}H-GTX in the external medium and the count in the effluent from the perfused axon, it is most likely that ^{3}H-GTX is exudated through the lipid phase of the membrane.

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PENTYLENETETRAZOL-INDUCED SINGLE CALCIUM CHANNEL CHANGES IN PRIMARY CULTURED NEURONS OF THE CEREBRAL CORTEX OF RATS. SEKIGUCHI,K., ITO,K., ISHIGE,A., TAKAGI,T*., KAJIWARA,K*., KOMATSUBARA,J*., SUGAYA,E*., SUGAYA,A.**, YUZURIHARA,M.**, TSUDA,T**. AND YASUDA,K**. Tsumura Res. Inst. for Pharmacology, Ami, Ibaraki, 300-11; *Knagawa Dental Col., Yokosuka, 238 and **Fuculty of Pharmaceutical Sci., Josai University, Sakado, Saitama, 350-02

To clarify the behavior of the single calcium channel during pentylenetetrazol (PTZ)-induced bursting activity in neurons, changes of the calcium channel of primary cultured neurons of the cerebral cortex of rats by PTZ were examined.

Dissected cortical area cells were prepared from 17th-day embryonic rats according to Asou's method. The isolated cells were plated on Eagle's MEM suspended in 20% calf serum. Two-day-old or three-day-old cultured neurons were used. Single calcium channel recordings were performed using patch electrodes containing $BaCl_2$ with a patch clamp amplifier.

When PTZ was applied to the cultured neurons, whole cell clamp recording showed bursting-like inward current. In the case of cell-attached single channel recording, the open time of the single calcium channel was prolonged and then showed burst-like open time prolongation.

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ACTION OF CYTOSKELETON ACTING AGENTS ON PRIMARY CULTURED NEURONS OF THE CEREBRAL CORTEX OF MICE. KAJIWARA,K., TAKAGI,T., KOMATSUBARA,J., SUGAYA,E., YUZURIHARA,M.*, TSUDA,T.*, YASUDA,K.*., SUGAYA,A.*, ASOU,H.**, OTA,A.** AND HIRANO,S.** Dept. of Physiol. Kanagawa Dental Col., Yokosuka, 238; *Fucult. of Pharmaceutical Sci., Josai Univ., Sakado, Saitama, 350-02 and **Dept. of Physiol. Toho Univ., Omori, Tokyo.

The relationship between morphological changes caused by cytoskeleton acting agents and neuronal gangliosides was examined to clarify the role of gangliosides in the development of neurites and also to elucidate the characeteristics of neurite development of El mice.

Primary cultured neurons of the cerebral cortex of ddY and El mice were used. When cytochalasin B was applied to primary cultured neurons, the neurites showed looping phenomena, the growth cone was not observed, and the GM_1 ganglioside dissapeared. When cholchicine was applied to the cultured neurons, neurite extension as well as content of the GM_1 ganglioside was reduced dose-dependently. The formation features of growth cones and neurites in EL mice were different from those of ddY mice.

These findings suggest that development of the growth cone is closely related to GM_1 ganglioside appearance, and characteristics of neurites and growth cones of El mice differ from those of normal ddY mice.

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VERATRIDINE-STIMULATION OF $^{22}Na^+$ INFLUX INTO CULTURED SUPERIOR CERVICAL GANGLION CELLS AND CAROTID BODY CELLS. SATO, M., YOSHIZAKI, K. and KOYANO, H. Dept. Physiol., Akita Univ. Sch. Med., Akita 010

It is known that carotid body (CB) glomus cells are responsive to hypoxia stimulus. But the mechanism of the chemoreception is still unclear. In this study, effect of veratridine (VER) on Na^+ influx into cultured CB cells was examined. CB from newborn rabbit is too small to get enough glomus cells to apply for protein assay. So that firstly micro-$^{22}Na^+$ influx assay was established in 1-week-cultured superior cervical ganglion (SCG) cells from newborn rabbit. Cultured cells prelabeled with ^{14}C-leucine were incubated for 20 min with $^{22}Na^+$ influx assay medium, with 10 μCi/ml of $^{22}Na^+$, in presence or absence of VER. $^{22}Na^+$ influx activity was obtained as a ratio of $^{22}Na^+$-radioactivity to ^{14}C-radioactivity in the cells. $^{22}Na^+$ influx activity attained nearly to plateau at the incubation period of 20 min, when an effect of VER on the secretion of ^{14}C-labeled materials from the cells was negligible. VER increased twice the $^{22}Na^+$ influx activity in the SCG cells, which was inhibited by TTX. Similarly in 1-week-cultured CB cells the $^{22}Na^+$ influx activity was increased nearly twice by VER. This finding suggests that CB glomus cells have veratridine-sensitive sodium channels.

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CALCIUM-ACTIVATED POTASSIUM CHANNEL IN SINGLE SMOOTH MUSCLE CELLS OF GUINEA-PIG VAS DEFERENS. MORIMOTO, K., *KUKITA, F., and YAMAGISHI, S. Dept. Physiol. Med. School, Kumamoto Univ., Kumamoto 860, *Dept. Cell Physiol. Natl. Inst. Physiol. Sci. Okazaki 444.

Dispersed single smooth muscle cells of guinea pig vas deferens obtained by collagenase treatment were used throughout the experiments. In Whole cell clamp experiment, the current voltage relation of peak outwared current shows typical N shape which has a maximum at about +60 mV and a minimum at about +100 mV. The N shaped relation was eliminated by external Co^{++} or removing Ca^{++} from the vasing solution. In excised patches, a highly K^+ selective channels with linear conductance of 80 pS was frequently observed. The probability of the channel being open (Po) increased when $(Ca)^{++}_i$ was elevated and /or when the membrane potential was made more positive. TEA (10 mM) applied to the extracellular membrane surface greatly reduced the amplitudes of the current and increased noise levels during the open-state. 4AP (2 mM) applied to the extracellular membrane surface also blocked the current by suppression of Po. Intracellularly applied TEA reduced the amplitudes of the current a little and clearly enhanced Po.

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BLOCKING ACTIONS OF BENZODIAZEPINES ON TWO TYPES OF CALCIUM CHANNELS IN NEUROBLASTOMA CELLS. WATABE, S.*[1], YOSHII, M., TSUNOO, A.* AND NARAHASHI, T.*[1] Meiji Inst. of Health Science, Odawara 250, and [1]Dept. of Pharmacology, Northwestern Univ. Med. Sch., Chicago, IL 60611, USA.

Neuroblastoma cells have two kinds of Ca channels: one generates a transient inward current (type I), and the other generates a long-lasting inward current (type II) (J. Physiol. 384, 571-585, 1987). In order to understand differential roles of Ca channels, we have examined the effects of benzodiazepines on the two types of Ca channels. Diazepam, nitrazepam and clonazepam were selected for the study because of different therapeutic profiles: diazepam is a sedative as well as an anticonvulsant; nitrazepam is a hypnotic with an antiepileptic property; clonazepam is an anti-convulsant with no remarkable sedative-hypnotic properties. Ca channel currents as carried by Ba^{2+}(50 mM) were recorded from neuroblastoma cells (N1E-115) using the whole-cell patch clamp technique. Diazepam (100 uM) reduced both types of current equally by 30%. Nitrazepam showed a similar but slightly less potent blocking action. Clonazepam (100 uM), on the contrary, reduced type I current by more than 50% without affecting type I current. Epileptogenesis may be related to the type I Ca channel activity.

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TWO TYPES OF CALCIUM CHANNELS IN NEUROBLASTOMA CELLS: THEIR ELECTROPHYSIOLOGICAL AND PHARMACOLOGICAL PROPERTIES. YOSHII, M., TSUNOO, A.* AND NARAHASHI, T.*[1] Meiji Inst. of Health Science, Odawara 250, and [1]Dept. of Pharmacology, Northwestern Univ. Med. Sch., Chicago, IL 60611, USA.

Our previous study has shown that neuroblastoma cells (N1E-115) have two types of Ca channels: one generates a transient Ca current (type I) and the other generates a long-lasting Ca current (type II) (Soc. Neurosci. Abstr. 10, 527, 1984). We have further characterized these Ca channels both electrophysiologically and pharmacologically. Under comparable membrane potential conditions, both channel types open equally fast but type II channels close 2.4 times faster than type I upon repolarization. Ba^{2+} was the most potent charge carrier among Ca^{2+}, Sr^{2+} and Ba^{2+} for type II channels, but type I channels were somewhat less selective for these three ions. Cd^{2+} preferentially blocked type II channels, whereas La^{3+} was a highly potent blocker for both types. Dibutyryl cyclic AMP (1 mM) caused a 30-50% increase in the amplitude of type II current, while failing to alter the type I component. Leu-enkephalin (25 nM) blocked type II channels in a time- and voltage-dependent manner. The effect was antagonized by 1 uM naloxone.

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TWO TYPES OF CALCIUM CHANNELS IN ISOLATED VASCULAR SMOOTH MUSCLES. KAWASHIMA, Y. AND OCHI, R. Dept. Physiol., Sch. Med., Juntendo Univ., Hongo, Tokyo 113

Single Ca channel currents were recorded by 50 mM Ba-containing pipettes under cell-attached configuration from smooth muscle cells isolated from the vena cava inferior of guinea-pig. On depolarization steps to above -50mV from a HP of -100 mV small elementary Ba currents with mean open time of 0.8 ms, and the unitary conductance of 12 pS appeared. Its mean current from multi-channel currents became maximal at -20 mV, was transient and was inactivated almost completely with shifting the HP to - 50mV. This channel seems to be T-type Ca channel. The other type, the 25pS channel had maximum amplitude at +20mV, inactivated more slowly and its mean open time was increased by BAY K 8644, so this channel was classified as L-type Ca channel. The steady-state inactivation curve of mean currents of L-type channel in the presence of BAY K 8644 showed half maximal inactivation at HP of -56 mV (Vh). The curve was shifted to the left with Vh of -62 mV by adding 1uM nitrendipine. These results suggest that two types of voltage-dependent Ca channels present in vascular smooth muscle cells are much like those found in cardiac myocyte. L-type channels supply Ca ions into the myoplasm, while T-type channels relatively rich in venous myocytes may contribute to spontaneous exitation in these muscles.

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MEMBRANE PROPERTIES OF PREGANGLIONIC FIBER OCCURRED IN BULLFROG LUMBAR SYMPATHETIC CHAIN. HASHIGUCHI, T., AND TOSAKA, T., Dept. of Physiol., Tokyo Medical College, Shinjuku, Tokyo 160

Membrane properties of preganglionic fibers in the bullfrog sympathetic chain were studied using an intracellular microelectrode and a sucrose-gap method. A single action potential recorded from a preganglionic fiber was characterized by the lack of afterhyperpolarization (AHP). In contrast, that from a cell body or a postganglionic fiber was followed by AHP. Both outward and inward rectifications occurred in preganglionic fibers, Supra-threshold current injection, which generated repetitive discharge, evoked slow AHP. Replacing external Na with Li abolished the slow AHP completely. Ouabain (10 μM) had an inhibitory effect on the slow AHP. These results suggest that the electrogenic Na/K pump was involved in the electrogenesis of the slow AHP. Cesium (5 mM) augmented the slow AHP. This augmentation of the slow AHP was not explicable on the basis of a change of the input resistance.

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LACK OF SCORPION TOXIN EFFECT ON NERVE FIBERS OF THE SCORPION.
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A neurotoxin was purified from the venom of a Chinese scorpion (Buthus martensi Karsch) by gel filteration chromatography and high performance liquid chromatography. The activity of the toxin was demonstrated in crayfish; the toxin dissolved in Harreveld's solution (0.3 uM) prolonged the duration of intracellularly recorded action potentials of giant axons in 5 to 15 min. However, this toxin dissolved in the same solution at the same concentration showed no effect on intracellularly recorded action potentials of abdominal nerve chord of the scorpion for more than 1 hr. The toxin applied at a concentration 300 times higher than this had no effect either. Sea anemone toxin (ATX II, 8 uM) also did not show any effect on scorpion nerve fibers. Tetrodotoxin (0.3 uM) or grayanotoxin (20 uM) reversibly suppressed the action potential, indicating that the Na channel is responsible for the action potential. We concluded that the Na channel of scorpion nerve fibers lacks the binding site for the scorpion toxin.

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CURRENT NOISE IN CRAYFISH NEURON SOMA.
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The electrical characteristics of crayfish neuron soma membranes were investigated by using a patch clamp technique. Isolated spherical neuron soma (20-30 μm in diameter) were obtained by treating an abdominal nerve cord with 0.1 % trypsin for 3-5 min at 31°C. The patch electrode (ca. 1 μm in tip diameter) was loosely or tightly (10-20 GΩ gigaseal) attached on the surface membrane of a neuron. The K channel current was measured while the membrane potential was shifted between -280 and 280 mV. Remarkable rectification was noticed in both outward and inward directions. The current was almost suppressed by application of 100 mM TEA. Both voltage and time dependent changes in open probability were demonstrated. These results of patch clamp correspond to those of whole cell current clamp. The relatively high channel conductance (17 pS at 280 mV) may facilitate the hyperpolarizing response.

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SOME CHARACTERISTCS OF THE KININASE FOUND IN RAT CEREBROSPINAL FLUID. YOSHIDA, T. AND NOSAKA, S. Dept. Physiol., Mie Univ. Sch. Med., Mie, 514.

In vitro incubation of synthetic peptides with rat cerebrospinal fluid (CSF) and analysis of the incubation mixture by reversed phase high performance liquid chromatography revealed the presence of a kininase II (angiotensin I converting enzyme)-like dipeptidylcarboxypeptidase (DCP) in rat CSF. As previously reported for the DCP from rabbit lung, NaCl, in a concentration range between 20 and 200 mM, exerted opposite effects on the bradykinin (BK) degradation and on the breakdown of a synthetic substrate, Hip-His-Leu, by the rat enzyme: a concentration dependent inhibition of the former but a concentration dependent stimulation of the latter. Further insight of the effect of NaCl on BK degradation by rat CSF-DCP indicated that NaCl was inhibitory to the first step of BK degradation, the cleavage at Pro^{7}-Phe^{8} bond, but stimulatory to the second cleavage at Phe^{5}-Ser^{6} bond of BK. The DCPs of rat CSF and serum were successively chromatographed on a gel filtration columun (TSK G3000sw) and on an anion exchange columun (Biorad MA7P) and they were indistinguishable in their behaviour in these chromatographic procedures. It was also demonstrated in present experiment that the relative activity of carboxypeptidase N (kininase I), another major BK degradating enzyme in plasma, to DCP was much smaller in rat CSF than in its serum.

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ANTAGONISM OF STRUCTURAL ANALOGUES TO THE TAURINE UPTAKE. TASAKA, J., SAKAI, S., TOSAKA, T. AND HASHIGUCHI, T. Dept. of Physiol., Tokyo Med. Coll., Shinjuku-ku, Tokyo 160

Effects of structural analogues on the uptake of ^{3}H-taurine into the isolated bullfrog lumbar sympathetic chain were studied. Glycine, DL-α-alanine, isethionic acid and cysteamine (5 mM) did not inhibit taurine (10.34 μM) uptake, while cysteic acid, γ-aminobutyric acid (GABA), DL-β-aminobutyric acid (BABA), L-2,4-diaminobutyric acid (DABA) and δ-aminovaleric acid (DAVA) reduced it by 15-35%. A Dixon analysis revealed that hypotaurine, β-alanine and GABA inhibited competitively the high affinity taurine uptake with the ratio inhibitor constant (Ki)/Km of taurine uptake of 1.0, 1.9 and 38 respectively. On the other hand, ^{3}H-GABA (5.14 μM) uptake was not antagonized by taurine, hypotaurine, β-alanine, DL-α-amino-n-butyric acid, α-amino-iso-butyric acid, BABA, DL-β-amino-iso-butyric acid and L-glutamic acid (1 mM), while only DABA and DAVA inhibited GABA uptake by half. It was thus concluded that taurine, hypotaurine and β-alanine share the high affinity taurine carrier system and GABA is incorporated through the highly specific GABA carrier system different from taurine one.

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INFLUENCES OF OXYGEN AT HIGH PRESSURE ON THE CENTRAL NERVOUS SYSTEM IN RAT: A NEUROCHEMICAL STUDY. SUGAWA, M., ISHIDA, Y.* AND NODA, Y.
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Influences of oxygen at high pressure(OHP) on the central nervous system were examined in terms of neurochemical changes in several regions of the rat brain. After single OHP exposure, the glutamic acid decarboxylase(GAD) and tyrosine hydroxylase(TH) activities were reduced in the parietal cortex and striatum, respectively, which recovered to normal levels within 3-6 days. The choline acetyltransferase(ChAT) activity, however, was not affected in the parietal cortex by single OHP. The influences of repeated OHP were complex; 1) ChAT activity were decreased in the parietal cortex, tuberculum olfactorium, striatum and globus pallidus, while being increased in the substantia nigra. 2) GAD activity were decreased in the substantia nigra and globus pallidus, while being increased in the parietal cortex, hippocampus and striatum. 3) TH activity were remarkably decreased in the substantia nigra, striatum, globus pallidus, tuberculum olfactorium and nucleus accumbens, while being increased in the hippocampus, hypothalamus and pons + medulla oblongata. Repeated OHP strikingly reduced the amount of dopamine and its metabolites in the substantia nigra and striatum and dopamine uptake in the striatum. These results suggest the differences of the vulnerability against OHP among brain regions and that repeated OHP may induce predominantly the degeneration of dopaminergic neurons.

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CONVULSIVE ACTIVITY OF 2-GUANIDINOETHANOL. II. EDAKI, A.*, WATANABE, Y.*, & YOKOI, I. Dept. of Neurochem., Inst. for Neurobiol., Okayama Univ. Med. Sch., Okayama 700

We have previously reported the convulsive activity of 2-guanidinoethanol (GEt) in rat. In this study, we examined the effects of GABA (1μmol), diazepam (DZP)(10mg/kg, i.p.), muscimol (50nmol), (3R)-(-)-4-amino-3-hydroxybutanoic acid (L-GABOB)(1μmol), phenobarbital (PB)(20 mg/kg, i.m.), diphenylhydantoin (PHT)(20mg/kg, i.p.) or valproate (VPA) (200 mg/kg, i.p.) on spike discharges (Sp-D) induced by GEt.

In rats given muscimol topically together with GEt, Sp-D were not induced, and Sp-D induced by GEt were suppressed within 10 min by the supplimentation of muscimol. While VPA, L-GABOB and GABA showed a suppressive effect on Sp-D induced by GEt, GEt induced Sp-D after pre-application of these three substances. About 20 min after injection of PB, DZP or PHT, GEt was applied on the pia mater, but Sp-D were not induced. PB, DZP, PHT or VPA, applied 20 min after the application of GEt, suppressed Sp-D induced by GEt.

These findings suggest that GEt might act on the GABAergic system to induce convulsive activity.

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DEVELOPMENTAL CHANGE OF BRAIN GANGLIOSIDES IN MATERNALLY HYPERPHENYLALANINEMIC RATS. HARADA, Y., OHTA, M., ASOU, H. AND HIRANO, S. Dept. Physiology, Toho Univ. Sch. Med., Tokyo

The change of the brain gangliosides have been examined in the rats derived from dams which had received high dose of L-Phe(2000 mg/kg) from day 10 to 14 of pregnancy. The brain weight consistently showed low value at the mantle region of cerebrum up to day 49 after birth. The concentration(n mol./g w.w.) of gangliosidic N-acetylneuramic acids(NANA) in the brain was decreased at the mantle region on day 49 after birth. The separation of gangliosides by HPTLC revealed that this was associated with reductions of GD1a, GT1b and GM1 which were reported to be candidates of markers for synaptogenesis. To examine this, subcellular fractions were prepared for gangliosides study. The concentration of gangliosides in the synaptosome was decreased by the treatment but the distribution pattern in which GD1a and GT1b were predominant was not changed. Golgi-Cox staining of cerebral cortex section also confirmed the possibility that the number of synapses or dendrites was reduced in the treated animals.

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ALTERATION OF CEREBRAL GANGLIOSIDE METABOLISM IN DEVELOPING SNELL DWARF MICE. SUGISAKI, T., KANAMATSU, T. AND NOGUCHI, T. Dept. of Physiol. Toho Univ. Sch. of Med. Tokyo 143

The ganglioside metabolism of the Snell dwarf cerebrum was examined on postnatal days 15 and 20, by monitoring the rate of incorporation of radioactivity into each ganglioside species from tritiated N-acetyl-D-mannosamine. It was found that the turnover rate of the GM3 ganglioside was reduced throughout the entire period of development, resulting in retardation of A pathway metabolism which becomes abundant during late cerebral development. In addition, the turnover rate of the GM4 species, which is considered related to myelin formation, was also found to be reduced throughout the entire period of cerebral development.

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REGIONAL DISTRIBUTION AND ONTOGENY OF CHOLINE ACETYLTRANSFERASE AND GLUTAMIC ACID DECARBOXYLASE IN CEREBRAL SUBDIVISION OF MACAQUE MONKEY.
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The activities of choline acetyltransferase (ChAT) and glutamic acid decarboxylase (GAD) were determined in various cerebral cortical subdivisions of the Japanese monkey, at three different stages: embryonic 4 months, embryonic 5.5 months and adult. At the adult stage, the highest ChAT activity occured in amygdala and the lowest was found in the occipital cortex. A relatively high level was observed in the hippocampus and temporal cortex. In contrast, GAD activities were distributed quite evenly. The development of ChAT activities were irregular among the cortical subdivision. In the postcentral gyrus and inferotemporal cortex, the levels of the enzyme activity at embryonic 5.5 months already reached those found in the adult. In contrast, GAD activities increased gradually between embryonic 4 months and adult. In conclusion, the distribution and the ontogenic changes of the ChAT activities were more irregular than those of the GAD activities. This may reflect that ChAT is present in fibers and GAD is present in the intrinsic neuron in the cerebral cortex.

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FEEDING BEHAVIOR RESPONDED TO HISTAMINE H_1-RECEPTORS IN THE RAT BRAIN.
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To clarify histamine-modulated feeding, histamine H_1- and H_2-receptor antagonists were infused into the rat third cerebroventricle. H_1-Receptor antagonists effectively elicited feeding at the early light period, but H_2-receptor antagonists showed no effect. Chlorpheniramine, H_1-receptor antagonist, induced feeding most potently at a dose of 0.26 μmol. Latency to eat was 38.6±3.1 min, and duration of a meal was 12.8±3.3 min. This feeding elicitation by H_1-receptor antagonist was attenuated by α-fluoromethylhistidine, suicide inhibitor of histidine decarboxylase. Under the same experimental schedule, blood samples were collected. Chlorpheniramine induced hyperglycemia, hyperlipidemia and hypoinsulinemia. These effects were attenuated by bilateral adrenomedullectomy. These results indicated that H_1-receptor antagonist in the brain which led to secretion of cathecholamine from the adrenalmedulla elicited feeding due to blockade of endogenous neuronal histamine.

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ELECTRON MICROSCOPICAL OBSERVATION OF IMMUNOREACTION OF ISOLATED SYNAPTIC VESICLES AND THEIR MONOCLONAL ANTIBODIES.
NISHIYE, H.[1], OBATA, K.[2], KOJIMA, N.[2], OZAKI, T.[3] AND UCHIZONO, K.[3] 1 Dept. Physiol., Sch. Med., Juntendo Univ., Tokyo 113, 2 Dept. Pharmcl. Gunma Univ. Sch. Med., Maebashi 371 and 3 Natl. Inst. Physiol. Sci., Okazaki 444

Synaptic vesicles(SVs) were isolated and purified from homogenates of guinea pig cerebra by using sucrose density gradient ultracentrifugation. And monoclonal antibodies(MAbs) were successfully produced against these SV fractions. Twenty-five hybridoma lines were judged to be producing SV-specific MAbs. The MAbs were obtained as culture supernatant or ascites fluid from the hybridoma-transplanted mice. Immunoreaction of isolated SVs and MAbs was successfully observed by electron microscope. At first, the SV suspension was dripped on specimen grid covered with Formvar membrane and SVs were dispersed as a monolayer on the grid. Then the immunoreaction procedures were done on the SV-dispersed grid. The immunoreacted SV specimen was faintly stained with 1% uranyl acetate solution and was given to the electron microscopic observation. Under the indirect immunoreaction using anti-mouse IgG, MAb-reacted SV was surrounded with a corona of ferritin particles which were attached to the surface of MAb-bound SV through avidin-biotin reaction. Four SV-specific protein components were immunobiochemically identified as SVP65, SVP38, SVP36 and SVP30 according to their molecular weights.

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AN IMMUNOHISTOCHEMICAL STUDY ON RABBIT OLFACTORY EPITHELIUM IN ADULTHOOD, DURING DEVELOPMENT, AND FOLLOWING UNILATIRAL BULBECTOMY, USING MONOCLONAL ANTIBODIES

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One monoclonal antibody, 112D5 (MAb 2D5), stained all of the olfactory receptor cells in the adult rabbit, whereas the other, 114G12 (MAb 4G12), stained the upper 2/3 to 3/4 of the receptor cell layer. MAb 2D5 stained all of the receptor neurons during development. 4G12-positive cells appeared in scatters in the epithelium of the embryonic day 17 fetus. At E25/26, 4G12-positive cells were situated in the superficial receptor cell layer. The arrangement in the 4G12-positive and -negative receptor neurons was 'superficial-positive' and 'deep-negative'. Thereafter, a gradual increase in the 'superficial-positive' cells was accompanied by a decrease in the 'deep-negative' cells. MAb 2D5 stained all receptor neurons, including degenerating neurons after the bulbectomy, but 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 3 months, 4G12-positive cells were arranged in a line at the apical region of the receptor cell layer, suggesting a recapitulation of the developmental pattern of the receptor neurons.

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H-NMR SPECTRA OF LIPIDS IN RAT TISSUES

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A variety of rat tissues such as the liver, the brain and the peritoneal body fat were analysed by H-NMR spectroscopy (Bruker's WP80SY-WG). They were prepared in 5 mm NMR tube each as the lipid sample of 10 mg extracted by Soxhlet's method and dissolved in 0.2 ml $CDCl_3$. In their spectra of 0 to 6 ppm were observed several peaks of 5 to 1250 in S/N and 0.05 to 0.2 ppm in width according to NMR activities of the $-CH_3$, $-CH_2-$, $CO-C-CH_2-$, $C-CH_2-C=$, $CO-CH_2-$, $=C-CH_2-C=$ and $-CH=CH-$ radicals. As the control, the authentic samples of oleic acid and linoleic acid were observed similarly. Between each of the experimental samples and each of the authentic were taken the difference spectra. There were found the experimental samples different from the controls especially in the methylene $-CH_2-$ peak, i.e., the brain and the body fat near to the oleic, and the liver near to the linoleic. The carbon and double bond numbers of the samples into which the proton numbers from each size of the radical peaks were converted by calculation were 14.5:0.8 in the liver, 17.6:1.0 in the brain and 19.1:1.4 in the body fat, while those of the authentic were 17.7:0.9 in the oleic (18:1) and 17.2:1.8 in the linoleic acid (18:2).

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EFFECT OF BRAIN ISCHEMIA ON ELECTRICAL ACTIVITIES STUDIED BY NMR.

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Complete cerebral ischemia, which showed the marked decrease in the concentrations of creatine phosphate (PCr) and ATP, was detected on the cat brain suppressed the blood supply from the carotid arteries, however, it was necessary to suppress the blood supply not only from the carotid arteries but also from the vertebral arteries on the rat brain. The concomitant decrease in the activities of electroencephalogram (EEG) and of somatosensory evoked potential (SEP) was observed even in the incomplete ischemia on the rat brain, which showed no decrease in ATP but slight decrease in PCr with cerebral acidification. When gas mixture 20-25 % CO_2 with rest O_2 was inhalated on rat, the cerebral acidification was observed with the decrease in the activities of EEG and SEP, suggesting the cerebral acidification as a cause for the decrease in the electrical activities of brain during cerebral ischemia in vivo.

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NERVE GROWTH FACTOR (NGF) INCREASES ACETYLCHOLINE CONTENT IN CULTURED RAT SEPTAL NEURONS. TAKEI, N., ISOBE, A.*, TSUKUI, H. AND HATANAKA, H. Dept. of Neurosci., Mitsubishi-Kasei Inst. Life Sci., Machida, Tokyo 194 and *Central Res. Lab., Mitsubishi Chem. Ind. Ltd., Yokohama, Kanagawa 227

NGF has been established to exist and to work on basal forebrain cholinergic neurons in CNS. We previously reported that NGF induces choline acetyltransferase (ChAT) activities in the cultured cholinergic neurons from embryonic and neonatal rat septum area. In the present study, we try to detect the contents of acetylcholine (ACh) itself in those cultured septal neurons. ACh was measured by HPLC with electrochemical detection combined with fixed enzyme column (B.A.S. Japan). After the extraction by 0.1N ice cold perchloric acid containing ethylhomocholine as internal standard, the homogenates were centrifuged. The supernatant was served for injection into HPLC system. NGF was found to markedly increase ACh contents as well as ChAT activities in the cultured septal neurons from 1-day-old rats. After the 10 days in culture, NGF (100ng/ml) increase 6-fold contents of ACh compared with culture without NGF. These data suggest that NGF increases cellular ACh contents which might be stored and available for neural transmition even in the cultured neurons.

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NEUROCHEMICAL STUDIES ON THE NEURONAL SURVIVAL FACTORS FROM RAT HIPPOCAMPUS. KOHSAKA, S., YOSHIDA, K.*, TAKAMATSU, K., IBATA, Y.*, OTANI, M., TOYA, S., AND TSUKADA, Y. Department of Physiology, and Department of Neurosurgery, Keio University School of Medicine, Shinjuku, Tokyo 160.

Previous studies from our laboratory have shown that the extract from rat hippocampus enhances the survivability of cultured neurons from rat embryonic cerebral hemispheres. The activity of the hippocampal neuronal survival factors (HNSF) was also found to be increased by a lesion of septo-hippocampal fibers, peaked at 14 days following the lesion. Analysis of various kinds of gangliosides in the extracts from 1 day and 14 days post-lesioned hippocampus by thin-layer chromatography revealed that GT_{1b} was significantly increased at 14 days. However, the addition of GT_{1b} in the medium did not enhance the neuronal survivability. The hippocampal extract was fractionated by HPLC (TSK-2000 SW column) and the each fraction was examined for the neuronal survival activity. The activity was recovered in three fractions corresponded to the molecular weights of 10-20K, 30-40K, and 50-60KDa. The hippocampal extract was also applied to the concanavalin A column, and the con-A binding fraction was examined for the neuronal survival activity. The activity was not recovered in the binding fraction, suggesting that the HNSF did not have sugar moiety.

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MUSCARINIC SUPPRESSION OF THE PERSISTENT CALCIUM SENSITIVE POTASSIUM CURRENT IN MYENTERIC NEURONS OF THE GUINEA-PIG ILEUM. TOKIMASA, T. AND NORTH, R. A.*, Department of Physiology, Kurume University School of Medicine, 67 Asahi-machi, Kurume 830, Japan and Neuropharmacology Laboratory, M.I.T. 56-245, Cambridge, MA 02139, U.S.A.*

Intracellular recordings were made from S and AH type myenteric neurons of the guinea-pig ileum maintained in vitro in Krebs solution containing 300 nM tetrodotoxin and 10 mM tetraethylammonium (TEA). Membrane currents were measured by using a single electrode voltage-clamp amplifier. Acetylcholine (ACh) was applied by perfusion (30 nM-3 μM). An inward rectification at potentials more negative than -85 mV was eliminated by extracellular cesium (2 mM). A transient or the A-current was blocked by 300 μM 4-aminopyridine (4-AP). An outward rectification at potentials between -60 and -40 mV was predominantly due to an activation of the persistent outward potassium current activated by intracellular calcium ions (North and Tokimasa, J. Physiol. 1987. in press). ACh or other muscarinic agonists such as oxotremorine suppressed the persistent calcium-sensitive potassium current without any significant effect on the inward calcium current. In S cells which lack the persistent calcium-sensitive potassium current or in AH cells perfused with calcium-free solution containing cesium, 4-AP, 2 mM cobalt and TEA, ACh depressed a time-independent leak current.

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INDIRECT REGULATION OF POTASSIUM CHANNELS BY MUSCARINIC RECPTOR IN CULTURED BULLFROG SYMPATHETIC GANGLIA

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Muscarine sensitive K channels, in cultured bullfrog sympathetic ganglia, were studied using a cell-attached patch clamp method (pipette solution: 2-118 mM K, TTX, TEA, Cd, apamin, and HEPES pH 7.2). There were four kinds of single channel current activities, sensitive to muscarine (10-20 uM) applied to a perfusing solution outside the patch pipette; 1) A voltage-independent channel having a single open state (0.3 ms: 100-130 pS) and two or three closed states, (I_{ME1}), 2) a voltage-dependent channel (20 pS) activated by membrane depolarization (on and off time constants; several seconds: IME2). 3) a voltage-independent channel which had a single open atate (60-80 pS: 0.6 ms) appearing in burst with two or three closed states (I_{MI1}) and 4) a voltage-independent channel of a long open state (30 pS and several seconds): (I_{MI2}). The activities of the former two were suppressed by muscarine: the open probability of I_{ME1} was reduced, its longer closed times increased, and the opening of I_{ME2} was totaly suppressed. The activities of the latter two were enhanced by muacarine: The open time of I_{MI1} was increased without a change in other parameters, and the open probability of I_{MI2} inceased. Thus, I_{ME1} and I_{ME2} may be responsible for the slow EPSP and the I_{MI1} and I_{MI2} for slow IPSP, although the extents of their contributions are not known.

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THE RESPONSES TO MUSCARINIC AGONISTS AND THE SLOW SYNAPTIC POTENTIALS IN THE SUBMUCOUS PLEXUS NEURONES OF GUINEA-PIG CAECUM. MIHARA, S. AND NISHI, S. Dept. Physiol., Kurume Univ. Sch. Med., Kurume 830

Intracellular recordings were made from neurones in the submucous plexus of the guinea-pig caecum. Muscarinic agonists produced a depolarization in the majority of neurones and a hyperpolarization or a biphasic response consisting of a hyperpolarization followed by a depolarization in the minority of neurones. The muscarinic depolarization or hyperpolarization were, respectively, due to a decrease and an increase in membrane potassium conductance. Low concentrations (30-100 nM) of pirenzepine or atropine completely antagonized both the depolarization and hyperpolarization. Lower concentrations (1-10 nM) of pirenzepine could block the hyperpolarization, while they could not affect the depolarization. Slow synaptic potentials could be evoked in the presence of an α_1 (prazosin, 1 μM) or an α_2 (idazoxan, 100 nM) blocker. Slow EPSP was only partially blocked by pirenzepine, suggesting that the slow EPSP is the mixture of a non-cholinergic and a cholinergic component. The slow IPSP was completely antagonized by pirenzepine (3-10 nM). It appears therefore that the submucous neurones are endowed with a system that produces the muscarinic slow IPSP in addition to those that elicit the noradrenergic slow IPSP and the non-cholinergic, non-adrenergic slow IPSP.

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THE FAST EPSP OF SYMPATHETIC PREGANGLIONIC NEURONES (SPN). INOKUCHI, H., YOSHIMURA, M. AND NISHI, S. Dept. Physiol., Kurume Univ. Sch. Med., Kurume 830

The fast EPSP of SPN in the transected slices of cat thoracic spinal cord was investigated with intracellular recordings to characterize the nature of the transmitter substance mediating the EPSP. Among the substances contained in the nerve terminals packed in the lateral horn, acetylcholine(ACh), serotonin(5-HT), noradrenaline(NA), substance P (SP), glutamate(Glu) and aspartate(Asp), produced depolarizations in SPNs. Since that the fast EPSP was unaffected by (+)-tubocurarine(50 μM) and atropine(10 μM) and that the 5-HT, NA and SP depolarizations were associated with an increased input resistance, ACh, 5-HT, NA and SP could be ruled out to be the candidate transmitter. The responses to Glu and Asp, particularly the former, were investigated in comparison with the fast EPSP. Glutamate blockers (cis-2,3-piperidine dicarboxylic acid and γ-D-glutamyl glycine) suppressed the amplitude of fast EPSPs. L-Aspartic acid-β-hydroxamate(0.1 mM), an amino acid uptake inhibitor, enhanced the duration and the amplitude of fast EPSP. DL-2-Amino-5-phosphonovalerate, an NMDA blocker, did not affect the fast EPSP although it completely suppressed the NMDA-induced depolarization. The fast EPSP was unaffected by a Mg-free solution. The equiribrium potentials for the fast EPSP and Glu-depolarization appeared to be -2.2±0.8 mV and -2.0±0.5 mV, respectively. These results suggest that the fast EPSP may be mediated by glutamate via a non-NMDA receptor on the SPN.

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AN ANALYSIS OF TRANSMITTER RELEASE AT THE NEUROMUSCULAR JUNCTION UNDER TREATMENTS WITH ADENOSINE AND THEOPHYLLINE. TAKEUCHI, N., TAKIKAWA, Y., YANA, K.* AND MINO, H. Dept. Physiol., Sch. Med., Juntendo Univ., Hongo, Tokyo 113 and *Dept. Electrical Eng., Col. Eng., Hosei Univ., Koganei, Tokyo 184

Spontaneous or evoked release of transmitter quanta was investigated at the frog neuromuscular junction. Adenosine, which has been known to be a functional modurator in several synapses, dose-dependently reduces the spontaneous (m.e.p.p.) and evoked quantal releases. In the presence of theophylline, which acts to increase in the m.e.p.p. frequency, log concentration of adenosine — the inhibitory effect curve was shifted to the right with a competitive manner. The dissociation constant for this competitive action of theophylline was in the range of 0.015-0.04 mM. This value was two orders lower than that for the theophylline effect for the m.e.p.p. frequency increase. When adenosine deaminase was applied in normal Ringer, an increase in the m.e.p.p. frequency was observed (the mean increase: 24 %). In 12 mM-K^+ solution, however, no marked increase in the frequency was observed by the application of this enzyme. These results suggest that 1) the concentration of endogenous adenosine in this tissue is approximately 1 μM, 2) theophylline acts at two different sites to increase the transmitter release, 3) depolarization of the nerve terminal membrane might elevate the adenosine deaminase activity.

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COMMON GTP-BINDING PROTEIN OPENS ALL K^+-CHANNELS COUPLED TO VARIOUS TYPES OF RECEPTORS. SASAKI, K., MATSUMOTO, M., TAKASHIMA, K., TAKAHASHI, J. and SATO, M., Dept. Physiol., Sch. Med., Iwate Med. Univ., Morioka, Iwate 020

Either acetylcholine (ACh) or Histamine (HA) and or Dopamine (DA) can produce slow hyperpolarization in each identified neuron of *Aplysia* ganglion. All responses are caused by a permeability increase toward K^+ following the activation of each receptor. Effects of intracellular applications of islet activating protein (IAP) and GTPγS were studied on each type of neuron under the modulated voltage clamp method: IAP (intracellular concentration, 2-5 μg/l) did not cause any change in the resting state of the membrane, but irreversibly blocked the transmitter-induced K^+-current within 30 minutes. Intracellular application of GTPγS alone (intracellular concentration, 5-10 μM) caused a very slow, irreversible increase in K^+-permeability of the resting membrane. All responses to the transmitters were depressed ultimately with the same time course as the changes in holding current. These results strongly suggest that a certain GTP-binding protein like N_i commonly regulates the opening of all K^+-channels coupled with these receptors. Supported by the I.M.U. Keiryokai Fund. No. 26.

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APPARENT AUGMENTING EFFECT OF LOW TEMPERATURE ON THE RESPONSES OF RECEPTORS WHICH ARE READILY DESENSITIZABLE. MATSUMOTO, M., SASAKI, K., TAKASHIMA, K., HAKOZAKI, S.* AND SATO, M. Dept. Physiol., Sch. Med., Iwate Med. Univ., Morioka, Iwate 020

GABA or ACh can induce a fast hyperpolarizing response in the identified neurons of Aplysia. These responses are caused by a specific permeability increase of the receptor membrane toward Cl^-. Characteristic nature of these receptors is to show a marked desensitization. The GABA- and ACh-induced currents were recorded under the voltage clamp at different temperatures. The amplitudes of both responses markedly increased when temperature was lowered from 22 °C to 12 °C, but decreased when raised to 30 °C. This temperature effect depended on the concentration of agonist used; the lower the agonist concentration, the greater increase in response at lower temperature. The rate of desensitization of GABA decreased at 12 °C to about a half of the control. Similar results were obtained from the ACh-induced responses. These results suggested that the augmenting effects of low temperature on these responses are mainly due to the decrease in the rate of desensitization.

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THE LONG-LASTING PSP INDUCED BY BRIEF EXCITATORY STIMULI IN THE AFFERENT SYNAPSE OF PLOTOSUS ELECTRORECEPTORS. OKANO, K., SUGAWARA, Y. and OBARA, S., Dept. of Physiol., Teikyo Univ. Sch. of Med., Tokyo 173

In the ampullary electroreceptors, brief excitatory stimuli often induce a complex PSP pattern, fast and slow PSP's, which outlasts the stimulus by a few hundred msec. The apparent PSP components were further examined in the isolated Plotosus receptors. With stimuli of about 50 msec, the fast and slow PSP's were readily distinguished. On increasing stimulus intensity, the time to peak of the fast PSP gradedly decreased to less than 10 msec, while in contrast that of the slow PSP increased over 100 msec. L-Asp prolonged the duration of the slow PSP at 100-300 μM, near threshold doses for excitation (1986), while had little effect on the fast PSP. Similar potentiation by L-Asp had been observed with iontophoretically-induced L-Glu response (Nagai, 1985). Kynurenic acid (Kyn), a competitive Glu antagonist in this synapse (1986), suppressed the slow PSP dose-dependently, with a suppression ratio of 19 ± 6 % (n = 7) at 0.1 mM and 74 ± 11 % (n = 11) at 1 mM. Kyn, however, had little effect on the fast PSP. Gamma-DGG showd similar but weaker effects. These results suggest that the synaptic responses involve at least two distinct receptors: one pharmacologically like Glu receptors for the slow PSP, and the other unknown receptors for the fast PSP.

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INHIBITORY MINIATURE POTENTIALS IN INSECT LEG MUSCLE FIBERS. WASHIO, H. Lab. Neurophysiol. Mitsubishi-Kasei Inst. Life Sci., Machida, Tokyo 194.

Miniature inhibitory junction potentials (MIJPs) were recorded from posterior coxal levator (182C,D) and coxal depressor (177d,e) muscles in the metathoracic legs of the cockroach, Periplaneta americana, with K-citrate and KCl electrodes. Frequent depolarizing and occasional hyperpolarizing potential changes were recorded at the resting potential. The hyperpolarizing potentials had relatively low frequency (< 1.0 per sec) and slow time course. When the muscle was bathed in glutamate saline (10^{-4}M) the depolarizing potential disappeared gradually. On the other hand, hyperpolarizing potentials were abolished in Cl-free saline and a saline containg 10^{-6}M picrotoxin. An increase in extracellular K and/or Ca concentrations increased the frequency of the hyperpolarizing potentials. Injection of hyperpolarizing DC current through a recording K-citrate electrode using a conventional bridge circuit converted the hyperpolarizing potential to the depolarizing. The reversal potential of the miniature potentials was within about 10mV of the resting potential more negative. All results have indicated that the hyperpolarizing miniature potentials observed in the insect muscle fibers are due to the spontaneous release of transmitter from inhibitory nerve terminals and that the transmitter substance predominantly increases the Cl-permeability of the postsynaptic membranes.

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EFFECTS OF NORADRENALINE ON CULTURED CHICK CEREBELLAR NEURONS. MORI-OKAMOTO, J. AND TATSUNO, J., Department of Physiology, National Defense Medical College, Tokorozawa, Saitama 359

The effect of noradrenaline(NA) on the responsiveness of cultured cerebellar neurons to excitatory amino acids were investigated intracellularly. The depolarization induced by iontophoretically applied of glutamate(GL) was enhanced by NA added to external medium to be 10 uM or lower. NA also enhanced aspartate(AS)-induced depolarization but to a smaller extent. NA alone slightly decreased spontaneous spike firing, induced small hyperpolarizations or slightly increased input resistance. Iontophoretically applied NA also showed similar effects by itself and potentiating actions. The site sensitive to iontophoresed NA were found not to be uniformly distributed but to be localized on the cell. The enhancement by NA of the GL or AS response was blocked by β-adrenergic antagonists (propranolol or pindolol), and mimicked by cAMP applied either extra- or intra-cellularly. These results suggest a possibility that NA physiologically modulates excitatory amino acid-mediating synaptic transmission in the cerebellum probably through intracellular cyclic nucleotide systems.

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EFFECTS OF SUBSTANCE P ON GLUTAMATE RESPONSES OF CULTURED RAT SEPTUM NEURONS. Iijima, T., Akita, K., Kudo, Y., Tsukui, H. and Hatanaka, H. Dept. of Neurosci., Mitsubishi-Kasei Inst. of Life Sci. Machida, Tokyo 194, Japan

The changes in membrane potentials (currents) and intracellular Ca^{2+} concentrations ($[Ca^{2+}]_i$) were detected with the whole-cell patch clamp and Ca^{2+} indicator dye Fura-2, respectively. All septum neurons examined were depolarized by L-glutamate. On the other hand, less than a half population of the neurons showed depolarizing responses when they were exposed to 0.3~3 μM substance P (SP). In every neuron, a pre-treatment with SP (30 sec exposure) largely changed the depolarization pattern of L-glutamate. The depolarizations of pre-treated neurons were generally enhanced and shortened (sometimes not enhanced but lengthened). The depolarizations of Pre-treated neurons accompanied with larger $[Ca^{2+}]_i$ increases than those in intact neurons. The treatment with SP itself didn't cause $[Ca^{2+}]_i$ change unless the neuron was depolarized by SP. One possible explanation for the lines of evidence is as follows: SP modulates the activity of glutamate channels directly or via some second messengors except Ca^{2+}. The alterations of the $[Ca^{2+}]_i$ change, the Ca^{2+} comes into the neurons through the glutamate channels initially, affect the activations of calcium dependent K^+ channels, which modulate the depolarization pattern in the septum neurons.

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THE CHANNEL CURRENTS ACTIVATED BY ADENOSINE 5'-TRIPHOSPHATE IN CULTURED XENOPUS SKELETAL MUSCLE CELLS. IGUSA,Y. Dept. of Physiol.,Jichi Med. Sch.,Tochigi-ken,329-04.

Single channel currents activated by ACh and by adenosine 5'-triphosphate (ATP;10^{-7}-10^{-3} M) were recorded in the cultured Xenopus muscle cells using the cell-attached patch clamp technique. Two types of ATP-activated currents ,High- and Low-conductance(γ) currents, were observed during 1-6 days cultures. Both types of currents were suppressed by 20-50μM curare and have the reversal potential around -10mV, suggesting that ATP activates the nicotinic ACh recepter channel. At 10^{-7}-10^{-5} M ATP the frequency of both currents increased linearly proportional to the logarithm of the concentration of ATP. The mean open time and slope conductance were 0.93ms, 59pS in High-γ current and 0.86ms, 42pS in Low-γ current. Mean open time and open probability were increased by hyperporalization and open times of both currents ,especially of Low-γ currents, were significantly shorter than that by 0.2μM ACh. At 10^{-7}-10^{-5} M ATP combined with 10^{-10} M ACh, frequencies of currents increased and were higher than those with ATP alone, indicating that ATP and ACh mutually facilitate the opening of ACh recepter channels. Frequencies of channel currents were decreased to 1-1.5 events/sec at 10^{-5}-10^{-3} M ATP with or without 10^{-10} M ACh. Adenylylimido 5'-diphosphate(AMP-PNP) was substitutive for ATP on Xenopus muscle cells.

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EFFECTS OF 5-HYDROXYTRYPTAMINE ON NEURONES OF THE RABBIT VESICAL PELVIC GANGLIA.
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Intracellular recordings were made from parasympathetic neurones of the rabbit vesical pelvic ganglia maintained in vitro. 5-hydroxytryptamine (5-HT) caused membrane depolarizations when applied either by superfusion or by brief pressure ejection pulse (20 kN m^{-2} for 50 ms) onto the soma membrane. The 5-HT depolarization was associated with an increase of both Na^+ and K^+ conductances. The depolarization was not eliminated in a solution which contained tetrodotoxin (TTX, 1 μM) or in a low calcium Krebs solution, suggesting that 5-HT directly depolarizes the post-ganglionic neurones. Methysergide (10 μM) caused no inhibitory action on the 5-HT depolarization. ICS 205-930 compound (0.01-1 nM), a potent antagonist of the 5-HT_3 receptor subtype, markedly depressed the 5-HT depolarization. From five experiments, ICS 205-930 (1 nM) produced a 82 ± 6 % depression. The effect of this antagonist is a concentration-dependent, with reduction in the amplitude of 5-HT response apparent at a concentration of 10 pM. The ICS 205-930 compound shifted in parallel the dose-response curve of the 5-HT depolarization to the right, compatible with competitive antagonism. These results suggest that 5-HT may increase the excitability of parasympathetic neurones in urinary bladder wall, by acting on a 5-HT_3 receptor.

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EFFECTS OF ω-CONOTOXIN ON ISOLATED RAT SUPERIOR CERVICAL GANGLIA.
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A peptide neurotoxin from fish-hunting cone snails (Conus geographus) is reported to block irreversibly a Ca channel which is involved in transmitter release. There are increasing evidence that Ca channel is classified to several types functionally. We observed effects of ω-conotoxin on isolated rat superior ganglia. The toxin blocked the EPSP evoked by electric stimulation of the preganglionic fibers. Calculated mean quantal content was decreased by the toxin, showing it also blocks a presynaptic Ca channel in rat sympathetic ganglion. However, the effective concentration was relatively high and the action was reversible. The toxin inhibited the peak amplitude of its action potentials and following after hyperpolarization. These action needed less concentration of the toxin than one which needed to block the presynaptic Ca channel. Different affinities and reversibilities of the toxin in these effects suggest ω-conotoxin inhibit, at least, two types of Ca channel in the ganglion, as well as species and tissue heterogeneities of each Ca channel type at molecular level.

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CHEMICAL CHARACTERIZATION OF A SPIDER TOXIN (JSTX) WHICH BLOCKS CRUSTACEAN NEUROMUSCULAR TRANSMISSION.
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A spider toxin derived from the venom of Nephila clavata(Joro spider) has been recognized as a potent inhibitor of the glutamate receptor . We purified the active principles from the spider venom. After venom glands were homogenized with 60 % acetonitrile and centrifuged, the supernatant fluid was analysed by reversed phase HPLC with an ODS column. By the repeated chromatography, at least 4 kinds of peaks were found to contain active substances. Measurement of ^{1}H-NMR spectra showed that these substances have similar pattern and the common signals around 6.5 and 7.0 ppm in D_2O. One of the active substances, JSTX-3 was further characterized using 1H-COSY-NMR. The spectrum showed that JSTX-3 is composed of 2,4-dihydroxyphenylacetylacetic acid, asparagine, cadaverine and polyamine. By similar NMR analysis of JSTX-4, 2,4-dihydroxyphenylacetylasparginyl-cadaverino moiety was commonly observed. Consequently this part is considered to be essential for revealing the biological activity.

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SUBSTANCE P AND NEUROKININ-A AUGMENTED A SLOW CALCIUM CURRENT IN VOLTAGE-CLAMPED SPINAL DORSAL HORN NEURONS OF THE RAT. MURASE, K., RANDIC, M. AND USUI, S., Information & Computer Sciences, Toyohashi Univ. Tech., Tempaku, Toyohashi 440 Japan.

Spinal dorsal horn neurons of 2-4 week-old rats in a slice preparation were studied by using the single-microelectrode sample-and-hold voltage-clamp technique, and by ionic substitution of the perfusing solution. In 2.4mM Ca and .2-1uM TTX, the cells were held at -75--55mV. 1s depolarizing voltage commands to -55--35mV induced slow inward current relaxations and inward current tails. Commands to -35mV or above evoked slow outward relaxations and outward tails. The latters seemed due to the activation of the Ca-dependent K conductance, because they were substantially reduced by 10-20mM TEA or by replacing Ca with Ba. Experiments in Ba-containing solution with zero Ca suggest the slow inward current relaxations and tails are due to the activation of a slow Ca current. They were dose-dependently increased by Ba; blocked by 10uM nifedipine, by removing Ba, or by replacing Ba with Co; slightly altered by substituting Na with Tris, or Cl with isothionate; unchanged by modifying K from 3.1 to 10mM. They activated at about -60mV and reached to the maximum at -45mV. Both consisted of two exponential components having time constants of T=.2-.4s and 2.5-5s. Substance P and neurokinin A cholecystokinin octapeptide enhanced the slow Ca and Ba current dose-dependently. Support by Jpn Ministry of Education to KM (#61750357), and JSPS to MR.

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CHANGES IN THE EXTERANAL POTASSIUM CONCENTRATION INDUCED BY ENDOGENOUS BIOACTIVE SUBSTANCES IN THE RAT SUPERFICIAL DORSAL HORN. TSURUHARA, H. AND TAKAHASHI, T. Dept. Physiol., Kyoto Univ. Fac. Med., Kyoto 606

The lumbar spinal cord was excised from the rat 2-3 weeks after birth. Intracellular potentials were recorded from glia cells in the superficial dorsal horn, and the external K^+ concentration around the same region was simultaneously measured with the K^+-sensitive electrode. Stimulation of the lumbar dorsal root produced a slow depolarization in glia cells, which was associated with a parallel increase in the external K^+ level. These responses disappeared when synaptic transmission was blocked by a Ca^{2+}-free solution. In a Ca^{2+}-free solution, however, the application of l-glutamate or substance P again induced glial depolarization and increased K^+ level. The two responses evoked by stimulation of the dorsal root were suppressed by met-enkephalin (m-Enk) or 5HT. The responses elicited by l-glutamate were also suppressed by m-Enk regardless of the presence or absence of external Ca^{2+}. In contrast, 5HT suppressed the glutamate-induced responses only in the presence of external Ca^{2+}. These results suggest that glial depolarization is produced by an increase in the external K^+ level at the superficial dorsal horn as a result of activation of interneurons involved in signalling nociceptive information and that inhibition of these neuronal activities by m-Enk and 5HT is based on different mechanisms.

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EVOKED RELEASE OF GLUTAMATE BY SUBSTANCE P FROM NEWBORN RAT SPINAL CORD. ONODERA, K., KAWAGOE, R. AND TAKEUCHI, A., Dept. of Physiol., Juntendo Univ. Sch. of Med., Hongo, Tokyo 113,

The actions of substance P (SP) on the motoneuron were investigated by the intracellular recording from the newborn rat spinal cord. When SP was applied the membrane potentials of motoneurons were depolarized, accompanied by an increase in the membrane potential fluctuations. At smaller doses of SP (5-200 nM), these potential changes were suppressed in low Ca and in TTX solutions. The SP induced depolarization was depressed by APV - a specific depressant for NMDA receptor. The release of endogenous glutamate and aspartate from the hemisected spinal cord were measured with mass fragmentography. A Ca-dependent release of glutamate was induced by dorsal root stimulation. Similarly, the bath application of SP caused the release of endogenous glutamate and this release was depressed or abolished in the low Ca and TTX solutions. These results suggest that low concentrations of SP cause a release of neuronal transmitter (possibly glutamate) and produced a depolarization of the motoneuron membrane, partly through the activation of NMDA receptor.

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NEURAL ACTIVITY AND ENERGY METABOLISM IN THE BRAIN SLICES OF THE WARM-BLOODED(GUINEA PIG) AND COLD-BLOODED(FROG) ANIMALS. OKADA, Y.,YONEDA,K., TANIMOTO, M., NISHIZAKI, T., MIYAMOTO, T., ARAKAWA, T., AND YAMAUCHI,R. Dept. Physiology, Sch. Med., Kobe Univ., Chuo-ku, kobe 650.

Thin brain slices(300-400um thick) were prepared from the hippocampus (HIP) and superior colliculus(SC) of the guinea pig and the tectum(FT) of the frog(summer). The neural activity(postsynaptic potentials,PSP) and the energy use rate of the slices were studied during the cooling and warming of the medium and during anoxia. PSP amplitude was highest at 33°C in the HIP and SC and at 26°C in the FT. Oxygen consumption of HIP and SC at resting was 1.2 umol $\sim O_2$/g protein/min(at 21°C), 3.3(at 28°C), 8.4(at 37°C), 12.3(at 42°C) and that of SC was 1.4(at21°C), 2.8 (at 28°C) and 8.2(at 37°C). The oxygen consumption of FT was 0.9(at 20° C), 2.7 (at 28°C) and 8.5(at 37°C). The results were in good agreement with those of ~P use rate obtained by measuring ATP, creatine-P and lactate of the slices during initial phase of anoxia.Thus the Q_{10} values of the guinea pig and frog brain slices were in the range of 2.1-3.5. During anoxia, PSP in the HIP and SC was abolished in 6 min at 36°C and in16 min at 28°. In the FT,anoxia abolished PSP in 70 min at 28°C.

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NMDA-RECEPTOR MEDIATES LONG-TERM POTENTIATED SYNAPTIC TRANSMISSION IN HIPPOCAMPUS. IZUMI, Y.*, MIYAKAWA, H., ITO, K. AND KATO, H. Dept. Physiol., Yamagata Univ. Sch. Med., Yamagata 990-23

High concentration of D,L-APV(>2mM), a selective NMDA receptor antagonist, applied before and after the tetanus reversibly reduced the postsynaptic response in CA1 neurons of guinea pig hippocampal slices. The population spikes during the long-term potentiation(LTP) after the tetanus fell to 60 % (n = 5) of the pre-LTP base line when the slices were made at room temperature. The same reduction was also observed by the application of 1 mM of D-APV. When slices were prepared at temperature of 6-7°C D.L-APV reduced the amplitude of population spike to the pre-LTP level due to the significantly small reduction below the control. These results suggest that the LTP is mediated by the NMDA receptor itself. In addition, there is a possibility that a certain LTP has been already induced during slice preparation before an electrical tetanus is delivered.

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CYTOPLASMIC CALCIUM ELEVATION IN HIPPICAMPAL CA1 NEURONS BY TETANIC STIMULATION STUDIED IN VITRO WITH FURA-2.
Kudo Y., *Ito K., *Miyakawa H., Ogura A. and *Kato H.,
Dept. Neurosci., Mitsubishi-Kasei Inst. Life Sci., Machida 194 and *Dept. Physiol., Yamagata Univ. Sch. Med., Yamagata 990-23

Tetanus induced changes of intracellular Ca^{++} concentration were measured simultaneously from many positions in CA1 area of guinea pig hippocampal slices by using Ca^{++} sensitive fluorescent dye, Fura-2. Electrical responses were also measured simultaneously. Tetanic stimulation (100Hz,1sec) applied to the Schaffer collaterals caused increment of $[Ca^{++}]_i$ in the str. radiatum (dendritic area) which lasted for 1-4 min after the cessation of the tetanus. The simultaneously recorded field potentials showed that the tetanus caused the Long-Term Potentiation(LTP). When Ca^{++} was removed from the bathing medium, no increment of $[Ca^{++}]_i$ was observed. These results suggest that regional calcium influx into CA1 neurons could be detected in relation to the LTP.

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NEUROTOXIC EFFECTS OF GLUTAMATE, KAINATE, AND N-METHYL-D-ASPARTATE ON THE HIPPOCAMPAL SLICES OF THE GUINEA PIG—THEIR EFFECTS ON THE NEURONAL ACTIVITY AND THE OXYGEN CONSUMPTION. NISHIZAKI, T., TANIMOTO, M., AND OKADA, Y., Dpt. Physiology, Sch. Med., Chuo-ku, Kobe 650

The effects of glutamate(Glu), kainate(Ka), and N-methyl-D-aspartate(NMDA) on the electrical activity(postsynaptic potential, PSP) and the oxygen consumption(QO_2) were investigated using hippocampal slices of the guinea pig. Bath application of Ka($1x10^{-9}$-$1x10^{-7}$M), NMDA ($1x10^{-9}$-$1x10^{-5}$M), and Glu($1x10^{-8}$-$1x10^{-4}$M) elevated the amplitude of PSP to 130% of the original level. PSP disappeared irreversibly(neurotoxicity) at the concentrations of $1x10^{-4}$M Ka, $1x10^{-3}$M NMDA, and $1x10^{-2}$M Glu. Q_{O_2} was increased dose-dependently by Ka($1x10^{-8}$-$1x10^{-6}$M), NMDA($1x10^{-6}$-$1x10^{-4}$M), and Glu($1x10^{-4}$-$5x10^{-4}$M), and was saturated at 140% increase from the resting state(8.43 μmol/g protein/min). The increase of QO_2 correlated well with the enhancement of the electrical activity. Removal of Ca^{++} from the medium protected against neurotoxicity by Ka, NMDA, and Glu, although Cl^- free medium enhanced neurotoxicity by these agents.

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ELECTRICAL ACTIVITIES OF HIPPOCAMPAL INTERNEURONS IN RABBITS. TAZAWA, Y. Dept. of Physiol., Nippon Med. School, 1-1-5, Sendagi, Bunkyo-ku, Tokyo, 113

It was reported that the intracellular counterpart of the interictal EEG spike was the inhibitory postsynaptic potential of the pyramidal cell, which was probably mediated by inhibitory interneurons. The present experiments were designed to know electrical activities of interneurons in various areas of the hippocampus, because the interneurons had been so far studied only in limited areas of the hippocampus, whereas the inhibitory EEG spike was detectable virtually throughout the hippocampus. Rabbits were lightly anaesthetized with Nembutal and the responses of interneurons to stimulation of the contralateral hippocampus were studied. Nine and 14 units were intra- and extracellularly recorded from CA1 and CA3 & CA4 region, respectively. CA1 interneurons tended to fire at a frequency lower (<400Hz) than CA3 & CA4 interneurons (>500Hz). In many cases two kinds of spikes, i.e., one with a short duration (about 0.5 msec) and the other with a long duration (more than 1 msec), existed in the same interneuron. The relationship between these two kinds of spikes was described.

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ROLES OF PROTEIN KINASES IN G-PROTRIN-MEDIATED NEUROTRANSMITTER RESPONSES IN XENOPUS OOCYTES INJECTED WITH BRAIN mRNA. Ito I.,Hirono C.,Sugiyama H. and Yamagishi S. Lab.Memb.Biol., Natl.Inst.Physiol.Sci., Okazaki 444.

Microinjection of rat brain mRNA in Xenopus oocytes induced ACh, neurotensin, serotonin, and glutamate receptors in the cells. These receptors stimulate a G-protein-mediated reaction pathway, including inositol phospholipid metabolism, production of inositol trisphosphate (IP3) and Ca^{2+} mobilization, and cause membrane current responses. In the present study, we examined the roles of several protein kinases in these responses, and obtained the following results:
(1)Calmodulin-dependent kinases may be directly involved in the reaction pathway, because trifluoperazine and/or general kinase inhibitors blocked the responses. (2)A-(or G-)kinases or C-kinase may not be involved in the pathway directly, but may modulate it by inhibiting the initial part of the pathway (receptors, G-proteins and/or phospholipase C), because activators of these kinases caused no responses, inhibitors did not affect but activators suppressed receptor-mediated responses, and current responses caused by IP3 injection were unaffected or enhanced by A-kinase or C-kinase activators, respectively.

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EXCITATORY AMINO ACID RECEPTORS INDUCED IN XENOPUS OOCYTES INJECTED WITH RAT BRAIN mRNA. HIRONO, C., ITO, I., YAMAGISHI, S. AND SUGIYAMA, H. Lab. Memb. Biol., Natl. Inst. Physiol. Sci., Okazaki 444

Three types of excitatory amino acid receptors were detected in Xenopus oocytes injected with rat brain mRNA. Type 1 and type 2 activate ion channels directly, and prefer kainate (KA) and quisqualate (QA) respectively. Type 3 is a new type of glutamate (Glu) receptors which prefer QA and activate inositol phospholipid metabolism. QA (Glu) did not activate KA receptors (type 1), but rather inhibited KA responses (type 1) in a competitive manner. JSTX irreversibly blocked responses of typel and type 2 but not type 3. γ-L-glutamylglycine suppressed responses of type 1 but not type 2 and type 3. Reversal potential of resposes of type 1, type 2 and type 3 were 0 mV, +10 mV and -35 mV respectively.

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KINETIC ANALYSIS OF ACH-INDUCED CHLORIDE CURRENT IN ISOLATED APLYSIA NEURONS. IKEMOTO, Y., AKAIKE, N., ONO, K. and ISHIZUKA, S.* Department of Physiology, Faculty of Medicine and Dentistry*, Kyushu University, Fukuoka 812, Japan

Single neurons were isolated from Aplysia ganglia treated with Dispase. Kinetic properties of ACh-induced Cl current was examined using the "concentration clamp technique", which allowed internal perfusion and rapid switching of the external solution within a few milliseconds. The activation phase of the I_{Cl} was single exponential and the time constant became smaller depending upon the ACh concentration but did not depend on the voltage. The Hill number for the peak current was estimated to be 2 and K_D 6.7 μM. In the majority of cells the I_{Cl} declined to a steady level during a continuous application of ACh, while in some cells it declined to almost null. Desensitization preceded double exponentially and was not affected by the membrane potential. The I_{Cl} did not cross-desensitize with glutamate or GABA-gated I_{Cl} in the same neuron. The current recovered from desensitization with two time constants. Noise analysis of the I_{Cl} evoked by low concentrations of ACh revealed that the single channel conductance was 23 pS.

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INFLUENCES OF PRESSURE-INJECTED INOSITOL TRISPHOSPHATE ON THE MEMBRANE OF IDENTIFIED NEURONS OF APLYSIA. SAWADA, M., ICHINOSE, M. AND MAENO, T. Dept. of Physiology, Shimane Medical University, Izumo, Shimane, 693

The ionic mechanism of the effect of intracellularly injected inositol trisphosphate ($InsP_3$) on the membrane of identified neurons of Aplysia was investigated with voltage-clamp, pressure-injection, and ion-substitution techniques. Brief pressure injection of $InsP_3$ into a neuron voltage-clamped at -40 mV induced an outward current associated with a conductance increase. The current was increased by depolarization and decreased by hyperpolarization up to -80 mV, where it disappeared. The $InsP_3$-induced current was blocked by 5 mM TEA but not affected by 5 mM 4-AP. The $InsP_3$-induced outward current recorded at a holding potential of -40 mV increased in amplitude in low-$[K^+]_o$ solutions and decreased in high-$[K^+]_o$ solutions. Alteration of $[Cl^-]_o$, as well as perfusion with Ca^{2+}-free plus 2 mM EGTA solution, did not affect the outward current. The $InsP_3$-induced outward current was found to disappear when the neuron was injected with EGTA. The calmodulin inhibitor W-7 (20 μM) inhibited both the $InsP_3$-induced and the Ca^{2+}-activated outward current. These results suggest that brief pressure injection of $InsP_3$ into identified neurons of Aplysia induces a 4-AP-resistant, TEA-sensitive K^+ current activated by increased intracellular free Ca^{2+}, and this increase might be the result of the mobilization of Ca^{2+} from intracellular stores by $InsP_3$.

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MECHANISM OF INHIBITION CAUSED BY N-ß-PHENYLPROPIONYL-L-TYROSINE (BPLT).
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A derivative of L-Phe-L-Tyr, N-ß-phenylpropionyl-L-tyrosine (BPLT) (L-Phe-L-Tyr without an amino group), produces a long-lasting inhibition of some Achatina neurones, for example, TAN (tonically autoactive neurone). To elucidate the ionic mechanism of BPLT inhibition, TAN current-voltage relationships (I-V curve) were measured under voltage clamping, in comparison with dopamine (DA) inhibition, which was due to the membrane permeability increase to the potassium. The inhibitions caused by BPLT and DA were long-lasting, suggesting that they were not due to the chloride. The TAN membrane resistance was reduced by BPLT, when measured near the resting potential (about -50 mV). However, the reversal potential of BPLT inhibition could not be seen up to -120 mV, though that of DA inhibition was observed at about -70 mV. This indicates that the BPLT inhibition was partly due to the potassium and partly to another factor, probably the permeability decrease of a cation.

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EFFECTS OF BIOLOGICALLY ACTIVE PEPTIDES ON MOLLUSCAN GIANT NEURONES.
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Thirty giant neurones have been identified in ganglia of an African giant snail (Achatina fulica Férussac). Effects of the following biologically active peptides on these neurones were examined: 1. peptides proposed as neurotransmitters in mammals (Met-enkephalin, substance P, neurotensin, LH-RH, [Gln^8] -LH-RH, oxytocin and Arg-vasopressin), 2. peptides proposed as neurotransmitters in invertebrates (proctolin and FMRFamide), and 3. natural venom peptides (bombesin, ranatensin C, vespakinin X and vespakinin M).

Of the peptides examined, the three, oxytocin, FMRFamide and proctolin, were effective on the neurones. Oxytocin tended to show excitatory effects, whereas FMRFamide tended to be inhibitory. Out of the thirty neurones, six were excited by oxytocin, but only one was inhibited by the same peptide. On the other hand, six neurones was inhibited by FMRFamide, but none was excited by this peptide. Proctolin affected (excitation) only one neurone. Other peptides examined had no effect on the neurones tested.

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EFFECTS OF ß-HYDROXYASPARTIC ACID (BHAA) AND ITS RELATED SUBSTANCES ON GIANT NEURONES SENSITIVE TO ß-HYDROXY-L-GLUTAMIC ACID (L-BHGA).
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The five identifiable giant neurones, PON (periodically oscillating neurone), d-RPLN (dorsal-right parietal large neurone), VIN (visceral intermittently firing neurone), RAPN (right anterior pallial neurone) and v-RCDN (ventral-right cerebral distinct neurone), of an African giant snail (Achatina fulica Ferussac) were markedly sensitive to ß-hydroxy-L-glutamic acid (L-BHGA); d-RPLN and RAPN were excited by L-BHGA, while PON, VIN and v-RCDN were inhibited. Effects of ß-hydroxyaspartic acid (BHAA) and its derivatives were examined on the five Achatina neurones. Threo-ß-hydroxy-DL-aspartic acid (threo-DL-BHAA) excited markedly d-RPLN and RAPN, which were excited by L-BHGA; while this compound inhibited slightly PON, VIN and v-RCDN, which were inhibited by L-BHGA. On the other hand, erythro-ß-hydroxy-DL-aspartic acid (erythro-BHAA) was almost ineffective, but slightly effective on v-RCDN as an exception.

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EFFECTS OF HYPERTONICITY AND TETANUS ON MINIATURE END-PLATE POTENTIALS AT THE FROG NEUROMUSCULAR JUNCTION. KAWASAKI, F., KITA, H. AND NARITA, K. Dept. of Physiol., Kawasaki Med. Sch., Kurashiki 701-01

Measurements were made on the amplitude and frequency of miniature end-plate potentials (MEPPs) recorded intracellularly from frog sartorius nerve-muscle preparations before, during and after soaking in hypertonic solutions made by adding 50 and 100 mM sucrose. The mean amplitude decreased transiently during the early period of hypertonicity with a corresponding increase in the mean frequency. Then it increased to a level slightly above the control and remained there for the rest of the period of hypertonicity, while the frequency was kept at an almost constant elevated level. On return to normal Ringer, both the amplitude and frequency returned to the initial level in most cases. The coefficient of variation (c.v.) of MEPP amplitudes was equal to, or a little below the control value during the initial period of hypertonicity, but it began to increase after 10-30 min with increasing occurrences of giant MEPPs. After soaking in hypertonic solutions for about 40 min, the elevated values of c.v. remained unchanged even in the control solution despite reductions in the amplitude and frequency. The same measurements were performed before and after tetanic stimulation (50 Hz, 3-10 min) of the nerve. Following tetanus, there was a decrease in the mean amplitude associated with an increase in c.v.

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EFFECTS OF Ca-ANTAGONISTS ON THE NEUROMUSCULAR TRANSMISSION OF THE FROG. TAKEUCHI,A., KAWAGOE,R. AND MINO,H. Dept.of Physiol., Juntendo Univ., Sch. of Med. Hongo, Tokyo 113,

The effects of the organic "Ca-antagonists" Diltiazem on the frog sartorius nerve-muscle preparation was investigated. During perfusion with Diltiazem(10~500μM),the amplitude of end-plate potentials(e.p.p.s) was decreased in dose-dependent manner. Frequency of spontaneous miniature end-plate potentials(m.e.p.p.s) was increased and the giant m.e.p.p.s tended to appear. The increase was independent of external calcium. The quantum content was increased to about 150% by 50μM Diltiazem. Postsynaptically,Diltiazem(20~100μM) reduced the amplitude of e.p.c. and m.e.p.c. recorded by voltage clamp and decreased the time constant of decay phase. Trains of Ach potentials induced by iontophoresis were depressed and the depression was more pronounced in successive Ach potentials compared with the initial one. When trains of stimuli were applied to the nerve,marked depression was not observed in successive e.p.p.s. These results suggest that decrease of e.p.p. amplitude by application of Diltiazem is caused mainly by its postsynaptic action.

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VOLTAGE-CLAMP ANALYSIS OF TAURINE-INDUCED SUPPRESSION OF EPSP AT FROG SPINAL MOTONEURON. HIRAKAWA, T., KUNO, M., MATSUURA, S., Dept. of Physiol., Osaka City univ. Med. Sch., Osaka 545

In the central nervous system, taurine has been considered to be a neuromodulator as well as an inhibitory transmitter. We studied mechanisms of taurine-induced suppression of excitatory postsynaptic potential (EPSP) and current (EPSC) at motoneurons in isolated, intra-arterially perfused spinal cord. Voltage-clamp was performed with two separate microelectrodes containing 2M K-acetate. Polysynaptic components of EPSP and EPSC were greatly decreased without any appreciable change in monosynaptic EPSC by low concentration of taurine(0.75mM), which hyperpolarized the cell with a slight increase in the membrane conductance (104-128%). Monosynaptic EPSC and spontaneous EPSC were suppressed by higher concentration of taurine(2~7.5mM) which depolarized the cell with an increase in membrane conductance (138-298%). Inward currents and an increment of conductance induced by glutamate(1mM) were reduced in the presence of taurine (2mM), both in standard and in 0.18mM Ca^{++} and 10mM Mg^{++} solutions. These results suggested that taurine suppressed EPSP both by inhibiting interneurons and by affecting generation of EPSC. Postsynaptic mechanism might be involved in the suppression of EPSC.

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DEPRESSION BY DOPAMINE OF THE FAST EPSP IN NUCLEUS ACCUMBENS NEURONS OF METHAMPHETAMINE-PRETREATED RATS. UCHIMURA, N.[1,2]; HIGASHI, H.[1], NISHI, S.[1] AND INANAGA, K.[2*] Departments of Physiology[1] & Psychiatry[2], Kurume University School of Medicine, Kurume 830

The effect of dopamine (DA) on the nucleus accumbens septi (NAS) neurons in brain slices of normal and methamphetamine (MAP)-pretreated rats was studied by intracellular recordings. In the slices of untreated rats DA and MAP showed almost no effect on the fast EPSP (presumably mediated by glutamate), whereas both substances markedly depressed the fast EPSP in MAP-pretreated rats. The minimal concentration of DA for the depression was 10 nM. In contrast, glutamate-induced depolarizations were unaffected by DA (>1 μM) regardless of MAP-pretreatment. These results suggest that the DA-induced depression of fast EPSP is most likely presynaptic in nature. It was also found that in the MAP-pretreated slices DA (≥10 nM) and also cyclic AMP (1 mM) depressed Ca^{2+}-dependent soma spikes as well as the fast EPSP. Haloperidol (D-1 and D-2 receptor antagonist) reversed the DA-induced depression of fast EPSP and Ca^{2+}-dependent spikes, while sulpiride (D-2 receptor antagonist) could not. The results altogether suggest that the MAP-pretreatment may produce a hypersensitivity of the D-1 receptor on the glutamate containing nerve terminals in the NAS, and that the depression of fast EPSP by DA may be due to a reduction of Ca^{2+}influx at the presynaptic nerve terminals which was caused by activation of the sensitized D-1 receptor thereupon.

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A SUM RULE OF SYNAPTIC CONDUCTANCE.

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Previously, the conservation law for the synapses between Cat's hair cell-spiral ganglion-a cochlear nucleus transmission was reported(J.Physiol.Soc.Japan,46,8,9, (1984)449): the sum of $1/\sqrt{m_i}\,\gamma_i$(of the i-th synapse)s is kept constant when the used neurons are varied with the change of stimulus intensity and sound frequency; here, $m_i$is the transmission rate defined as outputspike frequency/input one, and γ_i is the time constant of a psp of the i-th synapse. Now, the electrical model of synapse is introduced: the poralized potential causes the separation of positive charges and negative ones in a synapse and, if deporalized, those are diffused and a current happens. Consequently, the sum rule for the synaptic conductance is obtained:

$$\sum_i \sqrt{k/u}\cdot\frac{1}{A}\cdot z\cdot g_i = const.$$

u: the density of movable charges(Q) in a synapse. k: the constant, deporalized potential V=kQ/z. z: the distance of separation. A: the spatial constant of the decay of the potential conducted along a dendrite from a synapse to a cell body.

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RESPONSES OF SYMPATHETIC NERVE - BROWN FAT SYSTEM TO FOOD INTAKE: ROLES OF FOOD PALATABILITY. SAITO, M. AND MINOKOSHI, Y. Dep. Med. Biochem., Sch. Med., Ehime Univ. Shigenobu, Ehime 791-02

Thermogenesis in brown adipose tissue (BAT), which is under a direct control of sympathetic nerves, is known to contribute to keeping energy balance, so that it decreases and increases in response to , for example, fasting and hyperphagia induced by cafeteria-feeding regime, respectively. To clarify roles of palatability of food in the activation of the sympathetic nerve - BAT system, female rats were given a liquid diet orally or through a gastric tube for 3-12 days. The tube-fed rats weighed more than the orally fed rats largely because of increased white adipose tissue, and their interscapular BAT contained more triglyceride despite of less DNA and protein. These changes in BAT were quite similar to those found after surgical sympathectomy. In BAT of the tube-fed rats, the rate of norepinephrine turnover, a good index of the sympathetic nerve activity, was almost equal to that in the fasted rats, and was about one-fourth of the rate in the orally fed rats. There was no significant difference, however, in the norepinephrine turnover rate in the heart and pancreas between the tube-fed and orally fed rats. These results suggest an important role of oro-pharyngeal sensations of food in activation of sympathetic nerve - BAT system.

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UNDIMINISHED REFLEX RESPONSES OF ADRENAL SYMPATHETIC NERVE ACTIVITY TO STIMULATION OF BARORECEPTORS AND CUTANEOUS MECHANORECEPTORS IN AGED RATS. KUROSAWA,M., SATO,A., SATO,Y. and SUZUKI,H. Dept. Physiol., Tokyo Metropol. Inst. of Gerontol., Tokyo 173.

It has been reported that adrenal sympathetic nerve efferent unitary activity at resting conditions was increased during aging[1]. Causative factors to explain this increase might include an age-related decrease in arterial baroreceptor sensitivity, a decrease in central inhibitory mechanisms on the sympathetic neurons, or/and an increase in central excitatory mechanisms on those neurons. In the present experiments, reflex responses of adrenal sympathetic nerve activity to stimulation of baroreceptor and cutaneous mechanoreceptors were compared in young adult (4 months old) and aged (26 months old) rats, under strictly controlled conditions for anesthesia, respiration and body temperature. Under these conditions the reflex depression to baroreceptor stimulation and cutaneous brushing and reflex excitation to cutaneous pinching were quite well maintained during aging.

1) Ito,K., Sato,A., Sato,Y. and Suzuki,H., Neurosci. Lett., 69 (1986) 263-268.

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UPTAKE OF [3H]DOPAMINE IN ADRENAL CHROMAFFIN CELLS OF THE MOUSE DURING DARK AND LIGHT PERIOD. HIRANO,T.,*NAGAI,K. AND NIIJIMA,A. Dept. Physiol. Niigata Univ. Sch. Med. Niigata 951 and Div. Protein Metab., Protein Res. Inst. Oosaka Univ. Suita 565*

Uptake of [3H]dopamine in adrenal chromaffin cells of the mouse was examined by autoradiography under 12-h light and 12-h dark cycle in an attempt to examine the effects of circadian changes in humoral and neural factors on dopamine uptake. Male mice of ddY strain was used. Experiments were carried out between 1 to 3 h before dark-light alteration. Left adrenal nerves were cut 2 weeks before the experiment. [3H]dopamine was injected i.p. (8uCi/gbw). Thirty min after the injection of the isotope, mice were perfusion-fixed with glutaraldehyde followed by postosmication. After dehydration and embedding, sections were cut and they were processed for autoradiography.

The uptake of [3H]dopamine was markedly suppressed in the dark period in both A and NA cells. Adrenal denervation prevented the suppression. In denervated chromaffin cells, there was no significant difference in the uptake of dopamine between dark and light. It is suggested that there is a neurally mediated suppression of [3H]dopamine uptake by chromaffin cells in the dark period.

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EFFERENT PROJECTIONS OF THE NUCLEUS TRACTUS SOLITARII RELATED TO CIRCULATORY AND RESPIRATORY RESPONSES IN CATS STUDIED BY THE WGA-HRP METHOD. MIURA, M. AND TAKAYAMA, K., Dept. Physiol., 1st Div., Gunma Univ. Sch. Med., Maebashi 371

Using chloralose-anesthetized cats, efferent projections from the nucleus tractus solitarii (NTS) were studied in relation to circulatory and respiratory responses to microstimulation of the NTS. A small amount of WGA-HRP was iontophoretically injected into 3 distinct regions of the NTS: [1] the rostral regions with pressor and apneustic responses; [2] the intermediate regions with depressor and apneic responses; [3] the commissure regions with depressor and hypopneic responses. HRP-labeled axon terminals were sought in the serial frontal sections of the spinal cord, medulla oblongata and pons. Clearly, the distribution of labeled axon terminals were restricted in a strip of structure running from the NTS to the ipsilateral ventrolateral medulla (VLM) and the ipsilateral parabrachial nuclei of the pons. Through the traversing fibers, some projections were observed in the contralateral VLM. Most prominent site of labeled axon terminals was C1 area which is controversial on its role of the circulatory and respiratory control. The concentration of labeling was heavy in the case of [1], while weak in the case of [3].

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VENTROLATERAL MEDULLA OF THE RAT: THE FUNCTIONAL SUBDIVISIONS DETERMINED BY CIRCULATORY AND RESPIRATORY RESPONSES TO ELECTRICAL STIMULATION. SAJI, M., ONAI, T. AND MIURA, M. Dept. Physiol., 1st Div., Gunma Univ. Sch. Med., Maebashi 371

Using normotensive (WKY) and spontaneously hypertensive (SHR) rats anesthetized with urethane (500mg/kg) and chloralose (80mg/kg), functional subdivisions of the ventrolateral medulla (VLM) were studied in relation to the circulatory and respiratory responses to electrical stimulation. The results were: (1) effects of electrical stimulation of VLM were classified into four types, (a) intense pressor response with apnea and tachycardia was elicited in the lateral area of the caudal VLM (CVL) (similar to A1 area), (b) moderate pressor response with apnea and tachycardia was elicited in the area lateral and dorsal to the nucleus ambiguus (AMB) of the rostral VLM (RVL), (c) small pressor response with tachypnea and bradycardia was elicited in the ventral surface of RVL (similar to C1 area), (d) depressor response with apnea was elicited in the area medial and ventral to AMB; (2) among three types of pressor response, both pressor response with apnea of CVL and that of RVL showed a similar relationship to stimulus-intensity and -frequency despite the difference in sensitivity. There was no significant difference in the VLM circulatory and respiratory responses between WKY and SHR rats.

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CENTRAL RESPIRATORY DRIVE RELATED RHYTHM IN THE RAT'S SYMPATHETIC NERVES. KOSHIYA, N. AND NUMAO, Y. Inst. of Basic Med. Sci., Univ. of Tsukuba, Ibaraki-ken 305

In halothane anaesthetized, vagotomized, SA-denervated rats, various major sympathetic nerve activities have been analyzed with respect to central respiratory drive(CRD) related discharge pattern in which phrenic activity was recorded as an indication of CRD. The cervical and lumbar sympathetic nerves fired maximally following phrenic discharge and the former less during phrenic activity. On the other hand, the splanchnic, cardiac, renal and adrenal nerves exhibited maximal activity during inspiratory phase. Either altering the level of halothane anaesthesia or switching off of halothane to another anaesthetic agent (pentobarbital, urethane or alpha-chloralose) modified these variable patterns but could never disrupt the non-uniformity. Such distinct firing profiles were also resulted in after ganglion blockade with hexamethonium in the mixed pre- and postganglionic fibre preparations indicating that activities of a group of sympathetic preganglionic neurones are responsible for the discharge patterns and the regional differences.

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PROJECTION TO VENTROLATERAL MEDULLA OF NEURONS WITHIN SOLITARY TRACT NUCLEUS INFLUENCED BY HEPATIC VAGAL AFFERENTS IN RATS.
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Effects of the hepatic vagal afferents on neurons which project to the ventrolateral medulla (VLM) were investigated within the nucleus tractus solitarius (NTS) in urethan-chloralose anethetized rats. Forty one neurons which were responded antidromically by electrical stimulation of the VLM were recorded within the NTS. Antidromic responses were confirmed by collision tests. The mean value of antidromic latencies is about 10.9 msec. Electrical stimulation of the hepatic branch of the vagus nerve elicited facilitation (n=15), suppression (n=2), or both (n=2). Furthermore, two neurons which were facilitated by electrical stimulation of the hepatic branch of the vagus nerve decreased in discharge rates in response to portal infusion of hypertonic saline.

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CHANGES IN FOOD AND WATER INTAKES FOLLOWING HEPATIC VAGOTOMY AT A STAGE OF DEVELOPMENT IN RATS.
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Changes in food and water intakes after hepatic vagotomy were examined in the body weights of three different rats (about 100, 200 and 280g). Cumulative food and water intakes 2 or 12 day following the vagotomy were significantly reduced compared to the sham operated group only in the 100-g animals. These findings support our previous view that function of the hepatic vagus varied according to developmental stages, and suggest that the vagus nerve is active in stimulating normal feeding and drinking in an earlier stage of development.

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NORADRENALINE-RESPONSES OF HAMSTER SUBMANDIBULAR GANGLION CELLS.
SUZUKI, T., SAITO, T. AND SAKADA, S. Tokyo Dent. Coll., Chiba 260

The subtypes of α-adrenoceptors associated with noradrenaline (NA)-responses of the submandibular ganglion cells were investigated using intracellular recording technique. NA and $\alpha_{1,2}$-adrenoceptor agonists were applied to cells from micropipettes by means of a pressure ejection system. NA either depolarized or hyperpolarized the ganglion cells. The responses of some cells were biphasic. The depolarization and hyperpolarization were prevented by prazosin (10 μM) and yohimbine (10 μM), respectively. Phenylephrine and clonidine caused depolarization and hyperpolarization alone, respectively. The both responses were accompanied by decreased G_m. The depolarization possessed a reversal potential near K-equilibrium potential. However, the K channels responsible for NA-depolarization were not affected significantly by TEA, Cs^+, Ba^{2+}, 4-AP and quinine, and probably is not M channels. Generation of the depolarization was independent of Ca^{2+} ion. The K channels responsible for NA-depolarization might be voltage-insensitive channels similar to those of ganglion cells on cat urinary bladder.

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EFFECTS OF APAMIN ON THE LONG LASTING HYPERPOLARIZATION IN THE ELECTRICAL ACTIVITIES OF RABBIT OTIC GANGLION NEURONS. YOSHIZAKI, K., SATO, M. and KOYANO, H. Dept. of Physiol. Akita Univ. Sch. of Med. Akita 010

The long lasting hyperpolarization (LLH) following the afterhyperpolarization (AHP) is produced by an increase of Ca^{2+}-dependent K^+ conductance (g_{K-Ca}). The effects of apamin, a blocker of small g_{K-Ca}, on LLH and AHP were examined in existence or absence of tetraethylammonium (TEA), a blocker of large g_{K-Ca}. Apamin (5 nM) partly reduced LLH and AHP in amplitude and duration. TEA (10 mM) reduced LLH partly but increased the AHP duration and also in some neurons the AHP amplitude. Application of both apamin and TEA completely blocked LLH and partly the AHP amplitude. The residual AHP which was not blocked by both apamin and TEA was mostly blocked by addition of Co^{2+}, except for a residue of a small hyperpolarization which was not blocked even by 4-aminopyridine (4-AP). These results suggest that LLH is due to an increase of both the apamin-sensitive g_{K-Ca} and the TEA-sensitive g_{K-Ca}, and AHP is attributable to an increase of the apamin-sensitive g_{K-Ca}, the apamin- and TEA-insensitive g_{K-Ca} and an unknown conductance not blocked by Co^{2+} and 4-AP.

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INTRACELLULAR CALCIUM CONCENTRATION OF GUINEA-PIG MYENTERIC NEURONS MEASURED BY FURA-2. TATSUMI, H., HIRAI, K. AND KATAYAMA, Y. Dept. Autonom. Physiol., Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo 101

The concentration of intracellular free calcium, $[Ca^{++}]i$, was measured by the calcium sensitive fluorescent dye, fura-2, and the membrane potential was recorded simultaneously with intracellular electrodes. Guinea-pigs were sacrificed by heavy stunning on the head and bleeding from the neck. Myenteric plexus-longitudinal muscle preparations of the ileum were made and superfused with Krebs solution. Fura-2 was injected by negative currents from the recording electrode. The resting $[Ca^{++}]i$ in normal Krebs solution was about 80 nM. A somatic action potential of AH cells caused a transient increase in $[Ca^{++}]i$. $[Ca^{++}]i$ was increased by a membrane depolarization by outward currents through the recording electrode and the $[Ca^{++}]i$ increase was enhanced in high Ca^{++} solution (12.5 mM). The superfusion of high K^+ solution (20 mM) elicited a membrane depolarization and an increase in $[Ca^{++}]i$, whereas it did not change $[Ca^{++}]i$ when the high K^+ depolarization was manually nullified. Supported partly by Nakatani Electronic Measuring Technology Association of Japan.

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PROPAGATION OF NEURAL EXCITATION WITHIN THE MYENTERIC PLEXUS OF THE GUINEA-PIG ILEUM. KATAYAMA,Y., HIRAI,K. AND TATSUMI,H. Dept. Autonom. Physiol., Med. Res. Inst., Tokyo Med. and Dent. Univ., Tokyo 101.

Intracellular recordings were made from neurons of myenteric plexus-longitudinal muscle preparations of the guinea-pig ileum. Transmural stimulation caused synaptic responses (fast EPSP, slow EPSP and IPSP). In S cells, three types of the synaptic responses were evoked by single- or repetitive-pulse stimulation at distance about 8 mm (up to 15 mm) either oral or aboral from the neuron impaled. In AH cells, slow EPSPs were caused by repetitive stimulation at distance 10 (mean) ± 0.4 (SEM) mm (n=10, up to 12 mm) oral or 5.1 ± 0.4 mm (n=8, up to 8 mm) aboral from the impaled neuron; IPSPs were only occasionally observed. Focal stimulation within the ganglion in which the impaled neuron located was most effective in producing the synaptic responses, and there was no preferred location of stimulus electrodes, whether they were placed orally or aborally from the neuron impaled. By using intracellular staining with the fluorescent dye Lucifer yellow, the longest processes of S cells were observed to be aborally directed more frequently (13 out of 43 cells) than orally (5 out of 43 cells).

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ANALYSIS OF SHORT-TERM (STV) AND LONG-TERM (LTV) HEART RATE VARIABILITY IN ADULTS. YAMAMOTO, S., SUGIURA, Y. AND SHOZUHARA, H. Depart. of Neurosurg. Yaizu Municipal Hosp., Yaizu Shizuoka 425. UEMURA, K., NINCHOJI, T. AND RYU, H. Depart. of Neurosurg. Sch. Med. Hamamatsu Univ., Hamamatsu Shizuoka 431-31

The normal heart does not beat at a constant rate. Instead, there is a continuous change in heart rate on a beat-by-beat basis. We analyzed adult heart rate variability by examining short-term variability (STV) (beat-to-beat), and long-term variability (LTV) (range over 30 seconds) as fetal heart rate moniter-ing. CNS damage, such as ICH, was associated with decreased heart rate variability. (Normal $\fallingdotseq$ Subcortical Hemorrhage $\geqq$ Putaminal Hemorrhage > Thalamic Hemorrhage > Pontine Hemorrhage > Brainstem Death) Especialy the relationship between loss of LTV and brainstem damage was noted. On the other hand, high LTV and STV was thought to be the result of parasympathetic stimulation.

This investigation confirms its potential usefulness in the study of patients with brainstem dysfunction.

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Plasma catecholamine changes in spontaneously hypertensive rat (SHR) to foot shock.

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The previous reports demonstrated that sympathetic nerve activity (SNA) increased in SHR to various stimuli. To confirm this hyper-responsiveness in SHR to stress, we compared the conscious SHR with foot shock to that without it. The concentration of plasma catecholamines were measured with HPLC-ECD method. The plasma catecholamine in resting SHR was not different from that in WKY. Following foot shock, plasma norepinephrine increased more in SHR (2995 ± 227 pg/mℓ) than in WKY (1560 ± 197 pg/mℓ). This result suggests that SHR appears to exhibit increased SNA to stress, providing increased plasma catecholamine.

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THE EFFECT OF ALPHA-ADRENERGIC AGONIST (MIDODRINE HYDROCHLORIDE) ON MUSCLE SYMPATHETIC ACTIVITY IN MAN. IWASE, S., MANO, T., ISHIDA, G., TSUKAHARA, R., INAMURA, K. Res. Inst. Environ. Med., Nagoya Univ., Nagoya 464

Midodrine hydrochloride (midodrine) is a precursor of selective α_1 adrenergic agonist, possessing continuous pressor effect. To determine the effect of this drug on the sympathetic nervous system in humans, muscle sympathetic nerve activity (MSA) and its responses to stepwise passive and static head-up tilting (at the tilting angles of 0°, 10°, 20°, 40°, 60°, and 90°) were analyzed microneurographically before and after the intravenous injection (IV) of 5 mg midodrine, using a double blind method, in 10 healthy male volunteers with prior informed consent. The MSA innervating the triceps surae was recorded at the popliteal fossa using tungsten microelectrode. The spontaneous discharges of MSA in supine position were significantly suppressed after midodrine IV ($p<0.005$ after 30 min, $p<0.05$ after 90 min of IV), however there were no significant changes in systolic and diastolic blood pressures and in heart rates. The MSA in upright position was not significantly influenced by midodrine IV. Consequently, the slope of the regression line established between the sine of the tilting angle and the burst rate of MSA was significantly elevated by midodrine IV ($p<0.005$ after 30 min of IV). It is concluded that midodrine hydrochloride suppresses the MSA to maintain the hemodynamic homeostasis against peripheral vasoconstrictive action of this drug.

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CHANGE IN THE CARDIO-RESPIRATORY FUNCTION FOLLOWING GUSTATORY STIMULATION OF THE ORO-PHARYNGEAL MUCOSA. YONEMURA, K. AND ISHIKO, N. Dept. of Physiol., Miyazaki Medical College, Miyazaki 889-16

Rats anesthetized with urethane-chloralose were used. The femoral arterial blood pressure (BP), respiration rate (RR), heart rate (HR), ECG and end-tidal CO_2 were monitored. The lingual nerve containing the chorda tympani, the IXth and superior laryngeal nerve (SLN) were exposed, cut peripherally and stimulated electrically, while the efferent Xth nerve activity was recorded from the cervical trunk. An increase in stimulus intensity to the lingual nerve caused a gradual rise in BP and HR without change in RR. Similar changes in BP and HR with decrease in RR were obtained after the IXth stimulation. While SLN stimulation resulted in a rise of HR and a decrease in RR, a slight rise followed by a prominent decrease in BP occurred with increasing stimulus intensity. These changes in the autonomic function were usually accompanied with a depression of the Xth nerve activity. A rise in BP and HR also occurred following application of 1 M NaCl and 30 mM HCl to the oral cavity. The effect was most apparent in the presence of the IXth nerve. Little change was observed by 1 M sucrose, 30 mM quinine and cooled solution.

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PARTICIPATION OF SYSTEMIC BARORECEPTORS ON RENAL SYMPATHETIC NERVE ACTIVITY DURING PORTAL VEIN DISTENSION. Koyama, S., Kanai, K., Aibiki, M. and Miyakawa K. Shinshu University School of Medicine, Department of Physiology, Division 2., Nagano 390, Japan

This study was designed to determine neural control mechanisms on renal nerve activity during portal vein distension in anesthetized dogs. Following the inflation of a balloon in the main portal vein of animals with the neuraxis intact, mean blood pressure (MBP) fell significantly and renal nerve activity (RNA) increased significantly. This significant increase in RNA during the inflation of the balloon was not eliminated by either carotid sinus nerve denervation or vagotomy. However, reflex increase in RNA in both CS and V groups were significantly lower than those in animals with the neuraxis intact. Even when proximal portal vein pressure at the site of mesenteric area was controlled to the pre-distension level by means of artificial bypass between the mesenteric vein and femoral vein in CSV group, the increased response during the balloon inflation remained. Hepatic denervation in CSV group caused no significant changes in RNA. The results of this study indicated that increases in RNA during portal vein distension may be modified by systemic baroreceptors and local reflex systems. The local reflex system may be comprised of hepatic sympathetic afferents which is activated by decrease in portal vein pressure in the liver.

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EFFECTS OF FAMOTIDINE, PIRENZEPINE AND TETRODOTOXIN ON PENTAGASTRIN-INDUCED GASTRIC ACID SECRETION IN DOGS. FUJII, K., KAWAHORI, K.* AND OKAJIMA, M.* Dept. of Physiol. and Surg.*, Hiroshima Univ. Sch. Med., Hiroshima 734

In order to clarify the cholinergic mechanisms of gastric acid secretion in the gastric phase, the effects of famotidine, a histamine H_2-receptor antagonist, pirenzepine, a specific blocker of acetylcholine muscarinic receptor in the parietal cells, and tetrodotoxin (TTX) on pentagastrin-induced gastric acid secretion were investigated in gastric fistula dogs.

Gastric acid secretion induced with pentagastrin(2-4 μg/kg, s.c.) was strongly reduced by intravenous injection of famotidine(0.3 mg/kg). The remaining components which were not inhibited by famotidine were abolished by pirenzepine(3 mg/kg, i.v.) or TTX(10μg/kg /h, i.v.). However, the gastric acid secretion induced by bethanechol(5 μg/kg) was unaffected by TTX.

These results suggest that the pentagastrin stimulates the cholinergic nerve endings in the intramural nervous plexus and releases acetylcholine(Vizi et al., 1973), and consequently, activity of the parietal cells was augmented by released acetylcholine.

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EFFECTS OF GABA ON THE NON-ADRENERGIC NON-CHOLINERGIC INHIBITORY POTENTIALS IN THE CIRCULAR SMOOTH MUSCLE OF THE GUINEA-PIG DUODENUM.
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The effects of GABA on the non-adrenergic non-cholinergic inhibitory potentials (NANC i.p.s) in the circular muscle of the guinea-pig duodenum were investigated intracellularly. The amplitude of the NANC i.p.s was increased by GABA and baclofen and the excitatory action of GABA was almost disappeared by the treatment with picrotoxin and δ-aminovaleric acid (AVA). In the presence of atropine, GABA slightly increased the amplitude of i.p.s. In the presence of AVA and atropine, the amplitude of the i.p.s was decreased by GABA and baclofen while, in the presence of picrotoxin and atropine, it was increased. From the results, it is suggested that GABA increases the i.p.s mainly due to inhibition in acetylcholine release via $GABA_B$-receptors on the cholinergic neuron and that GABA increases the release of the NANC inhibitory neurotransmitter via $GABA_B$-receptors and decreased it via $GABA_A$-receptors on the NANC inhibitory neuron, respectively.

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EFFECT OF STIMULATION OF SP-NERVES CONTAINED IN THE MESENTERIC NERVE ON THE MOTILITY OF ISOLATED GUINEA-PIG ILEUM.
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Effects of hexamethonium(C_6), capsaicin and substance P desensitization were tested on the cholinergic contractile response to mesenteric nerve stimulation (MNS) in the four differently innervated loops of isolated guinea-pig ileum. Effect of oral MNS was more intensive than that of anal MNS in 80 % of preparations with oral and anal mesenteric nerves(MN). This result indicates that the innervation of oral MN is more dominant than that of anal MN. Moreover, the overlap of the innervation of oral MN and anal MN was found. The responses to oral MNS and anal MNS were not affected by C_6, but the respective responses to bidirectional MNS and oral and anal MNS were significantly reduced to about 60 and 50 % of the control. Effects of capsaicin or substance P desensitization on the response to each MNS showed no differences between the four differently innervated loops.

Furthermore, the longitudinal muscular response and myenteric neural electrical response could be actually evoked by MNS in the longitudinal muscle-myenteric plexus preparations innervated with bidirectional MN.

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RESPONSE OF UTERINE AFFERENTS IN THE HYPOGASTRIC AND PELVIC NERVE OF THE RAT TO ALGESIC CHEMICAL SUBSTANCES.
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The purpose of the present experiment was to study the responses of afferent fibers of the uterus in the hypogastric and pelvic nerves to algesic chemical stimuli. The uterus, together with distal portions of the hypogastric and pelvic nerves and the uterine blood supply, were dissected from the anesthetized rat and placed into an *in vitro* chamber. The algesic chemicals used were bradykinin (brad), 5-hydroxytryptamine creatine chloride (5-HT) and potassium chloride (KCl). All of these algesic substances produced an increase in activity in both nerves. For KCl and brad the response pattern were similar in the two nerves, while, in the case of 5-HT, the pattern was different. These responses to algesic substances in the pelvic and hypogastric nerves suggest that both nerves contribute to pain sensation.

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EFFECTS OF HYPOTHALAMIC STIMULATION ON VESICAL AND RECTAL MOTILITIES VIA THE PELVIC NERVE IN DOGS. YAMANE, M. Dept. Physiol., Kawasaki Med. Sch., Kurashiki 701-01

In urethane-chloralose anesthetized dogs, effects of hypothalamic electrical stimulation on vesical and rectal motilities via the pelvic nerve were studied. After cutting the lumbar colonic and bilateral hypogastric nerves, vesical outflow in the pelvic nerve and intravesical pressure (UB) and the rectal outflow and intrarectal pressure (R) were recorded. Electrical stimulation (ES) of the hypothalamus (0.15 mA, 30 Hz, 3 msec) produced excitatory or inhibitory responses of UB and R. Weak excitatory responses were obtained by ES in a wide area of the hypothalamus. Remarkable excitatory responses in UB and R were elicited by ES of the preoptic area, anterior hypothalamus and middle hypothalamus. Moderate excitatory response in UB was also elicited by ES of the posterior hypothalamus. Inhibitory response in UB was induced by ES of the dorsal part of the middle hypothalamus and the anterior part of the posterior hypothalamus, whereas that in R was induced by ES of the middle and posterior hypothalamus. Latencies of the excitatory responses of vesical and rectal branches of the pelvic nerve were 80-160 and 160-240 msec, respectively. Reflex responses of the pelvic nerve to the afferent stimulation of the right pelvic nerve were also increased or decreased by ES of the hypothalamus.

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THE EFFECT OF PARTIAL DENERVATION ON THE EFFERENT PATHWAYS TO THE URINARY BLADDER. MASAHITO KAWATANI and DE GROAT W. C.*, Dept. Physiol., Sch. Med., Showa Univ., Shinagawa, Tokyo and *Dept. Pharmacol., Sch. Med., Univ. Pittsburgh, PA. 15261, U.S.A.

Clinical observations suggest that injury to the parasympathetic innervation of the urinary bladder can lead to the unmasking of excitatory sympathetic inputs to the bladder. In this study using cats, unilateral transection of sacral ventral roots(S_1-S_3) was performed 2-48 weeks prior to the experiments. In these cats stimulation(stim) of the normal pelvic nerve, but not the denervated pelvic nerve, elicited bladder contactions. Repetitive stimulation(10-30 Hz) of the HGN ipsilateral to the denervation (DEN) produced a bimodel bladder contraction consisting of a large early contaction(EC) and small late contraction(LC). HGN-stim on the normal side produced only the EC. The LC, detected 4-48 weeks after denrvation, was blocked by atropine(10-20mg/kg i.a.) but was not changed by α-adrenrgic locking agents(phenoxybenzamine 0.5mg/kg). The EC was not affected by these drugs. HGN-stim on the DEN-side also elicited a discharge in ipsilateral bladder postganglionic nerves(latencies of 25 msec and at thresholds of 1V). The discharge was blocked by hexamethonium(1-10mg/kg) indicating it was synaptically mediated. In summury, interrution of the sacral preganglionic outflow to the urinary bladder led to the reorganization of synaptic connections in the bladder ganglia which was reflected in the formation of sympathetic cholinergic excitatory inputs.

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DEVELOPMENT OF NEURONAL PROPERTIES OF RAT DORSAL MOTOR NUCLEUS OF THE VAGUS (DMV). FUKUDA, A., NABEKURA, J., ITO, C. AND OOMURA, Y. Dept. Physiol., Fac. Med., Kyushu Univ. 60, Fukuoka 812

Functional characteristics of the nervous system change with age, and these changes can be observed in the DMV. Intracellular recordings were made from DMV neurons in slice preparations from 2 days before to 5 weeks after birth (Ab). Input membrane resistance decreased and membrane capacitance increased with age. Unmasked Ca^{2+} spikes, as well as Na^{+} spikes, were observed up to a few days Ab. Duration of action potentials and inter-spike intervals decreased with age. Up to 7-10 days Ab, afterhyperpolarization (a.h.p.) was simple; only late component was evident, which was attenuated by Cd^{2+}, but not by 4-AP. Later, a.h.p. contained early and late components, which were attenuated by 4-AP and Cd^{2+}, respectively. Tetanic stimulation caused late depolarization and delayed spontaneous e.p.s.p.s only in young preparations, but spontaneous and evoked i.p.s.p.s were characteristic in contrast to adults (e.p.s.p. predominant). Noradrenaline depolarized all neurons tested and increased frequency and amplitude of spontaneous i.p.s.p.s up to 7 days Ab, in contrast with previous studies in adults. Results suggest that membrane properties, synaptic inputs, and responses to putative transmitter develop gradually with some being completed 1-3 weeks Ab.

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CENTRAL CONNECTIONS OF THE VAGAL COMPLEX IN THE RAT. OKUMURA, T. and SUGAYA, K. Depts. of Med. and Physiol., Asahikawa Med. Col. Asahikawa 078

In this study, we have studied axonal projections to and from the vagal complex by means of HRP tracing method. An HRP-filled micropipette was stereotaxically inserted into the vagal complex and HRP was microinjected there iontophoretically. After survival of 48 hours, the rats were sacrified by cardiac perfusion under nembutal anesthesia. Retrogradely labeled cells were obserbed mainly in the ipsilateral central n. of amygdala, paraventricular n. of hypothalamus, central gray, medullary reticular formation, and contralateral sensory cortex and interpositis cerebellar n.. HRP labeled fibers coursed from vagal complex rostrally and ventrolaterally through ventrolateral reticular formation in the medulla and caudal pons, dorsolateral reticular formation in the rostral pons and mesencephalon, and then to lateral hypothalamic area. Labeled presumed axon terminals distributed mainly in the ambiguus n., lateral parabrachial n., paraventricular thalamic n., bed n.of the stria terminalis. Among a variety of nuclei studied, a significant number of labeled neurons and terminals were found in the paraventricular n. of hypothalamus and the lateral parabrachial n.,respectively. From all these results, the function of the vagal complex in visceral regulation was discussed.

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IDENTIFICATION OF CELLS OF ORIGIN PROJECTING TO THE HEPATIC BRANCH OF THE SPLANCHNIC NERVE IN THE RAT. KINO, S. and SUGAYA, K., Departments of Surgery and Physiology, Asahikawa Medical Collage, Asahikawa, 078

In this study, we identified cells of origin projecting their axons to the hepatic branch of the splanchnic nerve (HBSN) and compared these results with those projecting to the hepatic branch of the vagus nerve (HBVN). HRP was applied to the HBSN and to the HBVN in 7 and 2 rats, respectively. After survival time of 48 hours, the animals were sacrificed for histological analysis. Cells of origin projecting to the HBSN were found in the celiac ggl. (n=90), in the suprarenal ggl. (right;n=124, left;n=136) and in the thoracic sympathetic trunks (right;n=75, left;n=67). These neuronal structures belong to the sympathetic nervous system. In addition, a few HRP labeled cells were found in the left dorsal motor nucleus of vagus in 2 rats and many cells (n=118) in the left nodose ggl. in 5 rats. In rats with HRP injection to the HBVN, 1154 and 197 labeled cells were observed in the left nodose ggl. and in the left dorsal motor nucleus of vagus, respectively. A few labeled cells were also observed in the celiac ggl., in the suprarenal ggl. and in the sympathetic trunks. These results demonstrated that cells of origin projecting to the HBVN virtually belonged to the parasympathetic nervous system. In contrast, those projecting to the HBSN belonged to both the sympathetic and parasympathetic nervous system.

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A1 AND C1 AREA OF THE VENTROLATERAL MEDULLA IN RELATION TO SITES OF AXON TERMINALS FROM THE FASTIGIAL PRESSOR AREA IN THE CAT. TAKAYAMA, K. AND MIURA, M., Dept. Physiol., 1st Div., Gunma Univ. Sch. Med., Maebashi 371

Recently, using the WGA-HRP method, we found that labeled axon terminals from the fastigial pressor area are located in the area lateral and ventral to the lateral reticular nucleus (Lr) of the medulla of the cat. A question arose whether the above-mentioned area corresponds to the catecholaminergic A1 and/or C1 area. Since we have a few information on these neurons of the cat, we used the peroxidase and antiperoxidase immunohistochemical method, and tried to make a precise topographical map of these neurons in the ventrolateral medulla of the cat. Dopamine β-hydoxylase (DBH) and phenylethanolamine-N-methyl transferase (PNMT) were used as immunological markers of noradrenaline and/or adrenaline. The noradrenaline neurons were distributed in the areas dorsal to Lr and ventrolateral to the nucleus ambiguus (AMB), mainly at the level between the obex and 1.0 mm rostral to the obex, while the adrenaline neurons were distributed in the areas dorsolateral to Lr and ventrolateral to the nucleus retrofacialis (Rf), mainly at the level between 1.2 mm and 2.4 mm rostral to the obex. The adrenaline neurons were also located in the reticular formation surrounding Rf. Considering these anatomical data, we suggest that A1 and C1 areas may not be the sites for relaying fastigial pressor outflow.

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RESPONSES ON RENAL NERVE ACTIVITY AND PHRENIC NERVE ACTIVITY TO HEMORRHAGIC HYPOTENSION IN ANESTHETIZED RABBITS

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This experiment was designed to elucidate responses of renal nerve activity (RNA) and phrenic nerve activity (PNA) during hemorrhagic hypotention in anesthetized rabbits. The experimental animals were divided two groups: group 1(nerve activities disappeared within 20 min), group 2(nerve activities were maintained over 20 min) which hypotension was maintained by using Servo-controller system. In both groups, RNA showed a triphasic pattern: an initial increase due to baroreceptor reflex and a second increase followed by a profound decline, which might be contributed to brain ischemia. PNA remained to near control level until the late stage of intervention. In almost animals, the supression of PNA occurred prior to that of RNA, at when blood pressure level was below 20 mmHg. These results suggest that 1) during hemorrhagic hypotension, central inspiratory neurons might be more fragile than vasomotor neurons, 2) there might be a critical blood pressure level for deterioration of RNA and PNA output.

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SYMPATHETIC NERVE RESPONSE TO BRAIN ISCHEMIA IN RABBITS

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Efferent activities of renal sympathetic nerve(RSNA), cardiac sympathetic nerve(CSNA) and lumber sympathetic nerve(LSNA) with systemic arterial pressure(SAP) were measured simultaneously in Urethan anesthized rabbits during two different periods of complete brain ischemia. Short term brain ischemia caused significant increase in discharges of RSNA(355% of control level), CSNA(309%), LSNA(441%). SAP also raised to 170% of control level. The depressed period were observed in all measured nerves just after resumption of blood flow in baro-receptor intact animals. During long term brain ischemia, however, discharges of RSNA, CSNA and LSNA initially increased likely the short term brain ischemia. There followed a gradual decreased below the control level. SAP fell simultaneously with decrease in sympathetic nerve. These results suggest that the difference of lasting time for brain ischemia may correlate to changes of sympathetic nerve output through the central nervous system.

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THE INFLUENCE OF HEART BEAT AND RESPIRATORY RHYTHM AND THE EFFECT OF ACUPNCTURE STIMULATION ON PERIPHERAL SYMPATHETIC ACTIVITY IN MAN.

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We analyzed the effect of acupuncture stimulation on the action potential of posterior distal fibers of human sympathetic ganglia. On the basis of these results, the effect of acupuncture, a technique in Oriental medicine, was experimentally studied in five healthy adult men. Muscle sympathetic activity(MSA) is spontaneos and varies in correspondence with the changes in arterial pressure that occur with heart beat and respiration. As s result of the present experiment, MSA was found to be suppressed by acupuncture stimulation and then to recover gradually.

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CORTICALLY EVOKED RESPONSES ON SINGLE SUPERIOR SALIVATORY NEURONS IN THE CAT. ISHIZUKA, K., MURAKAMI, T. AND NAKAYAMA, K
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Cortically evoked responses on single superior salivatory (SS) neurons were studied in the cat lightly anesthetized with urethane-chloralose or Ketamine-HCL. Many SS neurons responded polysynaptically to stimulation of ipsilateral anterior part of coronal (72%) and orbital gyrus (61%). Some neurons were activted by stimulation of medial part of coronal (26%) and presylvian gyri (26%). The mean latencies of these reseponses were 22.8, 29.0, 25.2 and 22.6 msec, respectively. These were significantly longer than those evoked by stimulation of ipsilateral chorda tympani or lingual nerve. Majority of SS neurons (75%) responded to the cortical and peripheral stimulations. These results indicate that SS neurons mainly receive inputs from coronal and orbital gyri, and these also receive those from peripheral sensory nerves.

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ELECTRICAL ACTIVITIES OF SYMPATHETIC AND PARASYMPATHETIC FIBERS INNERVATING THE SUB-MANDIBULAR GLAND IN GUSTATORY-SALIVARY REFLEX OF HAMSTERS. MATSUO, R. AND YAMAMOTO, T., Dept. of Oral Physiol., Faculty of Dentistry, Osaka Univ., 1-8 Yamadaoka, Suita, Osaka 565, Japan

This study was designed to evaluate the neural control mechanisms subserving the gustatory-salivary reflex in the lower brain stem. Using urethane anesthetized and decerebrate hamsters, efferent neural activities in sympathetic and parasympathetic fibers innervating the submandibular gland were recorded when taste stimulation was applied to the tongue. Afferent activities in gustatory-salivary reflex arc were also recorded from the chorda tympani (CT) and the glossopharyngeal nerve (GN).

By electrical stimulation of the tongue, the parasympathetic and sympathetic fibers responded with latencies of about 50ms and 150ms, respectively. The para-sympathetic fibers showed tonic discharges, and the sympathetic fibers showed irregular burst discharges by taste stimulations. The magnitude of parasympathetic efferent activity was statistically significantly correlated with the magnitude of CT afferent discharge. The GN afferent was less concerned with the parasympathetic activity. On the other hand, the sympathetic efferent was mainly activated by high concentrations of HCl(0.03M) and NaCl(1M) solutions. The magnitude of sympathetic activity was correlated with the GN activity rather than CT activity.

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UPTAKE OF [3H]2-DEOXY-D-GLUCOSE IN STOMACH, DUODENUM AND PANCREAS IN THE MOUSE. HIRANO,T.,FUKUDA,A. AND NIIJIMA,A. Dept. Physiol. Niigata Univ. Sch. Med., Niigata 951

Uptake of [3H]2-deoxy-D-glucose (2DG) in stomach, duodenum and pancreas was examined by autoradiography in an attempt to measure glucose consumption in these organs. Male mice of ddY strain was used. The isotope was injected i.p. Forty five min after the injection of [3H]2DG, mice were perfusion-fixed with a mixture of glutaraldehyde and potassium dichromate. Sections were cut and processed for autoradiography.

In the stomach, mucous cells and chief cells were heavily labelled while parietal cells were less heavily labelled. Smooth muscle cells exhibited higher radioactivity. In the duodenum, highest radioactivity was demonstrated in goblet cells. Paneth cells were also heavily labelled, while absorptive cells were less heavily labelled. In the crypt, high radioactivity was demonstrated in the secreta. In the pancreas, acinar cells incorporated higher radioactivity, while islet cells took up less [3H]2DG. In the pancreatic duct, higher radioactivity was also demonstrated in the secreta.

The result shows that [3H]2DG was accumulated mainly in exocrine cells. These cells may have ability to select deoxyglucose from other usable sugarsand discard it into gut lumen.

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AN EXCITATION OF THE CANINE JEJUNAL MOTILITY BY SUBSTANCE P NEURONS. MIZUTANI, M., NEYA, T. AND NAKAYAMA,S. Dept. Physiol., Okayama Univ. Med. Sch. Okayama 700.

In urethane-anesthetized intact dogs as well as vagotomized and sympathectomized dogs 23-52 days before experiments, mesenteric nerve stimulation produced the jejunal contraction(MNSC) sensitive to C_6(70-140nmol,i.a.) and atropine(70nmol,i.a.). SP antagonist([D-Pro^4,D-Trp^{7,9}]substance P(4-11), 140nmol,i.a.) and capsaicin(70nmol,i.a.) inhibited reversibly MNSC by 40-60% and by 85% or more in untreated and pretreated animals. An excitatory effect induced by vagus stimulation was sensitive to C_6, atropine, and capsaicin but resistant to SP antagonist. Antidromic stimulation of the dorsal root(T7-12) had no considerable effect on the jejunal motility, although ventral root stimulation produced an inhibition frequently and an excitation infrequently.

From the results, it is revealed that SP neurons produce the jejunal contraction through nicotinic and cholinergic mechanisms, and may be considered two possible pathways: (1) Sympathetic postganglionic cholinergic neurons which connect to preganglionic cholinergic neurons from the ventral root in celiac ganglion excite intrinsic cholinergic motor neurons, resulting in the jejunal contractions sensitive to C_6 and atropine. (2) SP neurons(maybe sensory) originating in celiac ganglion and running through the mesenteric nerve terminate intrinsic cholinergic interneurons, which excite cholinergic motor neurons.

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ROLE OF GABAERGIC NEURON IN THE BOMBESIN-INDUCED CONTRACTION OF INTESTINE. TANIYAMA, K. Dept. Pharmacol., Kobe Univ. Sch. Med., Kobe 650

The mechanism of action of bombesin was examined in the longitudinal muscle with myenteric plexus (L-M) preparation from guinea pig ileum. Bombesin ($3x10^{-10}$ - $3x10^{-7}$M) induced the contraction, in a concentration dependent manner. Tetrodotoxin (TTX) inhibited completely the bombesin-induced contraction. Scopolamine inhibited completely the contractions induced by bombesin at low concentrations, but did partially those by high concentrations. Bombesin evoked the Ca^{2+}-dependent and TTX-sensitive release of acetylcholine (ACh) from the L-M preparation preloaded with ^{3}H-choline. Scopolamine and hexamethonium did not alter the bombesin-evoked ACh release. The prior application of bombesin induced the desensitization of response to subsequent application of bombesin. Bicuculline inhibited the bombesin-evoked contraction and ACh release. Bombesin evoked the Ca^{2+}-dependent and TTX-sensitive release of GABA. Bombesin-evoked release of GABA was not altered by scopolamine and hexamethonium, but inhibited by the prior application of bombesin. These results indicate that bombesin induces contraction mainly through cholinergic neuron and partially through non-cholinergic excitatory neuron. The GABAergic neuron may be involved in a part of bombesin-mediated stimulation of cholinergic neuron.

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EFFECTS OF MIANSERIN ON THE NICOTINIC TRANSMISSION IN BULLFROG SYMPATHETIC GANGLIA. ARIYOSHI, M. AND AKASU, T., Department of Physiology, Kurume University School of Medicine, 67 Asahi-machi, Kurume 830

The effect of mianserin, an antidepressant, on cholinergic transmission was investigated with intracellular microelectrode techniques in bullfrog sympathetic ganglia. At a concentration of 0.5-100 μM, mianserin did not change the resting membrane potential and resistance of the ganglion cell. Mianserin blocked the action potential elicited by the stimulation of preganglionic nerve fibers. The amplitude of fast excitatory postsynaptic potentials (fast EPSPs) was depressed by mianserin. The mean quantal content of fast EPSPs calculated by the variance method was depressed during a mianserin treatment. Mianserin depressed the acetylcholine (ACh) induced potentials (ACh potentials) produced by an iontophoretic application of ACh in a Ringer solution containing atropine, while it had no effect on the muscarinic ACh action. These results suggest that mianserin depressed both the sensitivity of the nicotinic ACh receptor and the ACh-release from presynaptic nerve terminals resulting in a blockage of the nicotinic transmission in sympathetic ganglia.

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INFLUENCE OF NGF ON DIFFERENTIATION OF RAT SYMPATHETIC NEURONS.
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The neuronal phenotypic differentiation of precursor cells is assumed to start after their final proliferation. In the present study we examined the influence of exogenous NGF on the time of the last DNA replication of superior cervical ganglionic neurons in rat embryos. Using monoclonal antibodies against BUdR, the replicating cells were detected by demonstrating immuno-histochemically the incorporation of BUdR into their nuclear DNA(Gratzner, 1982). Embryos were labelled at different stages of development by a single intravenous injection of BUdR to their mothers. Ganglion was isolated from the fetus after stage E15 and subsequently the cells were cultured. After the morphologic characteristics of the neurons were identified in cultur, the cells were fixed and examined. The exogenous NGF supply brought significant reduction in the percentage of labelled sympathetic neurons, while there was no significant difference in sensory neurons with or without NGF supply. This observation suggests that NGF may contribute to promote the differentiation of sympathoadrenal precursors into neurons in addition to as a survival factor.

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TWO TYPES OF NERVE FIBER REGENERATION FROM TRIGEMINAL SENSORY CELLS OF SHREWMOUSE IN A CHEMICALLY-DEFINED TISSUE CULTURE CONDITION. FUKUDA,J., AOSAKI,T., KEINO,K. and YAMAGUCHI, T.*, Dept. of Physiol., Fac. of Med., Univ. of Tokyo, Bunkyo-ku, Tokyo 113 and * Dept. of Biochem., Tokyo Women's Med. Coll., Shinjuku-ku, Tokyo 162.

Nerve cells isolated from trigeminal ganglia (TRG) of shrewmouse of various ages (newborn, adult and aged) were cultured in a serum-free medium, and the regeneration of neurites was compared between cultures made with and without nerve growth factor (NGF, from adult mouse salivary glands). The **first** finding is that the nerve cells are classified into two types, L-cells (cells with long neurites) and S-cells (those with short neurites) on the basis of growth patterns of neurites (the total length of neurites, number of arborization in each neurite, length of inter-arborization, number of neurites in each cells). The **second** finding is that the NGF-dependence is different between the L-cells and S-cells. Namely, although the S-cells of newborn animals were totally NGF-dependent, those of adult and aged animals were independent of the NGF. In contrast, L-cells of the newborn and the adult animals were dependent on the NGF. The L-cells, however, became finally independent of the NGF in the aged animals. **It is thus concluded** that the two types of sensory nerve cells underwent the different ways of changes in the NGF-dependence in association with aging.

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LOCAL PREMOTOR FUNCTION OF CRAYFISH ASCENDING INTERNERONS. NAGAYAMA, T. AND HISADA, M.
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Ascending interneurons originating from the last abdominal ganglion of the crayfish, Procambarus clarkii receive sensory input from the tactile hairs on the uropods. In addition to the documented characteristics of these interneurons as the secondary sensory interneurons, we found that they also function as the premotor interneurons to the uropod motoneurons through the local circuits. Presence of the output synapses on the dendrites revealed by EM supplements this physiological finding. The ascending interneurons are found to have monosynaptic direct connections as well as multisynaptic indirect connections via local non-spiking interneurons. They are also frequently mutually interconnected through monosynaptic and multisynaptic pathways. Complex interconnections between the ascending interneurons and other classes of neurons appears to be quite extensive, and seem to be necessiating a revision of the classical functional categorization of various classes of neurons.

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AUTOTOMY AND NEURONAL SPONTANEOUS HYPERACTIVITY IN SPINAL CORD FOLLOWING PERIPHERAL NERVE SECTION OF THE RAT.

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Autotomy of rats induced by peripheral nerve section can be considered to be an animal model of phantom limb pain or sensation in man.

In the behavioral study of the rats sectioned the sciatic and saphenus nerves unilaterally, the daily strong electrical stimulation(ES) (30Hz, 1hour/day) near the stump or to the contralateral limb suppressed the appearance of autotomy. The daily weak ES near the stump accelerated it.

In the electrophysiological study, units, having high level spontaneous discharge with dramatic increases(30-200 spikes/sec) , were found in the spinal cord (L3-L5) 5 - 39 days after sciatic nerve section. These units with spontaneous bursting activity were found more in autotomy rats than in no-autotomy ones. Such hyperactivities were never found in intact rats. The spontaneous hyperactivities of some units were suppressed for a few minutes after strong train ES to the cut nerve or to the contralateral sciatic nerve. Weak train ES to the cut nerve showed suppression or facilitation on hyperactivities of some units.

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SYNAPTIC INPUTS FROM THE TRIGEMINAL AFFERENTS TO THE AXOTOMIZED SPINAL ACCESSORY MOTONEURONS OF CATS.

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Synaptic potentials in the spinal accessory(Acc) motoneurons of cats anaesthetized with pentobarbital sodium were recorded on stimulation of the infraorbital branch of the trigeminal nerve(IO) after axotomy. By stimulation of the ipsilateral IO, the EPSPs with latencies of 2.5-6.0 msec(N=17) were evoked. Furthermore, ipsilateral IO stimulation evoked the IPSPs with latencies of 4.0-13.8 msec in 68 neurons(81%) out of the 85 neurons. Stimulation of the contralateral IO produced also polysynaptic IPSPs as well as EPSPs. The IPSPs had the latencies of 4.5-12.5 msec in 41 neurons(77% of 53 neurons). As is distinct from the axotomized facial motoneurons, there was no reduction in the number of the IPSPs elicited in the Acc neurons after axotomy. The time to peak of the IPSPs ranged from 5.0 to 11.3 msec(mean 9.4 msec, N=28), while it was 8.3 msec on the average in the normal Acc neurons. It can therefore be presumed that the inhibitory volleys originated from the trigeminal afferents impinge upon the distal part of the dendrites of the Acc neurons rahter than the soma and the proximal part of the dendrites.

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Activities of the dendrites of spinal motoneurons in cats

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Spinal motoneurons of normal infant pigs could show spikes of about 2 msec in duration and less than 5 mV in amplitude which were referred to as D-spikes (Fujita et al., J. Physiol., London, 383: 171-190, 1987). In chronically stimulation motoneurons, more D-spikes were encountered and there occurred all-or-none slow waves (duration: more than 10 msec, amplitude: 2-12 mV) which were referred to as D-waves. There was evidence indicating that both D-spikes and D-waves originated in the dendrites. In a decerebrate, non-anaesthetized state spinal motoneurons of normal cats could exhibit 2-5 different D-spikes and/or 2 different D-waves in the same cell, as judged from differences in threshold and waveform. D-waves were thought to represent some kind of plastic changes induced in the motoneurone during development. D-spikes of normal motoneurons were round-peaked, making a conspicuous contrast to sharp-peaked dendritic spikes in axotomized motoneurons as studied by other investigators, although sharp-peaked D-spikes were seen also in normal motoneurons. It was further shown that all-or-none potentials were superimposed on the A-spike to trigger the B-spike. It was possible to explain these potentials as originating in the dendrites.

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DEVELOPMENT OF LOCOMOTOR ACTIVITY IN THE LUMBAR SPINAL CORD OF RAT FETUSES. KUDO, N., AND YAMADA, T. Dept. of Physiol., Inst. of Basic Med. Sci., Univ. of Tsukuba, Ibaraki 305, Japan.

The development of rhythmic motor activity was studied using isolated lumbar spinal cord preparations of rat fetuses (embryonic day (E) 14.5-20.5). Rhythmic motor activity was evoked by bath application of N-methyl-D,L-aspartate (NMA) and monitored by means of glass suction electrodes through the ventral roots on both sides of the fourth lumbar spinal cord. It was found that rhythmic activity in the ventral roots was elicited by bath-applied NMA (15-30 μM) at and after E15.5. The mean frequency of the rhythmic activity increased with age, from 0.05 Hz at E15.5 to 0.44 Hz at E20.5 (NMA 20 μM). The rhythmic activity was also evoked at all stages after splitting the spinal cord midsagittally, indicating that each side of the spinal cord has neuronal circuits for rhythm generation. The phase relationship of the rhythmic activities between the two sides of the ventral roots was synchronous at E15.5 and E16.5, independent at E17.5 and alternating at E18.5-20.5. At E17.5, the addition of strychnine changed the independent rhythmic activities between the two sides to a synchronous pattern, while at earlier stages it had no effect. This suggests that some inhibitory pathways begin to play an important role for functional coupling between the two sides of neuronal circuits at this stage.

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PROJECTION LEVELS OF DESCENDING PATHWAYS ELICITING FORELIMB STEPPING IN THE CAT CERVICAL CORD. Mitsuyo HISHINUMA* AND Takashi YAMAGUCHI. Institute of Basic Medical Sciences, University of Tsukuba, Sakura, Niihari, Ibaraki 305, JAPAN.

It was shown descending pathways eliciting forelimb stepping are located in the C1-C3 lateral funiculus(LF). To know their entry segments from the LF into the grey matter, we studied effects of lesions on forelimb locomotion in decerebrate cats with the lower thoracic cord transected. Three kinds of lesions were made: LF transection in the C1-T2, parasagittal cut(each cut, ~10 mm long) between the LF and grey matter in the C1-C6 and transverse cut of the middle part of the spinal cord(midsection), including the dorsal column, grey matter and the whole or a part of the ventral funiculus(VF), in the C1-C6. LF transections at the level below the C8 hardly affected locomotion, but those at the C5-C7 made eliciting locomotion markedly difficult. Parasagittal cut and midsections saving the ventromedial VF never abolished locomotor rhythm at any segments in the C1-C6. Further, parasagittal cut or LF transections including a medial part of the C1-C4 LF(not C5-C6) weakened limb flexion during stepping. The midsections including the whole VF weakened extension, while the rhythm remained. It was concluded (1)the LF-descending pathways, probably important for rhythm generation, project into the C6-C7, partly C5 and C8; (2)the medial LF-system, probably related to flexion, seems to project into the caudal C4; (3)the VF-system mainly regulates extensor activities.

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THE ROLE OF COLLATERAL SPROUTING IN THE FUNCTIONAL RECOVERY OF CORTICOSPINAL CONNECTIONS AFTER SPINAL HEMISECTION IN MONKEYS.
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We investigated whether the corticospinal(CS) fibers increase their connections with lumbosacral neurons after spinal hemisection, using the retrograde and anterograde HRP methods. In one group of monkeys several months after spinal hemisection at the lower thoracic cord, HRP was injected into the lumbosacral cord unilaterally on the hemisected side at a level caudal to the lesion. Control injections were performed in intact monkeys and in monkeys immediately after hemisection. In all animals, CS neurons in the motor cortex were retrogradely labeled bilaterally. However, in the chronically spinal hemisected monkeys, the number of the labeled neurons was significantly increased on the side ipsilateral to the lesion. In other group of chronic monkeys, WGA(wheat germ agglutinin)-HRP was injected to the motor cortex on the side ipsilateral to the lesion. Labeled CS fibers were traced anterogradely in lumbosacral segments on the hemisected side and the distribution of terminal fibers was examined. It is suggested that CS connections to lumbosacral motoneurons are newly formed on the hemisected side and this fiber distribution may be due to collateral sprouting of intact CS fibers.

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

Lumbar spinal cord was divided longitudinally in order to investigate if bilateral coordination of the hindlimbs were affected by the section. The separation was performed aseptically from L_1 through L_5 in 6 cats as a first step of the investigation. After the cats recovered from the operation, they were repeatedly tested for as long as 3-4 months on phase relations between left and right hindlimbs as well as fore- and hindlimbs using the methods as was reported earlier (Kato et al, 1984). Accuracy of the foot placing was tested by encouraging the cats to walk on the grid (Kato, 1986). The cats were also encouraged to stand on force plates (Kato et al, 1985) and electric stimulation was applied to one hindlimb to test the response pattern of the four limbs. All of these investigations revealed the response patterns of the chronic cats were those of the spinal intact cats. Therefore tentative conclusion is this part of lumbar segments play little role for coordination of the limbs.

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DISTRIBUTION PATTERN OF COLLATERAL BRANCHES OF UPPER CERVICAL INSPIRATORY NEURONS IN THE CAT SPINAL CORD. SASAKI, S.-I., EDAMURA, M. AND AOKI, M. Department of Physiology, Sapporo Medical College, S.1, W.17, Chuo-ku, Sapporo 060 Japan.

To investigate intraspinal branching patterns of single upper cervical inspiratory neurons, we recorded extracellular spike activities from cell bodies of 23 neurons in the lateral border of the grey matter of C1, C2 spinal cord in anesthetized cats and mapped the distribution of effective stimulating sites for antidromic activation in and around the phrenic nucleus of C5, C6. Three out of 23 units tested were found to have collateral branches in C5, C6. These collateral branches were mainly distributed in the medial part of the grey matter, and some were in the ventral funiculus. Twenty units were found to have no branches and passing stem axons were located in the ventro-lateral funiculus. These results suggested that the cervical inspiratory neurons terminate on the dendrites of phrenic motoneurons. Cross-correlations of the 7 single cervical inspiratory units were examined with the nerve discharge of phrenic nerve and 4 units with the external intercostal nerve discharge. However, so far, no positive evidence of monosynaptic connections has been obtained. Recording sites of 17 neurons were histologically identified, which were localized in the margin of intermediate zone of the grey matter, with some in the white matter.

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CORTICOSPINAL AND RUBROSPINAL EFFECTS ON INTERNEURONES MEDIATING SKIN REFLEXES IN THE FORELIMB SEGMENTS OF THE CAT. HONGO, T., OHKI, Y. AND SASAKI, M. Dept. Neurophysiol., Institute of Brain Res., Sch. Med., Univ. of Tokyo, Tokyo 113

Descending effects from the corticospinal and rubrospinal tracts on interneurones in the skin reflex paths to forelimb motoneurones were studied in cats anesthetized with chloralose or Nembutal. Stimulation of these tracts facilitated skin reflexes at the interneuronal level. Polysynaptic reflex actions were facilitated from both the tracts, whereas disynaptic reflex actions were affected from the corticospinal but rarely from the rubrospinal tract. Retrogradely labelled neurones after HRP injection into the T1 motor nucleus distributed in laminae IV-VII of mainly C6-C8 segments. Neurones excited from skin afferents and antidromically activated from the T1 motor nucleus or the C8-T1 lateral funiculus were found in the same areas. They were thought to be the last order neurones in the skin reflex paths, since mapping experiments showed that five of the six examined neurones had low thresholds foci in the motor nucleus. The antidromically activated neurones with monosynaptic skin input were excited from the corticospinal but scarcely from the rubrospinal tract, while those with polysynaptic skin inputs were affected from both. Differences in neuronal organizations of the corticospinal and rubrospinal actions on skin reflex pathways are discussed.

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SYNAPTIC ACTIONS OF THE CONTRALATERAL Aδ AND C FIBERS ON CAT HINDLIMB MOTONEURONS. HORI, Y., *ENDO, K. AND WATANABE, S. Dept. Physiol., Sch. Med., Kyorin Univ., Tokyo 181 and *Dept. Physiol., Fac. Med., Kyoto Univ., Kyoto 606

Synaptic actions of the contralateral high-threshold afferent fibers on hindlimb motoneurons were studied in the cat anesthetized with sodium pentobarbital. Stimulation of Aδ fibers in the contralateral sural nerve produced EPSPs in 18% of flexor and 24% of extensor motoneurons tested, whereas IPSPs were produced by Aδ volleys in 23% of flexor and 13% of extensor motoneurons. EPSPs with longer latencies and longer durations were evoked by C volleys in the contralateral sural nerve in 25% of flexor and 31% of extensor motoneurons. C volleys in the contralateral sural nerve produced IPSPs in 16% of flexor and 9% of extensor motoneurons. In the late phase of PSPs evoked by C volleys, a significant increase in membrane resistance was observed, showing the probable existence of disfacilitatory or disinhibitory synaptic effects near the motoneuronal soma. Reciprocal patterns between PSPs evoked by Aδ and C volleys in the ipsilateral and the contralateral sural nerve were observed only in 8% of motoneurons tested.

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FACILITATORY EFFECT OF CGRP ON THE RECOVERY OF REDUCED TWITCH AFTER TETANIC STIMULATION. KUWAZAWA, J., SATO, M., KAWATANI, M. AND TAKESHIGE, C. Department of Physiology, School of Medicine, Showa University, Shinagawa, Tokyo, 142.

Tetanic 10Hz stimulation was applied fo about 60 minutes to the gastrocnemius muscle of gunea pig anesthetized with nembutal. The reduced twitch height after tetanic stimulation was estimated to indicate pain of the muscle. Reduced twitch height after tetanic stimulation was recoverd by oblique needle insertion to the muscle. Similar effect was produced by intraarterial injection of 0.3ml saline, 19ng prostaglandin E2 or 60ug isoproterenol. Stimulation of sciatic nerve to the muscle under treatment of d-tubocurarine produced similar effect to the needling and this effect was abolished by atropine. Both substance P(SP) and calcitonin gene-related peptide(CGRP), produced similar effect. The effect of SP was not, but that of the CGRP was abolished by atropine.

Relief of the muscle pain by needling to the muscle might caused by the mechanism that needling stimulated the CGRP containing primary afferent nerve ending in the muscle and excitation propagated to the axon-colaterales attached to the cholinergic nerve endings facilitating the release of acetylcholine to dilate the artery in the muscle, since it was previously found that denervation or treatment of capsaicin or atropine abolished needling effect.

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PATTERNS OF HEAD-TURNING INDUCED BY ELECTRICAL STIMULATION OF THE SUBSTANTIA NIGRA REGION. OHNO,T., AND TSUBOKAWA,H. Dept. of Physiol., Inst. of Basic Med. Sci., The Univ. of Tsukuba, Ibaraki 305

It has been suggested that contraversive head-turning(cHT) induced by repetitive electrical stimulation of the caudate nucleus(Cd) on one side is brought about by way of a pathway through the substantia nigra pars reticulata(SNr) and the superior colliculus(SC). Since the synaptic action of Cd output neurons on SNr neurons is inhibitory in nature, it will be expected that the activation of SNr neurons induces ipsiversive HT. In this study, however, unilateral stimulation (100 Hz, 200 pulses, less than 150 μA) of the SNr region in the alert cats induced cHT. Similar results were obtained in cats in which the frontal cortex (Cx) and Cd had been lesioned. Therefore, it was assumed that SNr-induced cHT was not brought about as the effect of the activation of cortico-tectal fibers passing through SNr or afferents from the Cd. The effect of repetitive stimulation of the SNr on SC neurons was examined in acute experiments with anesthetized cats. In the majority of SC neurons sampled from cats with lesions in the Cx and the Cd, the firing frequency was increased by repetitive stimulation of the SNr region, even with the intensity which induced inhibition or excitation-inhibition sequence with single shock. This increase in the firing rate of SC neurons during repetitive stimulation may at least in part account for the direction of the HT.

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EFFECTS OF LESION OF THE PARAMEDIAN PONTO-MEDULLARY RETICULAR FORMATION ON THE VISUALLY GUIDED ORIENTING MOVEMENT OF THE HEAD IN CATS. ISA, T. AND SASAKI, S. Dept. of Neurophysiol., Institute of Brain Res., Sch. Med., Univ. of Tokyo, Tokyo 113

Cats were trained to fixate their eyes on a light spot in the center of the perimeter and then to rapidly orient the head laterally toward another spot in the periphery. Cats turned the head slowly at first, beginning 0-50 msec before the accompanied saccadic eye movements, and then quickly to the target. The maximum angular velocity of the head turning linearly related to its amplitude (slope; 9-10°/sec/deg). A burst EMG response in the ipsilateral m. splenius and suppression of EMG activity in the contralateral m. splenius and bilateral m. biventer cervicis preceded the saccades by 0-90 msec, 50-150 msec and 80-150 msec, respectively. A fairy localized lesion in the paramedian ponto-medullary reticular formation (PPMR) (Horsley-Clarke plane, P4-P8, from midline to 2 mm laterally, sparing the abducens nucleus) was made unilaterally by injection of kainic acid (0.1%, 3-6 μl). After the lesion, the orienting movement to the intact side was unchanged both in speed and amplitude, but the cat couldn't move to the lesioned side in most trials. When occurred, the movement was very slow (3-4°/sec/deg) and without saccades. The results suggest the involvement of PPMR in the visually guided movement of the head.

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INHIBITION OF MICTURITION, DEFECATION, STRAINING AND JAW-OPENING REFLEXES BY STIMULATION OF THE MIDBRAIN IN DECEREBRATE DOGS. FUKUDA, H. AND KOGA, T. Dept. of Physiol., Kawasaki Med. School, Kurashiki 701-01

Micturition, defecation and straining reflexes elicited by stimulation of pelvic afferents were inhibited by stimulation of the periaqueductal gray of the midbrain and the reticular formation ventro-laterally adjacent to the gray in decerebrate dogs. Since both midbrain areas correspond to the region concerning with endogenous analgesia, the analgesic system seems to inhibit transmission of pelvic sensory impulses in the spinal cord. This possibility was examined in this study. Jaw-opening reflex elicited by tooth pulp stimulation was also suppressed by stimulation of both midbrain areas with similar threshold intensity. Centrifugal discharges in pelvic vesical and rectal branches evoked by pontine stimulation were not reduced by stimulation of both midbrain areas. In the contrast, field potential evoked by stimulation pelvic afferents and recorded from the lateral funiculus at the C3 segment was suppressed by stimulation of both midbrain areas still after ipsilateral hemisection of the C2 segment. However, naloxone (3 mg/kg, i.v.) did not block the inhibition of these 4 reflexes by both midbrain stimuli.

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THE [14C]2-DEOXYGLUCOSE TRACER ANALYSIS ON SUPRASPINAL MECHANISMS INVOLVING IN FORELIMB STEPPING OF THALAMIC CATS. KOGURE I., FUWA T. AND SHIMAMURA M. Dept. of Neurophysiol., Tokyo Metro. Inst. for Neurosci., Fuchu-city, Tokyo 183 (Japan)

Trace amounts of [14C]2-deoxyglucose (2-DG) were used to detect supraspinal areas involved in forelimb stepping in thalamic and low spinal cats. Under ether anesthesia, cats were transected at stereotaxic A12 level and Th10 segemnt. Two hours later, 50 uCi/Kg of 2-DG was infused i.v. and one of four procedures was followed: three cats stepped on a motor-driven treadmill (Stepping), three were kept in a stationary standing position (Rigidity), and two were stimulated in the mesencephalic locomotor region (MLR-induced). Absolute optical densities of the autoradiograms corresponding to identified anatomical structures of the brainstem, were generally in the following order; Stepping > MLR-induced > Rigidity. In the stepping cats both on moving treadmill and by MLR-induced, the 2-DG ratio, relative to the pyramidal tract, was highest in the cuneate nucleus, paramedian reticular formation, lateral reticular formation, lateral vestibular nucleus and pontine tegmental field. In the Rigid cat the 2-DG ratio was highest in the medial vestibular nucleus, ventral tegmental nucleus and periaqueductal gray. These results suggest that those nuclei in the brainstem may be related the supraspinal control on the rigidity and stepping of the thalamic cats.

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EFFECTS OF CEREBELLER NUCLEUS INTERPOSITUS STIMULATION ON TRIGEMINAL MOTOR SYSTEM. KATAYAMA, T., HASHIMOTO, N., ISHIWATA, Y* AND NAKAMURA, Y. Depts. Physiol. and *Orthod. II, Fac. Dent., Tokyo Med. Dent. Univ., Bunkyo-ku, Tokyo 113

Effects of stimulation of the medial part of the lateral group of the deep cerebellar nuculei (corresponding to the nucleus interpositus, NIP, of other rodents) were studied on jaw-closing (JCR) and -opening reflexes (JOR) and the intracellular activity of masseter (MAs) and digastric motoneurons (DIs) identified by antidromic responses to stimulation of the masseter and digastric nerves, respectively, in ketamine-anesthetized guinea pigs. JCR was monitored by the masseter EMG evoked by stimulation of the ipsilateral trigeminal mesencephalic nucleus, and JOR was monitored by the field potential of the anterior digastric motoneuron pool evoked by stimulation of the ipsilateral spinal trigeminal nucleus. The following results were obtained. 1) NIP stimulation evoked a short-latency suppression followed by a facilitation of the JCR, and a short-latency, rather long-lasting facilitation of the JOR, bilaterally with an ipsilateral dominance. 2) NIP stimulation evoked a short-latency hyperpolarizing potential in MAs which was reversed to a depolarization by Cl^- injection and abolished by strychnine. 3) NIP stimulation evoked a short-latency depolarizing potential in DIs, whose amplitude was decreaced and increaced by intracellular de- and hyperpolarizing current injection, respectively. We conclude that NIP stimulation evokes a short-latency reciprocal effect on trigeminal motoneurons, inhibition of MAs and facilitation of DIs, which is responsible for the NIP induced depression of JCR and facilitation of JOR after a short-latency.

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LOCALIZATION OF CENTRAL RHYTHM GENERATOR AND ITS INPUT PATHWAY INVOLVED IN MESENCEPHALICALLY INDUCED RHYTHMICAL MASTICATORY MOVEMENT IN THE GUINEA PIG. HASHIMOTO, N., KATAYAMA, T., ISHIWATA, Y* AND NAKAMURA, Y. Depts. Physiol. and *Orthod. II., Fac. Dent., Tokyo Med. Dent. Univ., Tokyo 113

We reported that electrical and chemical stimulation of the dorsolateral part of the mesencephalic reticular formation (mesencephalic masticatory region, MMR) in guinea pigs induced a rhythmical jaw movement resembling mastication, and that the MMR-induced rhythm could be generated centrally in the brain stem. In the present study, we investigated the localization of the central rhythm generator and its input pathway from the MMR in ketamine-anesthetized guinea pigs. The following results were obtained: 1) The MMR-induced rhythm was unaffected by a bilateral lesion of the pyramidal tract at the pontine level, but it was abolished by a midline section through the mesencephalon. 2) Repetitive MMR stimulation induced a field potential in the oral portion of the nucleus reticularis gigantocellularis (GCo), which periodically fluctuated in the masticatory rhythm coincident with the rhythmical mutiple unit activity in the digastric motoneuron pool (DIG-MUA). 3) After lesions of the GCo, the rhythmical DIG-MUA was no longer induced by the MMR stimulation. We conclude that the effect of the MMR stimulation is mediated to the GCo for the rhythm generation by way of the contralateral mesencephalon and of a route other than the pyramidal tract.

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DISCHARGE PATTERNS OF THE MESENCEPHALIC TRIGEMINAL NEURONS DURING MASTICATORY JAW MOVEMENTS IN THE RABBIT. NAGASHIMA, T., YOSHIDA, M.*, MASUDA, Y., INOUE, T. AND MORIMOTO, T. Dept. Oral Physiol., Osaka Univ., Faculty of Dentistry, Osaka 565

Contribution of muscle receptors to the control of masticatory jaw movements were studied in the urethane anesthetized rabbit. Unit discharges were recorded from the trigeminal mesencephalic nucleus (Mes V) during rhythmic jaw movements elicited by applying a thin test substance between opposing molars. These Mes V units showed discharges locked to certain phases of a single masticatory cycle. They were classified into 4 types, depending on the time relation between unit discharges and the jaw-movement; 1) those fired predominantly on the jaw-opening phase, 2) those fired on the jaw-closing phase, 3) those excited once in each phase and 4) those fired within the period of the masseteric burst. Since the three former were readily activated by slight depression of the mandible, they were regarded as muscle spindle units. On the other hand, the last type of the units showed the higher threshold for the same stimulus and was thus regarded as tendon organ units. The putative muscle spindle units which were excited perior to or during the jaw-closing muscle burst may contribute to the facilitation of jaw-closing muscles during chewing the test substance.

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PHYSIOLOGICAL PROPERTIES OF TRIGEMINAL NEURONS PROJECTING TO MESENCEPHALIC PARABRACHIAL AREA. HAYASHI, H. AND TABATA, T. Dept. Physiol. Sch. Dent. Tohoku Univ. Sendai 980

Retrograde and orthograde tracing experiments show a large bilateral projection arising from all spinal segments with particularly heavy termination in the mesencephalic parabrachial area (MPBA) including the mesencephalic parabrachial nucleus, lateral periaqueductal gray matter and nucleus cuneiformis. The present study is concerned with the identification and characterization of the sensory trigeminal neurons projecting to MPBA. A total of 141 neurons were identified as trigeminomesencephalic projection neurons (86 in Vc and 55 in Vms to Vi). They were distributed within the nucleus, spinal trigeminal tract or in the adjacent area. Number of contralaterally projecting neurons was larger (81) than that of ipsilaterally projecting ones(60) and 18 neurons were projecting to the both sides. Sixty of them projected also to thalamus. Their receptive fields(RF) were distributed over the ipsilateral facial and/or oral area except 38 neurons which RF were not found. In Vc, nocireceptive neurons (NS and WDR) were predominant. In the rostral subnuclei number of nocireceptive neurons was significant, although LTM neurons were more than the other two types. It is suggested that significant contribution of this system to the sensory processing on pain.

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CALCIUM-DEPENDENT RESPONSES OF SUBSTANTIA NIGRA NEURONS STUDIED IN VITRO. MATSUDA,Y., FUJIMURA,K. AND YOSHIDA,S.
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Cationic Ca-channel blockers (Cd^{++}, Mn^{++}) or Ca^{++}-free saline were applied to neurons of the guinea-pig substantia nigra maintained in a slice preparation in order to study the contribution of Ca^{++} to electrophysiological responses of the neurons. In presumed dopaminergic neurons in the pars compacta, the procedures resulted in a shortening of the duration of the spike and afterhyperpolarization, suggesting the contribution of Ca currents and Ca-activated (K) currents to the generation of action potentials. Ca currents also appeared to underlie the depolarizing potential preceding the intrinsic spontaneous spikes and application of Cd^{++} or Ca^{++}-free saline suppressed the spontaneous activities. Ca^{++} was also necessary for the generation of the depolarizing potential which occurred as a rebound response on cessation of hyperpolarizing current pulse. However, the potential was not depressed by Cd^{++} ($\leqq$1mM). Ca^{++}-dependent but Cd^{++}-resistant potentials were also noted as a depolarizing after-potential in certain nigral neurons which were considered to be non-dopaminergic cells.

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IN VIVO DIALYSIS MEASUREMENT OF DOPAMINE AND ITS METABOLITES AROUND A TRANSPLANTED AREA IN THE RAT STRIATUM. NISHINO, H., ONO, T., SHIBATA, R. AND NISHIJO, H. Dept. of Physiol., Fac. of Med., Toyama Med. and Pharmaceu. Univ., Toyama 930-01

Cell suspension of fetal rat substantia nigra or newborn rat adrenal medulla was transplanted in the caudate nucleus of rats with unilateral lesions in the nigrostriatal dopamine pathway. In one third of the transplanted animals circling due to Met-amphetamine decreased in the 4th week after transplantation. Dopamine and its metabolites (DOPAC, HVA), measured by in vivo dialysis, recovered in behavior recovered animals to 30 to 50% of the levels in intact controls, and remained below 10% of control levels in nonrecovered animals. In recovered animals dopamine was increased to several times, and DOPAC and HVA decreased slightly by Met-amphetamine (5 mg/kg) or by increase of the arousal level. The effects of Met-amphetamine and arousal were detected in both nigral transplanted and medullary transplanted animals. Data suggest that transplanted nigral and medullary cells have metabolic turnover similar to that of intact dopamine cells.

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PLASTICITY OF CROSSED CORTICORUBRAL FIBERS IN KITTENS AFTER UNILATERAL LESIONS OF THE SENSORI-MOTOR CORTEX. HIGASHI, S.*, HIROSE, S.* AND MURAKAMI, F. Department of Biophysical Engineering, Faculty of Enginering Science, Osaka University, Osaka, Japan

Presence of crossed corticorubral (CR) fibers in the kitten whose sensorimotor cortex (SMC) was ablated unilaterally, has been attributed to collateral sprouting. The present study was undertaken to examine an alternative possibility that crossed CR fibers were caused by the retention of crossed projections present in normal neonatal animals. Plant lectin, phaseolus vulgaris leuco-agglutinin was injected iontophoretically into SMC of the kitten about 20 - 40 days after birth and CR fibers were stained immunocytochemically. Two weeks after injection, abundunt CR fibers with numerous varicosities were observed in the ipsilateral red nucleus (RN). CR fibers, although much fewer, were found in the contralateral RN, too. By contrast, many labelled fibers were seen in the contralateral RN of the kitten whose SMC had been ablated 20 - 40 days after birth. Therefore, the crossed fibers observed in animals with neonatal SMC lesion may be ascribed to both collateral sprouting and retention of crossed fibers.

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CENTRAL GRAY MATTER PROJECTION TO THE AMBIGUAL AND PERIAMBIGUAL REGIONS IN THE RAT. YAJIMA, Y. AND HAYASHI, Y. Dept. of Physiol., Hyogo College of Med., Nishinomiya, Hyogo 663

Neurons in and near the nucleus ambiguus(NA) showed repetitive burst firings prior to ultrasounds induced by stimulation of the central gray matter(PAG) in the rat. Some of them had spontaneous discharges associated with expiration(exp neurons) but some did not(silent neurons). Their electrophysiological properties and distribution in NA region were compared in chronic or acute anesthetized rats. Histological examination revealed that silent neurons tended to be found more frequently in NA while exp neurons in the periambigual region. As for repetitive discharges induced by PAG stimulation, silent neurons had shorter latency and higher discharge frequency than exp neurons. Laryngeal motoneurons activated by antidromic stimulation of the recurrent laryngeal nerve were almost exclusively located in NA and showed repetitive discharges by PAG stimulation with longer latency of about 200 msec. The results suggest that exp neurons located in NA were laryngeal motoneurons with excitatory input during expiration and those in the periambigual region extralaryngeal neurons including premotorneurons for expiration.

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MESODIENCEPHALIC NEURONS RELATED TO VERTICAL EYE OR HEAD MOVEMENTS: EXCITATORY INPUTS FROM VESTIBULAR NUCLEUS (VN). NAKAO, S., SHIRAISHI, Y. AND OIKAWA, T. Dept. of Physiol., Tottori Univ. Sch. of Med., Yonago 683

Extracellular spikes of single neurons related to vertical eye or head movements were recorded in the medial mesodiencephalic junction of chronic, alert cats with a stimulating microelectrode in the VN on each side. The nature of excitatory synaptic inputs to these neurons from the VN was investigated by measuring the latency of their VN-induced spikes. The following results were obtained. (1) Long-lead upward-preferred burst neurons received di- or polysynaptic inputs from the ipsilateral VN. (2) Most medium-lead upward- or downward-preferred burst neurons received polysynaptic inputs from the ipsi- and/or contralateral VNs. (3) Many downward-on burst-tonic neurons received monosynaptic inputs from the contralateral VN. (4) All tonic neurons received mono- or disynaptic inputs only from the contralateral VN. (5) Other neurons unrelated to eye movements, but responding to head rotation, also received monosynaptic inputs only from the contralateral VN. In conclusion, various types of vertical eye or head movement-related neurons in the mesodiencephalic junction differentially receive excitatory synaptic inputs from the VN.

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LOCATION AND PROPERTIES OF VESTIBULOCOLLIC NEURONS IN CAT ANTERIOR CANAL SYSTEM. ISU, N.[1], NAKASHIMA, H.[2], SATOH, S.[2], UCHINO, Y., ICHIKAWA, T., and WATANABE, S. Dept. Physiol., Kyorin Univ. Sch. Med., Mitaka, Tokyo 181, [1]National Aerospace Lab., Chofu, Tokyo 182, [2]Dept. Oto-Laryngol., St. Marianna Univ., Kawasaki, Kanagawa 213.

Unit activities of secondary vestibulocollic (VC) neurons sending axons to the C_1 neck extensor motoneuron pools, excitatory targets of the anterior canal, were recorded extracellularly. Twenty-three VC neurons sent axons to the ipsilateral extensor motoneuron pool via the lateral vestibulospinal tract, while 8 VC neurons via the medial vestibulospinal tract. None of them were activated from the oculomotor nuclei. Twenty-two of 23 neurons in the former group were located in the ventral part of the lateral nucleus. It was confirmed in 5 neurons that they produce monosynaptic EPSPs with fast rising and short half width in extensor motoneurons (16/16 motoneurons). The latter group of VC neurons were located in the descending nucleus and the ventral part of the lateral nucleus. They did not produce EPSPs in any extensor motoneurons (0/8 motoneurons). VC neurons sending axons to the contralateral extensor motoneuron pool and not to the oculomotor nuclei were not found.

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MEDIAL VESTIBULAR NUCLEAR NEURONS RECEIVING INHIBITORY INPUTS FROM FLOCCULAR MIDDLE ZONE IN CATS. YU SATO AND TADASHI KAWASAKI
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Previously, we reported that the Purkinje cells in the middle zone of the flocculus project to the medial vestibular nucleus (MV), and that electrical stimulation of the middle zone produced ipsilateral horizontal conjugate eye movement. In the present experiments, the neuronal pathway responsible for this eye movement was investigated. The activities of the MV neurons at the rostro-caudal level of the abducense nucleus were suppressed by stimulation of the middle zone. These neurons were antidromically activated by systematic microstimulation of the ipsilateral abducense nucleus, while stimulation of the rostral brain stem including the oculomotor nucleus was not effective for evoking antidromic spikes. These results suggest that the target neurons of middle zone inhibition in the rostral MV may project to the motoneurons and internuclear neurons of the ipsilateral abducense nucleus, and contribute to the mediation of the ipsilateral horizontal conjugate eye movement elicited from the middle zone of the flocculus.

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DOES CHOLINERGIC PROJECTION FROM THE BRAINSTEM CONSTITUTE THE ASCENDING RETICULAR ACTIVATING SYSTEM?

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In urethane-anesthetized rats single neuronal activity was recorded in the laterodorsal tegmental nucleus (LDT), which has a dense complement of cholinergic neurons with ascending projection. The most frequently encountered response of putative cholinergic neurons to noxious stimulation (tail pinch) was phasic excitation. This response was not parallel in time course with EEG desynchronization. Upon repetition of tail pinch the response tended to become weak or disappear while EEG desynchronization continued to appear on each occasion. In chronically prepared, unanesthetized rats only a few LDT neurons were tonically active during awake state and inactive during slow wave sleep. Many LDT neurons fired irregularly at a low rate and responded to light touch of the skin with one or a few spikes. This response habituated very quickly upon repetition. These observations suggest that the cholinergic projection from the LDT may play a role not as an activating system to maintain arousal state, but rather as an attention system.

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CHANGES IN SPIKE AND WAVE COMPLEX IN THE PRESENCE OF FLASH STIMULUS.

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The amplitude of the spike and wave complex(SW) in the cerebral cortex EEG, evoked by 3 Hz stimulation of the nucl. ventralis anterior(VA) of the rabbit, increased on attachment of a contact lens(CL) in the absence of flash stimulus, but decreased with CL in the presence of flash stimulus. The amplitude of SW increased when flash stimulus alone was given. The amplitude of SW increased by 3 Hz stimulus of the hippocampus(HPC) but decreased by 100 Hz stimulus of the HPC. The findings suggest that the increase in amplitude of SW by CL, in the absence of flash stimulus, corresponds to the effect of 3 Hz stimulation of the HPC and decrease in amplitude of SW by CL in the presence of flash stimulus corresponds to the effect of 100 Hz stimulus of the HPC, respectively. The results suggest that the previously reported decrease in excitability of the brain stem reticular formation(RF), by attachment of CL, in the absence of flash stimulus, and the increase in the presence of flash stimulus can be attributed to a rise in indirect inhibition of RF and decline in indirect inhibition of RF via the diffuse projection system.

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MULTIPLE-SITE OPTICAL RECORDINGS OF ELECTRICAL ACTIVITY IN THE EMBRYONIC CHICK BRAIN-STEM.

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Using a multiple-site optical recording system and a voltage-sensitive dye, we have obtained the first recordings of electrical activities from the embryonic central nervous system, in vitro. The brain-system with the trigeminal ganglion was isolated from chick embryos and stained with a merocyanine-rhodanine dye (NK 2761). Stimulation of the ophthalmic or maxillo-mandibular division of cranial nerve V from the ganglion, using a suction electrode, evoked changes in light absorption related to action potentials in 4-10-day old embryonic brain-stems. Optical signals were recorded via a 12x12-element photodiode array, and obtained in the marginal narrow area of the stimulated side in the brain-stem along both the cephalic and caudal directions with stimulations of either ophthalmic or maxillo-mandibular division. The area in which the signals were detected extended about 500μm in the cephalic direction and more than 1200μm in the caudal direction from the root of the attached trigeminal ganglion, in a 5.5-day old embryonic brain-stem. The conduction velocity was approximately 0.12m/sec in this preparation. The present study demonstrate the usefulness of the multiple-site optical recordings of neuronal activity in the analysis of developmental process of the functional organization in the embryonic central system.

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EFFECT OF THE CONTRALATERAL HYPOGLOSSAL AND GLOSSOPHARYNGEAL NERVES ON THE GLOSSOPHARYNGEAL-HYPOGLOSSAL REFLEX IN FROGS. MURAYAMA, N. and ISHIKO, N. Dept. of Physiol., Kumamoto Univ. Med. Sch., Kumamoto 860 and Dept. of Physiol., Miyazaki Med. Coll., Miyazaki 889-16

Bullfrogs, Rana catesbiana, immobilized with suxamethonium chloride (20 mg/kg b.w., i.p.), were used. By stimulating the glossopharyngeal (IX) nerve, reflex activities, composed of early (10-20 ms in latency) and late (>20 ms) components, were evoked in both protoractor branch (P. br.) and retractor branch (R. br.) of the ipsilateral hypoglossal (XII) nerve. Contralateral IXth nerve stimulation increased the reflex activities of both components in the P. br., whereas it increased the reflex activities of the early component in the R. br. but decreased that of the late one. On the other hand, stimulation of the contralateral XIIth nerve increased the activities of both components in the P. br. and those of the late component in the R. br., but did not affect the activities of the early component in the R. br. The present findings strongly suggest the existence of afferent fibers in the XIIth nerve.

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RESPONSE PROPERTIES OF NEURONES IN THE NUCLEUS PREPOSITUS HYPOGLOSSI AND UNDERLYING RETICULAR FORMATION TO OPTOKINETIC AND VESTIBULAR STIMULI. KANO, M., KUSUNOKI, M. AND MAEKAWA, K., Dept. Physiol., Jichi Med. Sch., Minamikawachi-machi, Tochigi, 329-04

Visual signals evoking optokinetic responses were suggested to be transferred through the nucleus prepositus hypoglossi (PH). However, its visual responses were not well studied. To examine the response properties of cells in the PH and underlying reticular formation (RF) to optokinetic (OKS) and vestibular (VS) stimuli, extracellular spikes (n=46) were recorded from left PH-RF in encephale isole, immobilized pigmented rabbits under gas anaesthesia (N_2O and halothane). OKS was delivered as constant velocity rotation of a drum with vertical black and white stripes (0.5-40°/s). VS was delivered as sinusoidal rotation of the animal with a turntable in the dark (p-p 50°, 0.01-0.2 Hz). About two thirds of the cells were excited with counterclockwise rotation of the drum, and clockwise rotation of the turntable (type II response). The rest of the cells preferred the opposite directions (type I response). Discharge rates of many cells were modulated in synchrony with the nystagmic rhythm elicited by either OKS or VS. About a half of the cells tested (n=10) was orthodromically excited with electric stimuli of the optic chiasm with 7.7 ms latency. These findings, combined with previous studies, suggest that PH-RF receives visual, as well as vestibular, signals and drives the neural circuit for the nystagmus.

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SYNAPTIC POTENTIALS IN CAT HYPOGLOSSAL MOTONEURONS DURING SWALLOWING TOMOMUNE, N. AND TAKATA, M. Dept. of Oral-Physiology, Sch. of Dentistry, Tokushima Univ., Tokushima 770

Synaptic potentials in genioglossus and styloglossus motoneurons (GG- and SG-Mns) during swallowing were studied. A GG- and an SG-Mn was identified by an antidromic spike and by recording an unitary discharge of a muscle unit followed induced-spikes of a motoneuron one for one. Swallowing was elicited by placing water on the dorsum of the tongue and was confirmed by a pattern of electromyographic activities of a GG- and an SG-muscle. As a result, we have demonstrated that during swallowing a depolarizing potential and a depolarizing-hyperpolarizing potential sequence was elicited in an SG- and a GG-Mn, respectively. By increasing the intracellular concentration of chloride ions, a hyperpolarizing potential elicited in a GG-Mn during swallowing was turned into a depolarizing potential. In addition, we found that in immobilized cats, a depolarizing potential and a depolarizing-hyperpolarizing potential sequence was induced in tongue retractor and protruder Mns by repetitive electrical stimuli of the ipsilateral superior laryngeal nerve at the optimum frequency and strength. In conclusion, we have demonstrated that during swallowing the SG- and the GG-Mn received an excitatory and an excitatory-inhibitory input from a swallowing center.

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CHEMOSENSITIVE NEURONS WITHIN THE AREA POSTREMA OF THE RAT.
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A total of 46 neurons within the area postrema was examined electrophysiologically. Among them, 25 neurons responded to electrical stimulation of the cervical vagal trunk. Chemical stimuli were applied by superfusion of the exposed IVth ventricle and/or intracarotid injection. Four neurons decreased and one neuron increased the discharge rates in response to glucose. Two neurons increased and two neurons decreased the discharge rates in response to hypertonic saline. One neuron increased and one neuron decreased the discharge rates in response to hypotonic saline. Two LiCl-responsive neurons were also observed. This evidence suggests enteroceptor mechanisms of the area postrema as well as CTZ for vomitting.

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EFFECTS OF LOCAL APPLICATION OF SEROTONIN ON THE TRIGEMINAL MOTONEURON ACTIVITY IN THE GUINEA PIG.
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Serotonin (5-HT) is known to play an important modulatory role in motor control in various animal species. The present study was undertaken to investigate the effect of local application of 5-HT on the activity of trigeminal motoneurons in chloralose-anesthetized guinea pigs. Multibarrel glass micropietts were used for extracellular recording of single unit activity and microiontophoretic application of glutamate, 5-HT, and methysergide (MSG, a specific antagonist of 5-HT). The glutamate-induced activity of a majority (26 of 34) of masseter motoneurons was enhanced by 5-HT, and it was inhibited by MSG in most (19 of 26) of these 5-HT sensitive masseter motoneurons. However, either 5-HT or MSG exerted no effects on the glutamate-induced activity of about 40% (17 of 39) of digastric motoneurons. Among the remaining 5-HT sensitive digastric motoneurons, 11 and 9 neurons showed excitatory and inhibitory responses to 5-HT, respectively. These results suggest that the excitability of jaw closer motoneurons is facilitated tonically by endogeneous 5-HTergic inputs and phasically by exogeneous 5-HTergic inputs. The sensitivity of digastric motoneurons to 5-HT seems to be lower than that of masseter motoneurons, and 5-HTergic inputs to jaw opener motoneurons may not play a leading part in jaw opening movements.

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INTRACELLULAR RESPONSE PROPERTIES OF TRIGEMINAL SENSORY NEURONS TO MECHANICAL STIMULATION OF THE FACE.
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The response properties of trigeminal sensory neurons to quantitative mechanical stimulation of the oral and facial regions were studied intracellularly in chloralose-anesthetized cats. Type I and Type II neurons in the spinal nucleus oralis (J. Physiol. Soc. Japan, 48: 246, 1986) showed different response properties to the stimulation of their excitatory receptive fields. Type I neurons responded with an EPSP and spike potentials followed by IPSPs; the IPSP was evoked even from the excitatory receptive field following each spike potential. A ramp-and-hold pressure application to the excitatory receptive field evoked spike responses at a much higher frequency coincident with the constant pressure increase than during the constant pressure application; the spike firing showed a rapid adaptation. Synaptic activation noise was also much larger in amplitude and higher in frequency during the ramp phase. In contrast, Type II neurons responded with a long-lasting EPSP superimposed by a train of spike potentials, showing no significant adaptation to the stimulus of a constant amplitude. The frequency of the spike potentials of Type I neurons tended to have a positive correlation with the velocity of the stimulus, while that of Type II neurons with its amplitude. The results suggest that Type I and Type II neurons in the trigeminal sensory nucleus play different functional roles in the transmission of the sensory information.

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LOCALIZATION OF CENTRAL RHYTHM GENERATOR AND ITS INPUT PATHWAY INVOLVED IN INTRAORAL INDUCTION OF RHYTHMICAL JAW MOVEMENTS IN GUINEA PIGS.

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We reported that rhythmical jaw movements (RJM) were induced by innocuous repetitive electrical stimulation in the oral cavity as well as microstimulation of the dorsolateral reticular formation (DRF) adjacent to the trigeminal spinal nucleus interpolaris (STN). In the present study, we investigated the localization of the central rhythm generator (MRG) driven by peripheral inputs and its input pathway in ketamine-anesthetized guinea pigs, with the following results: (1) Transection of the STN at the caudal pole of the facial nucleus abolished the RJM and the short-latency field potentials in the DRF elicited by ipsilateral buccal stimulation, without affecting those evoked by contralateral buccal stimulation. (2) Intraoral stimulation evoked spikes in DRF neurons that responded antidromically to stimulation of the oral part of the gigantocellular reticular nucleus (GCo), and they showed a rhytmical burst coincident with the RJM induced by repetitve stimulation of the cortical masticatory area (CMA) or spontaneous chewing. (3) Rhythmical intracellular potential in GCo neurons was induced by repetitive stimulation of the oral mucosa or DRF in pace with the rhythmical field potential in the digastric motoneuron pool, which was the same as in repetitive CMA stimulation. Averaging of the intracellular potential of GCo neurons by spontaneous spikes of DRF neurons revealed depolarizing potential about 1.5 ms after triggering spikes. We concluded that DRF neurons received intraoral mechanosensory inputs and monosynaptically drove the GCo neurons to generate the RJM.

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CHEMICAL STIMULATION OF THE PONTINE MICTURITION CENTER IN DECEREBRATE CATS

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In acute decerebrate cats, electrical stimulation to the pontine micturition center (PMC) resulted in micturition. Our recent study has demonstrated that the PMC corresponded to the nucleus locus coeruleus alpha. In this study, we tried to activate the PMC by focal injection of 4 different chemical substances. Microinjection of carbachol (10 n mole/0.1 µl) into the PMC resulted in micturition. The pattern of the changes in bladder pressure and the sphincter activity during carbachol-induced micturition was almost identical to those observed during electrically-induced micturition. Noradrenaline and acetylcholine injections into the PMC facilitated reflex micturition. Leucine-enkephalin injection into the PMC suppressed reflex micturition. These results suggest that cells in the PMC receive excitatory inputs for micturition from noradrenaline-containing cells in the cell groups A1 to 14, and from acetylcholine-containing cells in the reticular formation of the brain stem and sacral intermediate gray, and that they receive inhibitory inputs presumably from enkephalin-containing cells in the periaqueductal gray, nucleus parabrachialis lateralis, nuclei vestibularis and sacral intermediate gray.

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CHOLINERGICALLY ACTIVATED RETICULOSPINAL INHIBITORY PATHWAY TO HINDLIMB ALPHA-MOTONEURONS IN DECEREBRATE CATS.

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In reflexively standing decerebrate cats, microinjection of carbachol (long-acting cholinomimetic agent,injection dose :less than 4µg/0.25µl) into the nucleus reticularis pontis oralis (PoO) resulted in the long-lasting suppression of postural muscle tone in the bilateral hindlimbs. Postural suppression started within 1 minute after the bigining of carbachol injection and lasted for more than 2 hours. With the bigining of postural suppression, a group of PoO cells and cells in the nucleus reticularis gigantocellularis (Gc) started to increase their firing frequencies significantly. Averaging of intracellularly recorded membrane potential of hindlimb alpha-MNs, triggered by the spikes of a single Gc cell, revealed an existance of IPSPs (latency 4.0-7.3ms, segmental delay 1.2-2.2ms). Such IPSPs were recorded from plural alpha-MNs innervating both hindlimb extensor and flexor muscles. Furthermore, in lumbar segment (L6), there was an interneuron whose firing was synchronized with the firing of a Gc cell. Our preliminary study suggests that Gc cells exert non-reciprocal inhibitory effects upon hindlimb alpha-MNs and such an interneuron plays a role relaying signals from Gc cell to the target alpha-MNs.

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AXONAL PROJECTIONS TO AND FROM THE NUCLEUS RETICULARIS GIGANTOCELLULARIS IN CATS.
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In this study, axonal projections to and from the nucleus reticularis gigantocellularis (NRGc) were neuroanatomically studied. HRP injection into the NRGc resulted in the retrograde labeling of small and medium-sized cells (diameter less than 50um) in the pontine reticular formation (PRF). In contrast, HRP injection into the L1 spinal cord resulted in the labeling of large-sized cells in the PRF. HRP labeled fibers from the NRGc were found both rostral and caudal to the NRGc. In the caudal medulla ipsilateral to HRP injection site, labeled fibers were found in the ventrolateral MLF, ventromedial reticular formation. In the spinal cord, they were found in both the ventral and the ventrolateral funiculus. Contralaterally, labeled fibers were found in the dorsal portion of the MLF, and in the ventral funiculus of the spinal cord. PHA-L injection into the NRGc resulted in the orthograde labeling of fibers terminating on cells in the PRF. It also resulted in the labeling of fine nerve fibers in the lower cervical spinal cord. Labeled terminals were found in the Rexed's VIIth and VIIIth layers bilaterally. All these results suggest a possibility that there exists a reverberating neuronal circuit in the reticular core, and that the NRGc is one of the main component of it.

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EFFECTS OF STIMULATION IN THE N. RAPHE MAGNUS ON LUMBAR MONOSYNAPTIC REFLEX PATHWAYS IN THE CAT.
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We previously reported that the microstimulation in the N. raphe magnus produced the biphasic, facilitatory and subsequent inhibitory effects on lumbar monosynaptic reflexes in cats anesthetized with chloralose (50mg/kg) and urethane (500mg/kg). This study aimed to examine neural pathways contributing to their effects, and the distribution and the conduction velocity (CV) of the raphe-spinal neurons, which projected to the lumbar spinal cord, especially L7 segment, were investigated by using the antidromic stimulation and the retrograde HRP method. In the antidromic stimulation, 51 antidromic spikes were recorded in the N. raphe magnus. The mean CV was 38.4 m/s and they were evenly distributed throughout the nucleus. On the other hand, in the N. raphe pallidus, only 6 antidromic spikes were recorded and the mean CV was 17.4 m/s. In the injection of HRP into the unilateral lumbar segments, the number of HRP-labeled neurons was most numerous in the N. raphe pallidus and then the number was in the order of the N. raphe magnus, the N. raphe obscurus. These results support the view that raphe-spinal neurons could produce facilitatory and inhibitory effects on the lumbar monosynaptic reflexes.

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THE EFFECTS OF MORPHINE ON THE NEURONAL ACTIVITY OF THE NUCLEUS RAPHE DORSALIS IN AWAKE CATS
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Forty-nine neurons recorded within the nucleus raphe dorsalis (NRD) in awake cats were classified into two groups: 29 regularly firing (clock-like) and 20 irregularly firing (non-clock-like) neurons. Almost all clock-like neurons were influenced neither by noxious stimulation (0.1 ml of 5% formalin, s.c.) nor by a single dose (1 mg/kg, i.p.) or cumulative doses (0.25, 0.5, 1 mg/kg) of morphine injection. In contrast, about a half of non-clock-like neurons were activated both by noxious stimulation and by administration of morphine. The time course of formalin-induced activation of nociceptive non-clock-like neurons was correlated with that of behavioral pain rating (formalin test). Morphine-induced activation of non-clock-like neurons was dose-related and reversed by naloxone (0.2 mg/kg, i.p.). These findings suggest that clock-like neurons in the NRD are not involved in morphine analgesia. Non-clock-like neurons, however, may play a role in the mediation of such analgesia.

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SUBFORNICAL ORGAN AND PARAVENTRICULAR NUCLEUS CONNECTIONS WITH MEDIAN PREOPTIC NUCLEUS NEURONS: AN ELECTROPHYSIOLOGICAL STUDY IN THE RAT. SAITO, H., TANAKA, J., KABA, H., LI, C.-S., NOJIMA, K. AND SETO, K. Dept. of Physiol., Kochi Med. Sch., Nankoku, Kochi 781-51

In urethane anesthetized male rats, the majority (n=19) of subfornical organ (SFO) units (n=24) antidromically identified as projecting to the median preoptic nucleus (MnPO) were excited by microiontophoretically applied (MI-A) angiotensin II (AII) and the effect of AII was blocked by MI-A saralasin (Sar), an AII antagonist. These SFO units were also excited by intravenously injected AII. Electrical stimulation of the SFO produced excitation (n=14) or inhibition (n=7) of the activity of MnPO units (n=29) antidromically identified as projecting to the paraventricular nucleus (PVN). All MnPO units that were excited by SFO stimulation were also excited by MI-A AII, while the remaining units were not affected. The excitatory responses to SFO stimulation and MI-A AII were blocked by MI-A Sar, whereas the inhibitory responses were not affected. Microinjected AII into the SFO produced either an excitation (n=6) or no effect (n=5) in the activity of identified MnPO units. Microinjected AII into the MnPO evoked an excitatory response in the activity of 5 of 16 putative vasopressin (VP)-secreting PVN units with no effect on the remainder. These results suggest that AII sensitive MnPO neurons projecting to the PVN may act to enhance the excitability of VP-secreting PVN neurons in response to the excitatory inputs from SFO neurons that are activated by circulating AII.

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LOCATION AND DISCHARGE PATTERN OF PALLIDAL NEURONS WITH PREFRONTAL AND PREMOTOR CORTICAL INPUTS. JINNAI, K., NAMBU, A. AND YOSHIDA, S. Dept. of Physiol., Shiga Univ. of Med. Scien., Ohtsu, Shiga 520-21. Dept. of Physiol. Inst. for Brain Res., Fac. of Med., Kyoto Univ., kyoto 606.

Activities of pallidal neurons were studied in one awake monkey which were implanted with stimulating electrodes in the cerebral cortex and the striatum. Cortical and striatal inputs to each pallidal neurons were examined by responses to stimulation through these electrodes. Fifteen neurons which were inhibited by stimulation of the prefrontal area, premotor area and/or head of the caudate nucleus were located in the dorsal part of the pallidum. In reaction time task, most (8/11) of these neurons responded to visual cue stimulus at short latencies (80-180 msec). On the other hand, 31 neurons which were inhibited by stimulation of both the motor area and central part of the putamen were located in the ventral part of the pallidum. In the same task, most (20/22) of these neurons changed their firing rate after visual cue stimulus but at longer latencies than 180 msec, and these changes were correlated more closely to the response movements than to the visual cue stimuli.

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PATTERNS OF PROJECTION FROM VESTIBULAR NUCLEUS TO THALAMUS. MORI, A., YOSHIDA, T., MATSUURA, N. AND SUMINO, R. Department of Physiology, Nihon University School of Dentistry, Chiyoda-ku, Tokyo 101, Japan

We examined the projection pattern from vestibular nucleus the thalamus of cats. Under light ketamine anesthesia (35mg/kg), a tungsten-in-glass pipette microelectrode were inserted into the thalamus and used for both intracortical microstimulation (ICMS), and recording unitary and/or responsive spike. 6 other electrodes were inserted into the vestibular nucleus was fixed as it picked up a response to the stimulation of the vestibulum. The 6 microelectrodes were used for ICMS (30μA or less), and for recording responsive spikes. Antidromic activated neurons in the SVN and SMN responded to the stimulations of the VL, VPM and VPL. In addition, a few SVN and MVN neurons activated antidromically by ICMS of the Po and MGmc. Neurons of the inferior vestibular nucles (IVN) projected into the PL, VPM and VPL, but it did not project into the Po and MGmc. These neurons have large receptive fields. This suggests that neurons of the SVN,MVN and IVN send strong output to thalamic neurons and that thalamic neurons have function at lower level integration for both vestibular and somesthetic inputs.

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THE MULTIPLE SENSORY NEURONAL ACTIVITIES IN THALAMIC VB NUCLEUS AND THE ASCENDING INHIBITORY PATHWAY. NODA,K., AKITA,H., HOTSUMI,K., OGATA,M., HAMANAKA,S., KOBAYASHI,S.and AIKAWA,S. Dept. of Physiol., Sch. of Hygienic Sciences, Kitasato Univ., Sagamihara, Kanagawa and Dept. of ME, Seishin-Igaku Inst., Itabashi-ku,Tokyo

Unitary discharges were recorded extracellularly using multimicro-electrode technique in the thalamic ventrobasal complex in the cat.

In so-called spontaneous unitary discharges, some unit' were synchronized with heart beats. These neurons not only discharged synchronously to heart beats but also responded to its receptive fields on body surface(HBS). These HBS unitary discharges were inhibited by electrical stimuli to the receptive fields on body surface when the evoked discharges to electric stimuli preceded the HBS' with a given period.

These HBS unitary discharges disappeared after partial cervical cordotomy of the lateral part of anterolateral funiculus although the evoked discharges to the electric stimuli of the receptive field(SES) persisted. After the section of residual medial part of the funiculus, SES' were vanished.

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NOCICEPTIVE NEURONS IN THE VENTROBASAL COMPLEX OF THE PRIMATE THALAMUS.
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The ventrobasal (VB) complex comprises the nucleus ventralis posterolateralis (VPL) and somatosensory part of the nucleus ventralis posteromedialis (VPM proper). In the present study, the VB complex was explored for nociceptive units in Japanese macaques anesthetized with urethan-chloralose. Both nociceptive specific (NS) and wide dynamic range (WDR) units were found in the shell region of the VB complex. NS units were located in the caudal part, whereas WDR units were found in a narrow band just rostral to the NS zone. The dorsal shell region of the VPM proper is separated into medial and lateral parts. The medial part is dorsal to the nucleus pulvinaris oralis (PuO) and/or nucleus centrum medianum (CM), whereas the lateral part is dorsal to these nuclei. Similarly, the ventral shell region of the VPL is separated into medial and lateral parts. The medial part is dorsal to the nucleus ventralis inferior (VPI), whereas the lateral part is ventral or lateral to the VPI. Hence, the shell region of the VB complex in which nociceptive units were found, was discontinuous at two sites.

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RESPONSES OF HYPOTHALAMIC NEURONS DURING LICKING OF TASTE SOLUTIONS IN THE RAT.
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To reveal the functional significance of the lateral hypothalamic (LH) neurons during ingestive behavior, unit activities of the LH neurons were recorded with chronically implanted Pt-Ir fine wires during licking of various taste solutions in Wistar male rats. Implantation of the fine wires and other necessary surgical operations were performed under deep anesthesia with sodium pentobarbital and urethane. About half of the LH neurons (n=65) histologically indentified changed their spontaneous rates after onset of cue tone (4.5KHz) presented 5-10 sec before the start of licking. The change of activity seemed to reflect emotional (anticipatory) behavior and searching behavior including movement-related reaction and sniffing. LH neurons were classified into the 3 types according to their response properties during licking period: 1) Taste neurons (5%), which responded strongly to a specific taste quality. 2) Taste-hedonic neurons (35%), which showed differential response patterns depending on the palatability of taste solutions. 3) Neurons (60%), which showed no or non-specific responses during licking behavior regardless the taste qualities. These results suggest that LH neurons are responsible for arousal state expecting rewards, and licking behavior namely based on the hedonics of the rewards.

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VENTROMEDIAL HYPOTHALAMIC NEURONAL ACTIVITY RELATIONS TO RHYTHMICITY OF SLEEP-AROUSAL AND FEEDING IN FREELY BEHAVING RATS.
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Long term activity of single neurons in the ventromedial hypothalamus (VMH) was recorded through chronically implanted electrodes in freely behaving rats, and relations between neuronal activity and feeding behavior were analyzed. Activity of 57 of 78 recorded neurons changed with EEG (EEG related). Activity of 26/57 decreased only during feeding episodes, and none of these responded to intraventricular (i.c.v.) glucose infusion. Activity of 17/78 changed with light-dark cycle but not with EEG (EEG independent neuron); i.c.v. glucose increased activity of 11 in 3 groups: 3 responded to feeding but not to drinking (type 1), 5 responded to both feeding and drinking (type 2), and 3 responded to neither feeding nor drinking (type 3). Activity of type 1 was decreased by i.c.v. noradrenaline (NA) but not by i.c.v. NaCl. Types 2 and 3 responded to both i.c.v. NA and NaCl and to rise of ambient temperature. The results suggest that EEG related neurons are related to inner environmental rhythmicity of the sleep-arousal cycle, and EEG independent neurons are related to, and functionally differentiate information about blood glucose level, osmotic change and ambient temperature.

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LATERAL HYPOTHALAMUS INVOLVEMENT IN NOREPINEPHRINE INDUCED FEEDING BY RAT.

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It is well known that intrahypothalamic or intracerebroventricular (i.c.v.) infusion of norepinephrine (NE) induces feeding behavior, even in satiated animals. In the present study we recorded single neuron activity in the lateral hypothalamus (LHA) of freely behaving rats, and investigated relations between neuronal activity and feeding behavior induced by i.c.v. administration of NE. Of 47 LHA neurons tested during NE-induced feeding behavior, activity decreased in 12 and increased in 3. The duration of inhibition or excitation ranged from 10 to 55 min (mean: 30.5 min). The NE elicitation of feeding behavior and neuronal activity change was blocked by pretreatment with i.c.v. phenoxybenzamine, an α-antagonist of NE. Although i.c.v. dopamine induced feeding behavior in a few cases, neuronal activity was not affected (27/27). The results indicate that the LHA is implicated, directly or indirectly, in the process of NE-induced feeding behavior.

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GUSTATORY RESPONSES OF LATERAL HYPOTHALAMIC GLUCOSENSITIVE (GS) AND GLUCOSE-INSENSITIVE (GIS) NEURONS IN THE MONKEY.

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Single unit recordings from the monkey lateral hypothalamic area (LHA) during operant bar press feeding tasks as well as electric brain stimulations revealed details of the functional organization of the LHA GS- and GIS-neurons. To elucidate these neurons' specific function in the taste and odor information processing their activity changes for gustatory and olfactory stimulations were studied. For repeated applications of different taste-solutions the most GS-neurons (95% of neurons tested) responded, predominantly to two or more taste qualities, while fewer responses (59%) - ususally for one taste quality - of the GIS-neurons were seen. Since gustation and olfaction guide food searching and selecting behaviors together, odor stimulations were also performed. Corresponding to the functional relationship between these two senses, similar activity changes were found to those seen after taste stimulations. Furthermore, overwhelming majority of the GS-neurons showed "bimodal" taste and odor responsiveness (96%), in contrast with the GIS-neurons that responded prevailingly to either taste or odor. The GS-neurons of the LHA seem to integrate multimodal sensory informations in regulating feeding behavior, while the GIS-neurons distinguish specific sensory cues to control selection and acquisition of foods.

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FIBROBLAST GROWTH FACTOR (FGF) POTENTIAL PARTICIPATION IN THE REGULATION OF FEEDING.

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FGF is a potent mitogen which has been identified throughout the nervous system. Two forms of FGF (acidic and basic) have been purified, their amino acid sequences determined and their cDNAs cloned and sequenced. Brain-derived acidic FGF act as a survival agent, and it exhibits mitogenic activity for endothelial and glial cells *in vitro*. The *in vivo* role(s) of FGF in the nervous system is not known. Using a bioassay system (the depression of the feeding response of the *hydra japonica* elicited by S-methylglutathione), the presence of an acidic FGF-like activity in the cerebrospinal fluid (CSF) was investigated. In chronically cannulated rats, the acidic FGF-like activity in the CSF from III ventricle (n=8), and from cisterna magna (n=5) shows an increase from <0.1 pg/ml in 24 hr food-deprived rats to 262 ± 180 μg/ml after feeding with return to the basal levels 12 hr later. Since this evidence indicates that acidic FGF may participate in the regulation of feeding, male Wistar rats were subjected to intra-cerebroventricular applications of acidic FGF. The results show that some preparations of acidic FGF decrease food intake, whereas others did not. The significance of this variable effect and possible participation of acidic FGF in the regulation of feeding is currently investigated.

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NEURAL MECHANISM OF PAIN TRANSMISSION TO RAT LATERAL HYPOTHALAMUS. KAI, Y., NISHIMURA, H., KATAFUCHI, T., SHIMIZU, N. AND OOMURA, Y. Dept. Physiol., Fac. Med., Kyushu Univ., Fukuoka 812

In adult male anesthetized rats, the effects of LHA neurons were examined following electrical stimulation of periaqueductal gray (PAG) and dorsal raphe nucleus (DR). Of 234 spontaneously firing LHA neurons examined by electrical stimulation of the PAG, 70 (29%) were inhibited. Of 70 neurons, 65% cells were glucose-sensitive. Naloxone attenuated the inhibitory response to PAG stimulation, tail pinch and electrophoretic morphine application. Intracellular recording showed polysynaptic IPSPs. Of 287 by electrical stimulation of the DR, 73 (25%) were excited, 71% of them were glucose-insensitive, and 157 (55%) were inhibited, 51% of them were glucose-sensitive. The serotonin 1 receptor antagonist, lisuride and (-)-propranolol, attenuated both the inhibitory response to DR stimulation and electrophoretic serotonin application. However, the inhibitory effect of tail pinch was not attenuated by lisuride. Intracellular recordings with DR stimulation showed monosynaptic EPSP and IPSP. We conclude that LHA glucose-sensitive neurons receive inhibitory opiate inputs from PAG through noxious stimulation, while inhibitory inputs to glucose-sensitive neurons from DR are related to serotonin 1 receptors, but are not directly involved in the mediation of the noxious tail pinch.

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FEEDING RELATED LATERAL HYPOTHALAMIC NEURONS TO ODORS DEPENDS ON THE DEGREE OF SATIATION. SHIRAISHI, T. Dept. of Physiol. Tokai Univ. Sch of Med., Isehara, 259-11

It has been investigated feeding related LHA neuronal activity and responses to odor stimulation in rats at various levels of satiation. Extracellular responses of 168 neurons to three odors, isoamylacetate (AA), cineole (CL), and isovaleric acid (VA), were recorded from 168 LHA neurons of Wistar-SPF male rats. Of 168 units, 107 (63.7%) responded to from one to three odors, but not to light or phonic stimulation. Of the responding units, 94.4% (101/107) were excited, and 5.6% were inhibited.

In response to a single electrical stimulation (0.5ms, 1-10V) of the OB, 61 units were excited with latencies of 6 - 43ms (19.8±12.0ms, mean±S.D.) indicating compound OB-LHA relations-- mono- and polysynaptic through myelinated and nonmyelinated fibers. The results suggest predominantly excitatory effects of both electrical stimulation of the OB and odor stimulation on the LHA. Firing frequency in response to AA or VA was significantly ($p<0.05$) greater for the long fasting group (38 hr, LF, n=8) than for the NF (non-fasting, n=12) group; differences between the LF and MF (24 hr, n=6) groups were not significant. Glucose-sensitive neurons (GSN, n=19) responded more to odors than non-GSNs (n=86), and discharge frequency increase depended markedly on food deprivation. Food deprivation results suggest that responsiveness of feeding related LHA neurons to odors depends on the degree of satiation.

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EFFERENT PATHWAYS FROM THE LATERAL HYPOTHALAMIC AREA TO THE PARAVENTRICULAR NUCLEUS THROUGH SUBFORNICAL ORGAN NEURONS: AN ELECTROPHYSIOLOGICAL STUDY IN THE RAT. TANAKA, J., KABA, H., SAITO, H. AND SETO, K. Dept. of Physiol., Kochi Med. Sch., Nankoku, Kochi 781-51

The action of pathways from the lateral hypothalamic area (LHA) to the paraventricular nucleus (PVN) through subfornical organ (SFO) neurons on the excitability of antidromically identified phasically firing neurosecretory (putative vasopressin (VP)-secreting) neurons in the PVN was examined in urethane anesthetized male Wistar rats.

The activity of almost all (n=19) of SFO units (n=20) antidromically identified as projecting to the PVN was excited by microiontophoretically (MIPh) applied angiotensin II (ANG II) and the effect of ANG II was blocked by MIPh-applied saralasin (Sar), a specific ANG II antagonist. Electrical stimulation in the LHA evoked a prominent excitation in the activity of about half (n=11) of these identified SFO units with no effect on the remainder (n=9), and the excitatory responses were blocked by MIPh-applied Sar. Microinjection of ANG II into the SFO excited the activity of 9 of 13 putative VP-secreting PVN units tested.

These findings suggest the possibility that LHA efferent projections to the SFO may act to enhance the excitability of putative VP-secreting neurons in the PVN through an excitatory influence on ANG II sensitive SFO neurons projecting to it.

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INHIBITORY EFFECTS OF LONG-TERM ESTRADIOL TREATMENT ON DOPAMINE SYNTHESIS IN VITRO IN TUBEROINFUNDIBULAR DOPAMINERGIC NEURONS.

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The mechanism of the inhibitory effect of long-term estradiol treatment on dopamine synthesis in tuberoinfundibular dopaminergic (TIDA) neurons was studied by using hypothalamic slices of ovariectomized rats. Treatment for 6 weeks with 2 mg estradiol valerate (EV) increased the weight of anterior pituitaries and the concentration of serum prolactin. In vitro dopamine synthesis in TIDA neurons was estimated by DOPA accumulation in the median eminence after incubation of hypothalamic slices with NSD 1015. The basal rate of DOPA accumulation in the median eminence of hypothalamic slices obtained from EV-treated rats was smaller than that from control rats. Ca^{2+}-dependent DOPA accumulation, as determined by incubation in media containing depolarization agents such as 50 mM K^+ and veratridine or in Na^+-free media, and cAMP-dependent DOPA accumulation, as determined by incubation with dibutyryl cAMP or forskolin, were decreased in EV-treated rats.

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EFFECTS OF DN-1417 ON ELECTRICAL PHENOMENA IN KINDLED RABBITS.

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1) With kindled rabbits DN-1417(TRH-analog) gave effect of a rise in the threshold of each arousal reaction and evoked muscular discharge applying cortical stimulation at the dose of 2.0 mg/kg i.v. and lasted for 30 min. A reduction in afterdischarge duration was also seen together. But DN-1417 had no effect either at higher dose(20.0 mg/kg i.v.) or at lower dose(0.2 mg/kg i.v.).

In contrast pentobarbital had a dose-dependent effect.

2) The threshold of each arousal reaction and evoked muscular discharge by hippocampal stimulation made a decrease in the amygdaloid kindling rabbits while the threshold showed no change or an increase in no kindling ones.

3) Stomach ulcerative changes were also found in kindled rabbits. Especially, in amygdaloid and hippocampal kindled groups, such changes were more remarkable than in cortical one.

However, its rate in no kindling group was very low.

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NEURONAL ACTIVITY RELATED TO A NON-SPATIAL STIMULUS-RESPONSE ASSOCIATION TASK IN THE ENTO-/PERI-RHINAL CORTEX AND THE HIPPOCAMPUS OF THE MONKEY.

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To examine the functions of the primate hippocampus, the activity of 402 single neurons has been analyzed in the ento-/peri-rhinal cortex and the hippocampus of Japanese monkeys (Macaca Fuscata) learning and performing a stimulus-response association task. Ento-/peri-rhinal neurons (R-cells), which provide major input to the hippocampus, were sampled in the dorsal and ventral bank of the rhinal sulcus (A22-A14). 10.2% of R-cells responded in the cue period differentially between go and nogo trials and 5.3% of R-cells did so in the delay period. 10.6% of R-cells were related to reward and/or omission of reward. In the hippocampus more neurons responded in the delay period and less neurons in the cue period or to reward. 41 neurons were studied while the monkeys learned new associations between visual stimuli and motor responses. 12 hippocampal neurons modified their activity during the learning. However, no R-cell exhibited such modification except one marginal case. The differences between R-cells and hippocampal neurons may reflect information transformation within the hippocampus in the associative learning.

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EFFECT OF ZINC CHELATING AGENTS ON THE HIPPOCAMPUS OF A MOUSE BRAIN. EEG AND HISTOCHEMICAL STUDIES. MURAKAMI,T.H.,TOYOSHIMA,T,NEGI,T.AND HORI,Y. (Dept. of Biol., Phys. Ed. and Dept. of Physiol.) Kagawa Med. Schl. and Okayama Univ.,Kagawa 761-07,Okayama 700

It is well established that the hippocampus contains zinc. Following the intraperitoneal injection of chelating agents, dithizone, oxine, diethyldithiocarbamate and Ca-EDTA, were compared with the alteration of Timm's staining pattern and hippocampal EEG in mice. An injection of Ca-EDTA (500mg/kg) had no significant effect on the EEG and Timm's staining pattern. In contrast, dithizone (50mg/kg, 100mg/kg), oxine (200mg/kg) and diethyldithiocarbamate (500mg/kg or greater) produced dose-dependent significant decreases in hippocampal EEG and Timm's staining pattern from 10 to 90 min after injection. The maximal decreases were seen between 10 to 15 min in EEG and from 10 to 60 min in Timm reaction. In this period they produced almost a total loss of electrical activities and Timm reaction. In the recovery period, a waveform showed a shift to slower frequencies, and during this time Timm reaction remained negative. Although the abolished EEG by chelating agents administration were immediately recovered by zinc acetate or zinc sulfate application, while the histochemical zinc reaction remained negative. There was a difference between the result on the electrical activity and the histochemical reaction, however, we suspect that in each there is sensitivity.

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VARIOUS CONDITIONS TO INDUCE A CHANGE IN KINDLING ACQUISITON BY AMYGDALA STIMULATION. MATSUURA, S., KAWAWAKI, H., LEE, S. Dept. Physiol., Osaka City Univ. Med. Sch., Osaka 545

A decrease in blood glucose level by insulin application to suckling rats during kindling acquisition process by amygdala stimulation produced a marked enhancement in the duration increase of EEG afterdischages (ADs) by the kindling, but the progress of behavioral seizure stages showed no apparent changes. Kindling stimulations by 50-60 Hz electric pulses with a short interval such as 15 min produced an increase in ADs and an acquisition of kindling seisure in suckling rats but not in the adults. When entorhinal field potential (EFP) to amygdala stimulation was recorded during development of kindling effects, posttetanic potentiation (PTP) was usually observed after each kindring trial with high frequency pulses like 50 Hz and the EFP recorded just before each trial with one hour interval also showed an increase in amplitude, giving an evidence of long term potentiation (LTP). In the kindling trials by a low frequency of pulses such as 3 or 10 Hz, PTP was rarely observed, but LTP on repeated trials and a clear increase in FEP response during each kindling trial was usually observed in suckling rats. In many adult rats, kindling stimulation with 3Hz pulses failed to produce the facilitatory effect on EFP in each trial to result in no development of LTP and kindling effects.

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THE ROLE OF LIMBIC-HYPOTHALAMIC SYSTEM IN METABOLIC RESPONSES OF CITRATE TO COLD EXPOSURE. OHRI, A., KITAOKA, K., OHBA, C., EDASHIGE, N., LI, C.-H., SAITO, H. AND SETO, K. Dept. Physiol., Kochi Med. Sch., Kochi 781-51

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

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RESPONSES OF RAT LATERAL HYPOTHALAMIC NEURON ACTIVITY TO FASTIGIAL NUCLEUS STIMULATION. MIN, B., KATAFUCHI, T., KAI, Y. AND OOMURA, Y. Dept. Physiol., Fac. Med., Kyushu Univ., Fukuoka 812

Contralateral fastigial nucleus (FN) stimulation in anesthetized rat evoked three types of responses in 48% (115/240) of lateral hypothalamic area (LHA) neurons with an increase in blood pressure: inhibition with 10.9 ± 6.2 latency (71/115, 62%), excitation with 15.1 ± 12.3 latency (34/115.29%) and excitation-inhibition with 5.1 ± 3.9 latency (10/115, 9%). The neuronal responses were not affected by inferior cerebellar peduncle transection, though it resulted in a substantial fall of arterial pressure. Most Glucose-sensitive neurons were inhibited by FN stimulation, whereas only two of 18 Glucose-insensitive neurons responded to such stimulation. Intracellularly recorded IPSPs were considered to be monosynaptic since their latencies were constant when FN stimulus intensity was changed. The results suggest close functional connections between the LHA and the FN. These connections may contribute to functional modulation of the autonomic nervous system and the hypothalamus.

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CORRESPONDENCE BETWEEN THE VIBRISSAE REPRESENTATION AND BARRELOIDS IN THE RAT VENTROBASAL COMPLEX. SUGITANI, M., OOYAMA, H., YANO, J. AND SUGAI, T. Dept. Physiol., Kanazawa Medical Univ., Ishikawa 920-02

Recently, barreloids, similar structure to barrels in the somatosensory cortex, were reported to be seen in the ventrobasal complex (VB) of adult rats using cytochrome oxidase (CO) stain (Land & Simons, 1985). The arrangement of barreloids, however, does not agree with the somatotopic map of vibrissae representation revealed by Waite (1973), especially in the dorsoventral extent. Two series of experiments were carried out to solve this discrepancy. First, the vibrissal region of the VB was systematically re-mapped, and second, CO stain was applied after injecting dye to the recording sites of vibrissa neurons. Mapping experiments confirmed Waite's results, and further, showed that the cluster of neurons projected from any single vibrissa forms a column extending from anterodorsomedial to posteroventrolateral direction, and that these columns are piled up dorsoventrally and anteroposteriorly with ventral ones being shifted medially. Though numerous CO stained sections from 34 VB's were examined, it was possible to differentiate only a few barreloids with some confidence, if ever. The situation appears quite different from that on the barrels in the cortex. To establish the relation between the individual vibrissae and barreloids, some drastic technical alteration or quite a new method of approach seems to be necessary.

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NEURONS IN THE NUCLEUS VENTRALIS POSTEROLATERALIS RESPONSIVE TO VISCERAL AFFERENT INPUT. MASUDA, T., TAGUCHI, H., KOYAMA, N. AND YOKOTA, T. Dept. Physiol., Med. Coll. Shiga, Otsu 520-21

Neurons in the nucleus ventralis posterolateralis (VPL) which receive sympathetic visceral afferent input were studied in cats anesthetized with urethan-chloralose. A great majority of units recorded from the VPL were low-threshold mechanoreceptive units. None of them were responsive to electrical stimulation of the inferior cardiac (IC) or greater splanchnic (SPL) nerve. The remaining units were nociceptive specific (NS) or wide dynamic range (WDR) units. Both of them were located in the dorsal and ventral shell regions of the caudal VPL. Units responsive to sympathetic visceral afferents were found among these nociceptive units. Units exclusively responsive to sympathetic visceral afferents were not found. NS units responsive to IC stimulation had a cutaneous receptive field in the area corresponding to tactile dermatomes C5-T13. WDR units responsive to IC had at least a part of their receptive fields in the same area. Units responsive to SPL stimulation had a cutaneous receptive field in the area corresponding to tactile dermatomes C8-L3. WDR units responsive to SPL had at least a part of their receptive fields in the same area.

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PROTECTION BY CA-ANTAGONISTS FROM ELECTROPHYSIOLOGICAL DYSFUNCTION OF HIPPOCAMPAL NEURONS. SUGITA, S.[1,2]; HIGASHI, H.[1], NISHI, S.[1] AND KURAMOTO, K.[2]* Depts. Physiol.[1] & Neurosurg.[2] Kurume Univ. Sch. Med., Kurume 830

The effect of Ca-antagonists on the guinea-pig hippocampal CA1 neurons in in vitro preparations was studied by intracellular recordings. When the neurons were superfused with a high K^+ (60 mM) medium, the membrane potential was irreversibly reduced to approximately 0 mV. This cell deterioration by the high K^+ medium could be prevented by addition of Co (2 mM). Similarly, the solution containing verapamil (2.5 μM), D-600 (1 μM), flunarizine (1 μM), cinnarizine (1 μM), nifedipine (1 μM) or prenylamine (1 μM) could also prevent the cell deterioration. However, diltiazem at concentrations up to 5 μM could not prevent the high K^+-induced deterioration. Ca-antagonists (verapamil, D-600, flunarizine, cinnarizine, nifedipine, nicardipine, prenylamine, diltiazem) except for diltiazem reversibly depressed Ca-dependent TEA spike. D-600, flunarizine, nifedipine and prenylamine raised the threshold for generation of the Na-dependent spike. Prenylamine (1 μM) slightly reduced the amplitude of e.p.s.p.s, while other Ca-antagonists were without effects on e.p.s.p.s. These results suggest that the blockade by Ca-antagonists of voltage-dependent Ca-influxes may prevent the cell deterioration in the high K^+ medium.

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CHANGE OF EEG WAVES AND FIELD POTENTIAL IN ENTORHINAL CORTEX DURING AMYGDALA KINDLING. KAWAWAKI, H., LEE, S., MATSUURA, S. Dept. Physiol., Osaka City Univ. Med. Sch., Osaka 545

Development of afterdischarges (ADs) in the EEG waves and changes in the response pattern of entorhinal field potential (EFP) during the kindling process by amygdala stimulations were compared in adult and suckling rats. EFP recorded by a tungsten wire electrode (tip; 2-3 um) changed its response size and polarity, when evoked by an ipsilateral amygdala stimulation and obtained at different sites in the depth. Long term potentiation (LTP) was observed in the EFP during repeated kindling trials and more markedly induced in suckling rats than in adult rats and by stimulation with 10 Hz electric pulses than stimulation with 3 Hz pulses. In spite of the development of LTP during the repeated kindling trials, posttetanic depression was usually observed in the EFP after each kindling trial. The present observations show that the kindling effects by stimulating amygdala with a low frequency of electric pulses such as 3 - 10 Hz are obtained more easily in suckling rats than in adult rats and development of LTP in the entorhinal response may be involved in the mechanism of kindling aquisition by amygdala stimulation.

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LONG-LASTING REDUCTION OF THE DENTATE RECURRENT INHIBITION FOLLOWING HIGH-FREQUENCY STIMULATIONS OF THE PERFORANT PATH. MARU, E., ASHIDA, H. and TATSUNO, J., Dept. Physiol., National Defense Medical College, Tokorozawa, Saitama 359

Effects of high-frequency electrical stimulations of the perforant path (PP) on the dentate field potential were examined in the urethane-anesthetized rat. The dentate field potential consisted of the population EPSP and the population spike reflecting the synchronous discharge of granule cells. The high-frequency stimulations resulted in a strong potentiation of the PP-dentate excitatory synapses, and an enhancement of the granule cell excitability indicated by an increase in the ratio of the population spike height against the population EPSP strength, lasting for at least 120 min after the last pulse train. A paired-pulse stimulation of the PP fibers produced two distinctive inhibitions of the population spike in the second response, the "early recurrent inhibition" at an interpulse interval of 20-30 msec and the "late recurrent inhibition" at an interpulse interval of 200-6000 msec. The strength of the early recurrent inhibition decreased for at least 90 min after the last pulse train, while the late recurrent inhibition remained unchanged.

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MONKEY AMYGDALAR NEURON RESPONSES: TO COMPLEX SENSORY STIMULATION AND IN DELAYED COMPARISON TEST. NISHIJO, H., ONO, T., NAKAMURA, K. AND TAMURA, R. Dept. of Physiol., Fac. of Med., Toyama Med. and Pharmaceu. Univ., Toyama 930-01.

Single neuron activity in the monkey amygdala (AM) was recorded during operant bar pressing. Responses to visual, auditory, somesthetic and oral sensory stimuli, and in delayed comparison of pairs (DPC) among 4 colored lamps were analyzed. Of 585 neurons tested for sensory responses, 107 responded primarily to a single modality (40 vision, 26 audition and 41 ingestion), 117 responded transiently or tonically to all four modalities; 14 responded selectively to only one stimulus item. Of the 585 neurons, 423 were also tested in DPC, and 124 responded in one or more phases: 1) 17/30 vision related responded to 1st and/or 2nd cue lamps, and 4/30 responded throughout the 1st and 2nd cue and delay periods; 2) 0/21 audition related responded in DPC; 3) 4/30 ingestion related responded to 1st and/or 2nd cue lamps, and 30/30 responded in the ingestion phase; 4) 21/70 multimodal responded transiently and 47/70 responded tonically to the 1st and/or 2nd cue lamps (9/47 responded also in the delay period); 5) 4/14 selective neurons responded in ingestion phase in DPC only when the selective item was the reward. Conclusion: AM neuronal responses in the delay period were rare (13/423), suggesting that the AM is not involved in short term memory in DPC for familiar color matching.

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FUNCTIONAL CHARACTERISTICS OF CEREBELLAR GOLGI CELLS IN DECEREBRATE CATS. TAKAHIRA, H. Dept. of Physiol., Tokai Univ. Sch. of Med., Bohseidai, Isehara, 259-11, Japan

In the boundary area between Purkinje cell layer and upper granular layer of cat's cerebellar cortex, so-called 'multi-unit' type of recordings were obtained with single capillary microelectrodes. They are mossy fiber spikes, Purkinje cell spikes and Golgi cell spikes. Respective activities from different units could be discerned by their own functional characteristics. In this report, the characteristics of Golgi cell spikes will be described. The duration of extracellularly recorded spikes from Golgi cells was invariably longer than that from Purkinje cells: almost twice (3 ms) of that of Purkinje cells (1.5 ms). This is due to the difference of durations of intracellularly recorded spikes from two cells. Golgi cells never fired 'bursts' as those of Purkinje cells, but fired repetitive discharges in response to single shock in the cerebellar white matter or in the ipsilateral radial nerve. Identification of Golgi cell spike, distinguishable from Purkinje cell spike, thus quite clear, but these two cell spikes in addition to intradendritically recorded 'slow spikes' from Purkinje cells were only discernible intracortical cell spikes obtained in cat's cerebellar cortex. These results suggest that the other cerebellar cells; upper stellate cells, basket cells and granule cells, might be 'non-spiking' interneurones, transmitting averaged signals between 'spiking' input fiber and output cells.

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THE ORIGINS OF THE CLIMBING AND THE MOSSY FIBER INPUTS TO THE CEREBELLAR NODULUS IN RABBITS. KATAYAMA,S. & NISIMARU, N. Dept. of Physiol., Med. Coll. of Oita,Oita 879-56

The origins of the climbing and the mossy fiber inputs to the nodulus were studied by means of retrograde transport of horseradish peroxidase (HRP) in α-chloralose urethane anesthetized rabbits. The climbing fiber inputs showed topographically organized projections to longitudinally oriented zones. There are at least 5 zones in the nodulus. The nucleus beta of the inferior olive (IO) projects contralaterally to a most medial zone. The rostrolateral part of the medial accessory olive(MAO) projects to the most lateral zone. The dorsal cap of the principal olive (PO) projects to a zone located in the relatively wide intermediate zone. The dorsomedial cell column projects to a zone located between the rostrolateral MAO zone and the dorsal cap zone. Finally, the ventrolateral outgrowth of the PO projects to a zone located in the middle part of the dorsal cap zone. When HRP was injected in the lateral one-third of the nodulus labelled cells were also found in the vestibular nuclei(MV and LV), prepositus hypoglossal nucleus(PH),intercalated nucleus , Roller nucleus and medial longitudinal fasciculus. On the other hand, following injections of HRP in the medial part of the nodulus, labelled cells were found only in the MV, LV and PH, predominantly in the ipsilateral side. It is suggested that the mossy fiber inputs might terminate in longitudinally oriented zones in the nodulus.

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BRANCHING PATTERN OF SINGLE INTERPOSITUS AND DENTATE NUCLEUS NEURONS IN THE RED NUCLEUS Mitoma, H.,Futami, T. and Shinoda, Y. Dept. of Physiol., Sch. of Med., Tokyo Medical and Dental University, Yushima, Bunkyo-ku, Tokyo, Japan

Axonal branching patterns of physiologically identified cerebellar nucleus neurons were investigated in anesthetized cats, using methods of intraaxonal HRP injection and three-dimensional reconstruction on serial sections. Penetrated axons were identified as axons originating from dentate or interpositus neurons by their direct spike responses to stimualtion of individual nuclei at an intensity of 200 uA or less. Axons of dentate and interpositus neurons projected to the VL nucleus of the thalamus and on their way, several axon collaterals were given off from stem axons to the red nucleus. Axon terminals of interpositus neurons were very extensive and terminated as a sagittal sheet of arbolizations in the red nucleus. The approximate dimension of this sheet of arbolizations was 1 to 2 mm rostrocaudally, 200 to 500 um mediolaterally, and 500 to 800 um, dorsoventrally. Their terminal boutons made apparent contact with cell bodies and proximal dendrites of rubrospinal neurons. The axons from the dentate nucleus, passing through the caudal portion of the red nucleus, entered into the rostral portion of it and gave off axon collaterals there. These collaterals were very thin and axon terminals were usually very sparse. So far, we could not find any cerebellar nucleus neurons specifically projecting to the red nucleus without further projecting to the VL.

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PURKINJE CELL-CHARACTERISTIC P_{400} PROTEIN AND DENDRITE FORMATION OF PURKINJE CELL.
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P_{400} protein was purified from 6 weeks old mouse cerebella by consecutive column chromatographies. Two kinds of the proteins were obtained using Con A Sepharose(Con A-binding and -nonbinding P_{400}). Although both proteins have the same molecular weight of 250K, they were clearly separated by the two dimensional gel electrophoresis, and also gave the different patterns by the peptide map analysis. These results indicated that P_{400} protein consists of at least two proteins, which are highly related, but have different structures. A monoclonal antibody against Con A-binding P_{400} was obtained(10A6). In the immunohistochemical studies, 10A6 stained only Purkinje cells. In the staggerer mutant mouse where the dendrite arborization of Purkinje cell is poor, Con A-binding P_{400} was almost missing. Expression of this protein increased with the development of Purkinje cell's dendrite. These results suggested that Con A-binding P_{400} plays important role in the dendrite formation of Purkinje cells.

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TRANSPLANTATION OF DISSOCIATED CEREBELLAR CELLS INTO THE WEAVER MOUSE CEREBELLUM.
TAKAYAMA, H.[2], KOHSAKA, S.[1], SHINOZAKI, T.[2], INOUE, H.[1], NAKANO, Y.[2], OTANI, M.[2], TOYA, S.2 AND TSUKADA, Y.[1] [1]Dept. Physiol., [2] Dept. Neurosurg., Sch. Med., Keio Univ., Tokyo 160

Weaver mutant mouse is characterized by a degeneration of cerebellar granule cells in an early postnatal development. Normal cerebellar tissues were obtained from 15-day-old mouse embryos(CBA) and were dissociated by a treatment with trypsin. The dissociated cells were transplanted into the cerebellum of 5-week-old weaver mice. At 4th week after the transplantation, the grafted tissue was distinguishable from the host cerebellum, developing a trilaminar organization. Autoradiographic studies using ^{3}H-Thymidine revealed that implanted granule cells were actively proliferated in the host cerebellum. The formation of synapses by the implanted granule cells was analyzed immunohistochemically with antiserum against synaptic vesicle protein, Synapsin 1. Certain areas in the grafted tissue were intensely stained with Synapsin 1 antiserum.

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MICRO-COMPUTER ANALYSIS OF LINE-DRAWING TEST AS A MEASUREMENT OF CEREBELLAR DYSMETRY.
SHIMOYAMA,I., UEMURA,K., MORITA,Y., NINCHOJI,T.* and RYU,H. Hamamatsu Univ.,Sch.Med., Hamamatsu 431-31

There are no well-documented normal standards in a so-called Line-Drawing test, which has been used to detect cerebellar dysmetry clinically. This test can be performed quantitatively and the results can be analysed simultaneously under a simple system, in which minute slips of horizontal lines drawn between pre-determined two vertical lines can be fed through digitizer and detected by a micro-computer.

One hundred and three normal subjects, including 64 males and 39 females (ages ranged between 9 and 78 and their average was 35.7) were examined.

Age, sex, repetition of the test and distances between two vertical lines, all did not show any statistical differences. Regardless of age, sex, repeated trials and length of lines to be drawn, slips at the stop lines fell within $\pm$ 1.5mm of them.

In conclusion, this system can be used to test quantitatively one aspect of cerebellar function.

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POSSIBLE DEGENERATION OF THE INTERNAL GRANULE CELLS IN THE CEREBELLUM BY THE INJECTION OF TUNICAMYCIN INTO THE NEONATAL RAT. MITA,K., KOHSAKA,S. AND TSUKADA,Y. Dept. Physiol., Sch. Med., Keio Univ., Shinjuku, Tokyo 160

Previous studies from our laboratory have demonstrated that a single intracranial injection of tunicamycin(TM), an inhibitor of glycosylation, into the neonatal rat specifically impaired the postnatal development of cerebellum. The mechanism of the cerebellar maldevelopment by the TM treatment was further investigated. DNA content in the cerebellum did not change at 1 and 2 days after the injection, but significantly decreased from 3 days till 4 weeks. By the autoradiographic studies using ^{3}H-thymidine, it was clearly shown that the cell division of the external granule cell layer was not affected by the compound at the time of the injection. However, the number of the labelling cells in the internal granule cell layer was severely reduced at 7 days. These results suggest that glycoconjugates may play important roles in the survivability of granule cells after the migration.

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DIFFERENCES OF THE LAMINAR PROFILE OF NEURONAL ACTIVITIES IN THE PRIMATE MOTOR CORTEX UNDER ANESTHETIZED AND UNANESTHETIZED CONDITIONS. Matsumura, M., Sawaguchi, T. and Kubota, K. Dept. of Neurophysiol,, Primate Res. Inst., Kyoto Univ., Inuyama, Aichi 484

Differences of the laminar profiles of neuronal activities between awake and anesthetized conditions were analyzed in the primate motor cortex. Multiple neuronal activities were successively recorded while multi-barreled carbon fiber electrode was deepened at every 200 um step. In awake preparation, the neuronal activities were higher in the upper part of layer III and layer V. This laminar pattern of the activities was weakened by iontophoretically applied Bicuculline (<50 nA). In Halothane (1%) or Pentobarbital (35 mg/Kg) anesthetized condition, spontaneous activities were drastically decreased at every cortical layer. This trend was the most obvious in the layer V. These decreased activities were not recovered by Bicuculline application. These results were interpreted that lower activities in anesthetized condition were due to the lack of excitatory synaptic inputs. Intra-cortical GABAergic inhibition might be involved significantly to generate the laminar activity pattern of the motor cortex in awake condition.

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ELECTRICAL ACTIVITY IN THE PREFRONTAL CORTEX SPECIFIC TO NO-GO REACTION OF CONDITIONED HAND MOVEMENT WITH COLOUR DISCRIMINATION IN THE MONKEY. SASAKI, K. AND GEMBA, H. Inst. for Brain Res., Fac. Med., Kyoto Univ., Kyoto 606

Monkeys were trained to perform hand movements in a reaction time task with discrimination between go and no-go light signals, and field potentials in various cortical areas were recorded and analysed with chronically implanted cortical electrodes. The caudal part of the dorsal bank of the principal sulcus was found to be activated specifically on no-go trials and revealed a relatively sharp surface-negative, depth-positive potential at a latency of 110-150 ms after the onset of no-go light stimulus. Development and increase of the potential were closely correlated with the process of acquiring the discrimination. With reversal of the go and no-go signals, this potential was found to be recorded only on no-go trials, irrespective of the colour used for the stimulus. In all six monkeys tested, the potential was recorded in the caudal part of the dorsal principal bank in both hemispheres, and also the electrodes implanted in the rostroventral part of the inferior convexity of the prefrontal cortex in two monkeys revealed the similar potential on no-go reactions. It is suggested that the no-go potential in these prefrontal areas is related to the judgement not to execute the movement and the suppressor action of the prefrontal cortex on motor execution. Sasaki, K. and Gemba, H. (1986) Exp. Brain Res. 64: 603-606.

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FUNCTIONAL ORGANIZATION OF THE FRONTAL EYE FIELD IN MONKEYS. AZUMA, M., SASAKI, Y. AND SUZUKI, H., Dept. of Physiol., Hirosaki Univ. Sch. of Med., Hirosaki 036

In the periarcuate cortex of the awake macaque monkey, we localized the cortical extent in which saccadic eye movements were elicited by intracortical microstimulation (the frontal eye field, FEF). The FEF was extended along the inferior arcuate sulcus, into depth of its anterior bank up to its floor, and slightly onto the prearcuate cortical surface. In thus defined FEF, there was topographic organization with respect to the saccade vector: stimulation in the caudo-lateral portion elicited small-amplitude saccades, while the rostromedial portion large saccades. We further found a relation of generating saccade with the visual receptive field of the neurons recorded at the stimulating site. The saccade elicited by microstimulation brought the visual line of the animal into a specific area of the contralateral visual field, that was generally situated within the visual receptive field of the neurons.

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CONTINGENT NEGATIVE VARIATION (CNV) AND READINESS POTENTIAL IN THE FRONTAL LOBE OF MONKEYS.
GEMBA, H., TSUJIMOTO, T. AND SASAKI, K. Inst. for Brain Res., Fac. Med., Kyoto Univ., Kyoto 606

Monkeys were trained to lift a lever with wrist extension in response to the imperative yellow light stimulus (IS) of 500 ms duration that was preceded for 0.8-1 s by warning stimulus (WS) of green light (50 ms duration) or of 2000 Hz tone (10 ms duration). Field potentials evoked thereby were recorded with electrodes implanted chronically on the surface and at a depth of 2.0-3.0 mm in various loci of the frontal cortex. After short latency responses set up by WS, surface-negative, depth-positive slow potentials were started and maintained toward IS in the prefrontal, premotor, supplementary motor (SM) and motor cortices. The slow potential was, in general, much more predominantly induced by the light WS than the tone WS, and was different in shape and size in respective cortical areas. The potential is considered to be an electrical dipole due mainly to synaptic currents in cortical pyramidal neurones and to correspond to CNV of the human. The readiness potential prior to self-paced movements was significantly recorded with the same electrodes in the motor, somatosensory, premotor and SM areas, but not so with those in the prefrontal areas. The readiness potential became visible in the prefrontal areas after a monkey was exercised with the WS-IS task, but it was rather feeble and almost disappeared with repetition of self-paced movements.

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PRIMATE PREFRONTAL NEURONS RELATED TO THE 'ASSOCIATIVE SIGNIFICANCE' OF THE STIMULUS.
WATANABE, M. Dep. of Liberal Arts, Tokyo Engineering University, Hachioji, Tokyo 192

In the primate prefrontal cortex, those neurons are reported which code the 'behavioral significance' of the stimulus. This study was conducted to find out whether there are neurons in this area which code the 'associative significance' of the stimulus.

Two monkeys were trained on a lever-release response task which was overlapped by a stimulus-reward association learning; the animal could obtain the juice reward after the lever-release response only when a visual or auditory cue presented had been associated with the juice reward. About 30 % of task-related neurons were found to be related to this associative significance of the stimulus independent of its physical properties, and about 10 % were related to both the physical properties and the associative significance of the stimulus.

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RESPONSES OF THERMAL SENSITIVE TOOTH PULP DRIVEN NEURONS IN THE SI REGION OF CAT CEREBRAL CORTEX.
KOICHI IWATA, HIROYUKI MURAMATSU, HIROSHI ITOGA, AIKO SUZUKI and RHYUJI SUMINO
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Distribution and response properties of SI neurons responded to thermal stimulation of the tooth pulp were studied in the cat anesthetized with ketamine-HCL (initial dose: 50mg/Kg, maintenance dose: 20mg/Kg at every one hour) and immobilized with pancronium bromide (about 1mg/Kg at every one hour). A total of 96 TPNs which responded to electrical stimulation of the tooth pulp were tested for the thermal stimulation (10 - 55 ^{o}C) to the tooth pulp. 15 of 96 TPNs (16%) responded to thermal stimulation of the tooth pulp (TS-TPNs). Ts-TPNs were distributed in the cytoarchitectonic area 3b, while Thermal insensitive TPNs (Tins-TPNs) were in the areas 3a and 3b. 60 % of Ts-TPNs received noxious cutaneous inputs from the orofacial regions, while only 15% of Tins-TPNs received those inputs. All Ts-TPNs increased firing frequency depending on the intensity of thermal stimulation to the tooth pulp.

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PERCEPTUAL DEFICITS DEDUCED FROM MONKEY'S MANIPULATIVE BEHAVIOR. AN EFFECT OF MUSCIMOL INJECTION INTO THE SOMATOSENSORY CORTEX (SI).
IWAMURA, Y. TANAKA, M. AND HIRABA H. Dept. Physiol., Toho Univ. Sch. Med., Tokyo 143

Localized injection of muscimol (GABA agonist) into the monkey somatosensory cortex induced deficits in dextrity of hand and fingers to manipulate small objects such as diced apples. We noticed that after the injection animals often behaved as if they had a piece of diced apple in their hand irrespective of their failure to do so. In other occasions, they were not aware of the presence of the object in their hand. These behavioral signs of perceptual deficits appeared relatively quickly after the muscimol injection into the middle regions of area 2, where neuronal receptive fields covered the volar surfaces of either index or middle finger, or of multiple fingers. In more medial or lateral region of area 2, it took longer time, more than one hour, to be manifested. Similar observations were made only occasionally when muscimol was injected into area 3a or 3b. The results support our hypothesis derived from neuronal studies(Iwamura et al Exp Brain Res. 51:327) that area 2 is the site of processing information related to object discrimination or recognition.

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RESPONSE PROPERTIES AND MORPHOLOGICAL FEATURES OF PYRAMIDAL NEURONS IN THE CAT SOMATOSENSORY CORTEX.
SAMEJIMA,A., YAMAMOTO,T., AND OKA,H. Dept. of Physiol., Fukui Med. Sch., Fukui 910-11

Intracellular recording combined with HRP injection was performed in cat cortical areas 3,1 and 2 under Nembutal anesthesia(35mg/kg,i.p.). Responses in cortical neurons were examined by stimulations of the superficial radial nerve(SR), the ventrobasal complex of the thalamus(VB), the pyramidal tract or the pontine nuclei. Morphological identification of HRP-stained neurons was performed in various layers of the cortex. In layer V, two types of the pyramidal neurons were found as reported in the motor and parietal cortices; i.e. one has spiny apical dendrites and slow conduction velocity, and the other has aspiny apical dendrites and fast conduction velocity. Latencies of EPSPs in the two groups evoked by SR and VB stimulations had statistically non-significant difference. Mean latencies evoked by VB were 1.9, 1.6, 2.4 and 2.3ms in layers II, III, V and VI, respectively. Connections of the thalamocortical fibers with the layer III pyramidal neurons was presumed to be monosynaptic from the short latencies and extrapolating results. Mean latencies of EPSPs of non-pyramidal neurons in layers III and V induced by SR and VB stimulations were significantly shorter than those of pyramidal neurons.

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SPATIAL ORGANIZATION OF INTRACORTICAL MICROSTIMULATION EFFECTS IN THE DIGIT AREA OF MONKEY MOTOR CORTEX.
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Dept. Physiol., Sch. Med. Hokkaido Univ. Sapporo, 060

The effects of intracortical microstimulation were examined in the digit area of the precentral motor cortex of unanesthetized monkeys (Macaca fuscata). EMG recordings were made with wire elelctrodes chronically implanted in digit and forelimb muscles. The magnitudes of stimulus-evoked muscle responses were digitized and fed into a microcomputor along with data about locations of stimulating electrodes in x-y coordinate as well as their cortical depths. Stimulation (11x 0.2 ms-rectangular pulses at 333 Hz) with four different intensities was made after every 200 or 300 μm electrode advancement. All electrode tracks were reconstructed with the aid of microlesions (with iron deposits). The distribution of effects on individual muscles obtained in the entire digit area were plotted on an unfolded map of the precentral gyrus. Magnitudes of muscle responses were also plotted on a three dimensional display. As a result of these analyses, spatial organizations of the entire microexcitable digit areas were visualized.

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EXCITATORY SYNAPTIC ACTIONS BETWEEN PAIRS OF NEIGHBORING PYRAMIDAL TRACT CELLS IN THE MOTOR CORTEX. KANG, Y., KAYANO, F., ENDO, K. and ARAKI, T. Dept. Physiol., Kyoto Univ. Fac. Med. Kyoto 606

By spike triggered averaging, we documented recurrent individual EPSPs produced in 27 pyramidal tract (PT) cells by the activity of axon collaterals of neighboring single PT cells in the motor cortex of the cat. Recurrent individual EPSPs were produced in fast PT cells by activation of neighboring slow PT cells and also of neighboring fast PT cells. Some recurrent individual EPSPs were observed also in slow PT cells. The mean latencies of recurrent individual EPSPs produced by the activity of axon collaterals of slow and fast PT cells were 1.74 msec (n=18) and 1.17 msec (n=9), respectively. Their amplitude ranged between 30 and 390 μV (n=27). Their rise time observed in fast PT cells with activation of slow and fast PT cells ranged from 1.6 to 3.6 msec (n=17) and from 0.8 to 1.9 msec (n=7), respectively. It is suggested that axon collaterals of slow PT cells may synapse onto more distal dendrites of fast PT cells than axon collaterals of fast PT cells. Facilitation of recurrent individual EPSPs was observed in fast PT cells following averages selectively triggered from spikes of slow PT cells preceded by short interspike intervals (10-20 msec; 50-100 Hz) rather than those preceded by longer intervals.

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CYCLIC AMP GENERATING SYSTEM IN THE CEREBRAL CORTEX AFTER AN ANODAL POLARIZATION IN RATS. MORIWAKI, A., HATTORI, Y., HAYASHI, Y. 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 applied for 30 min to the surface of the left sensorimotor cortex (anodal polarization). One day after the anodal polarization, rats were decapitated and the cerebral cortex was dissected into four quadrants 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 adenosine after preincubation for 60 min, and then cyclic AMP contents were determined and compared among the cortical areas. In rats polarized with 3.0 or 30 μA, the ratios of cyclic AMP content in adenosine-treated slices to that in untreated slices were greater in the left anterior cortical area than in the right anterior. In rats polarized with 0.3 μA, there was no difference in the ratios between left and right anterior cortical areas. The changes in cyclic AMP response to adenosine appeared to be due partially to fluctuation of cyclic AMP levels in untreated slices.

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AUDITORY NEURONS IN THE CEREBRAL VOCALIZATION NUCLEUS OF THE CANARY. MASAO MAEKAWA and NOZOMU SAITO, Dept. of Physiol., Dokkyo Univ. Sch. of Med., Mibu, Tochigi, 321-02

The cerebral vocalization nucleus in the canary, the caudal nucleus of the ventral hyperstriatum (HVc), is well developed as a voco-auditory association area. Most auditory neurons in the HVc responded with a phasic pattern to pure tone (phasic auditory neuron). The phasic auditory neuron elicited an intracellular slow potential which underlied the phasic spike potential.

The neurons which elicited slow potential responded with a constant latency throughout 30 trials of pure tone stimuli, while the other neurons which did not elicit a slow spike (non-phasic auditory neuron) responded with an irregular latency.

By using intracellular HRP staining, the phasic auditory neuron was clarified to be a relatively large cell with large dendritic arborization, and was closely contacted to neighbering neurons which constituted a cluster. However the non-phasic auditory neuron was small with fewer dendrites and was isolated; not forming cell cluster.

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The Morphological Study of the Epileptic Neuron. KOYAMA,I.,NISHIOKA,S.[1],SHIMIZU,H.[2]*, ISHIJIMA,B.[2]*,SEKINO,Y.,and UEDA,K. Dept.of Physiol.,Tokyo Women's Med.College,[1]Mitubishi Kasei Soken,[2]Tokyo Metropolitan Neurol.Hospital

The cortical tissues,removed from the focus of temporal lobe epilepsy of man with theraputic purpose, had been stained by Rapid Golgi method. Our finding seemed similar to those found in the cobalt-induced epileptic focus of cat. Most importantly the alteration of the apical dendrite of PT cell;such as beadstring formation, decrease number in spine, and cell destruction appeared in close contact with the intact neurons. This morphological background related to occurence of epilepsy.

The present study is meant to know whether or not this damaged neuron can become hyperexcitable.For this purpose HRP is injected through recording microelectrode after the recording the burst activity of neuron in cobalt-induced focus of cat. HRP-stained cells were PT, stallate, and spindle neurons. Their configulation under the light microscope appeared rather normal, if any an alteration exsisted, it was not an advanced one. Therefore, epileptic firing may initiate from intact neurons that depolarized in the environment caused by the closely located destructed neurons.

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THE ORGANIZATION OF THE GUSTATORY CORTEX OF THE HAMSTER: AN ANATOMICAL AND ELECTROPHYSIOLOGICAL STUDY. KITAMURA, R.* AND YAMAMOTO, T. Dept. Oral Physiol., *Dept Oral Surg., Osaka Univ. Fac. Dent., 1-8 Yamadaoka, Suita, Osaka 565.

The gustatory cortex (GC) was delineated by mapping the evoked potentials which were induced by electrical stimulation of the chorda tympani and glossopharyngeal nerves. Injection of HRP to the GC showed that the neurons in this area sent axons to the ipsilateral parvocellular part of the ventralis posteromedial nucleus of the thalamus (VPMpc), the ipsilateral central nucleus of the amygdala (AM), the bilateral parabrachial nuclei (PbN) and the contralateral nucleus of the solitary tract (NTS). Injection of HRP to these corticofugal projection areas revealed that layers I and V received inputs from the GC, VPMpc, AM and PbN, layer II-IV from the GC and VMPpc, layer VI from the VPMpc and PbN, and the neurons in layers V and VI sent axons to all the 5 structures and VPMpc, respectively. Neurons in layer V tended to respond to one or two stimuli among the four basic taste stimuli, indicating that the corticofugal output neurons are narrowly tuned in their taste responsiveness.

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REORGANIZATION OF SENSORIMOTOR CORTEX CORRESPONDING TO CONVERSION OF FOOD INGESTIVE BEHAVIOR FROM SUCKING TO CHEWING DURING DEVELOPMENT OF GUINEA PIGS. IRIKI, A. AND NAKAMURA, Y. Dept. Physiol., Fac. Dent., Tokyo Med. Dent. Univ., Bunkyo-ku, Tokyo 113

We previously reported in guinea pigs that the origin of corticobulbar projections responsible for rhythmical jaw movement induction was transposed during the conversion from sucking to chewing. In the present study, the mode of reorganization of the sensorimotor cortex corresponding to this conversion was studied by systematically testing motor effects of intracortical microstimulation and sensory responses of single units in the cortex. The results are as follows: 1) The cortical area whose repetitive stimulation induced sucking movements in immature animals was situated in the motor representataion area of the jaw, face and tongue of the agranular motor cortex. Stimulation of the granular cortex never induced rhythmical jaw movements. 2) A circumscribed area with a less granular layer and with scarce peripheral inputs (disgranular area, DA) were found among the most rostral part of mature granular cortex, but not in immature one. The DA corresponded to the lower lip representation area laterally adjacent to the forepaw area of the immature primary sensory cortex; the lower lip area shifted laterally in mature animals and the DA occupied the region between the lower lip and forepaw areas. 3) In mature animals, train pulse stimulation of the DA induced EMG activities bilaterally in the digastric, lip and tongue muscles. Repetitive stimulation of this area, as well as a region within agranular motor cortex where the jaw, face and tongue were representated, induced chewing jaw movements.

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"OCULOMOTOR" CORTEX IN THE ANTERIOR ECTOSYLVIAN SULCUS OF THE CAT.
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The ventral bank of the anterior ectosylvian sulcus (AES) of the cat is important for the control of the eye movement since the cortex receives visual inputs and sends fibers to the frontal oculomotor cortices. In the present study, we demonstrated the eye movement following stimulation of the AES and its descending pathway.

Intracortical microstimulations of the AES zone evoked upward movements of both eyes when the eyes were directed downward. The latency of the eye movement was 40-60 msec and the intensity of the stimulation was 30-60μA. Antidromic spike of cortical neuron in the AES zone was evoked ipsilaterally by the stimulation of the reticular formation (RF) in the brainstem. Orthodromically labeled neural terminals were found in the RF, superior colliculus and pontine nuclei following injection of WGA-HRP in the AES zone at which the eye movement was evoked. These results suggest that the ventral bank of the AES may play a significant role in the control of the eye movements as an additional "oculomotor" cortex.

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RHYTHMIC DEPOLARIZING POTENTIALS OF DENDRITIC ORIGIN IN CAT MOTOR CORTICAL NEURONES DURING ELECTROCORTICAL TYPE II SPINDLES.
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Encéphale isolé cats were carefully maintained by monitoring the electrocorticogram with spontaneous sleep-waking cycles. Intracellular potentials were recorded from motor cortical lamina V neurones which responded to epicortical stimulation with slowly rising monosynaptic excitatory postsynaptic potentials (EPSPs). In these neurones, rhythmic depolarizing waves occurred closely in phase with spontaneous type II spindle bursts, composed of surface negative and deep positive waves. As we reported previously, the epicortically elicited EPSPs were of dendritic origin. Their amplitude was altered in proportion to the membrane potential which was changed spontaneously by excitatory bombardments onto the dendrites, but was insusceptive to the potential changes produced by current injection into the soma. These characteristics were all encountered in the rhythmic depolarizations during the spindle bursts. By assuming a linear relationship to spontaneous membrane potentials, the epicortical EPSPs and the rhythmic depolarizations in the same neurone yielded similar values of the "apparent" reversal potentials around -45 mV. These results indicate that the rhythmic depolarizations mainly consist of dendritic EPSPs caused by subcortical excitatory inputs to the cortical superficial layers.

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A PART OF THE PRIMATE CORTICOSTRIATAL PROJECTION IS SUPPLIED BY COLLATERAL BRANCH OF CORTICOSPINAL AXON FROM THE MOTOR CORTEX.
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To reveal innervation of the striatum by collateral branch of corticospinal (CSP) axon, we used two approaches using 3 monkeys (2 M. fuscata, 1 M. fascicularis). (1) fluorescent double labeling; Bisbenzimide labeling nucleus was injected into right spinal cord (SC, C3-C7) and Fast Blue labeling cytoplasm was injected into the left putamen. In the left motor cortex (MC), labeled corticostriatal (CST) cells were of medium size and scattered throughout layer V, while labeled CSP cells were large and located deep in layer V. 10-20 % of CST cells and 15-25% of CSP cells were double-labeled. (2) electrophysiology; stimulating electrodes were chronically implanted into right SC (C3-C7) and the left putamen. Animal was immobilized with Flaxedil and ventilated with a mixture of N_2O, O_2 and halothane. Action potential of left MC cells was recorded by an elgiloy microelectrode and examined to be antidromically evoked from SC and the putamen. Among 56 CST cells (latency, 7.9±3.7 ms) and 59 CSP cells (latency, 3.6±2.6 ms) thus identified, 5 cells were CSP cells with collateral branch to the putamen (latency, 4.1±2.6 ms from the putamen; 2.6±1.9 ms from SC). It was concluded that 15-25% of CSP cells in MC give collataral branch to the putamen, and thus a part of the motor command from MC to SC is transferred also to the putamen.

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EFFECTS OF DOPAMINE ANTAGONISTS ON NEURONAL ACTIVITIES RELATED TO THE DELAY OF A DELAYED RESPONSE TASK IN THE MONKEY PREFRONTAL CORTEX.

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To collect evidence that dopamine is involved in the spatial short-term memory mechanisms in the monkey prefrontal cortex, effects of dopamine antagonists were studied. While monkeys were performing a delayed response task, neuronal activities with changes during a delay period were recorded (n=32), and haloperidol, S-sulpiride, and fluphenazine were applied iontophoretically. Haloperidol and fluphenazine attenuated the delay-related activities in all of neurons tested (n=26, for haloperidol; n=6, for fluphenazine), while S-sulpiride did not affect those activities in all of neurons tested (n=25). Further, haloperidol attenuated the excitatory influence of dopamine on delay-relayed activities (n=3), but S-sulpiride did not (n=2). These data suggest that D-1 receptors may be involved in the neuronal processing of spatial short-term memory in the prefrontal cortex.

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ELECTRO-MYOGRAMMIC ANALYSIS ON THE HAND STIMULATION.

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How are the muscles of arms of the technician at the hand stimulation of technician for the case ? I examined it by the electro-myogramm. The muscles that I used on this occasion are the flexor, extensor of the forearm and the bicapitate, tricapitate muscle of the upper arm. The hand stimulations are the movable, balance and power ones. He gave them on the waist of the case. Then I recognized that at the mobilization of musscles group of arm and the technician gives stimulation to it with his both hands at the same time.

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BASIC STUDIES ON THE EMG COMPONENTS OF THE PHOTICALLY EVOKED LID POTENTIAL CHANGES, ESPECIALLY RELATED TO TECHNIQUES FOR LEADING.

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The EMG components of the average photically evoked lid potential changes were studied polygraphically under various conditions to determine the most adequate method to lead. In the evoked lid potential changes led off bipolarly the EMG components were decreased in amplitude. In the monopolar leads between auricles and different parts of the superior lids the EMG components were the highest in amplitude. The EMG components obtained by flash stimulation to a single eye disappeared almost completely in rabbits, though they appeared in human subjects. In dark adaptation the EMG components appeared more markedly than those obtained in light adaptation. They were usually increased in amplitude according to the intensity strengthened. The above results suggest that the EMG components of photically evoked lid potential changes as the indicator of orbicularis oculi reflex should be led off monopolarly with indifferent electrode on the auricle and the other exploring electrodes on the superior parts of the lid under dark adaptation, strengthening the stimuli, if necessary.

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A STUDY OF AVERAGED WAVE OF REFLEX DISCHARGE ON HYPOGLOSSAL NERVE BY ELECTRICAL STIMULATION ON GLOSSOPHARYNGEAL NERVE IN THE FROG.

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Reflex discharges were recorded from three branches,hyoglossal,intrinsic and genioglossal branch of hypoglossal nerve by stimulation to lateral and medial branches of glossopharyngeal nerve respectively. Reflex discharges were added thirty times by averager after treating through half wave rectifier. The averaged waves of reflex discharges have some characteristics. Latency of medial-hypoglossal reflex was shorter than that of lateral-hypoglossal reflex. Time from start to peak of discharge on hyoglossal branch was shortest among three branches. Duration of medial-hypoglossal reflex discharge was longer than that of lateral-hypoglossal one. But there is no difference on duration of reflex discharge in genioglossal branch between stimulation to medial branch and that to lateral branch. Area of averaged wave calculated by personal computer decreased with reduction of strength of stimulation. The rate of decrease of the area was slow in the cases of medial-hyoglossal,medial-intrinsic and lateral-genioglossal reflex. Threshold was low in the cases of medial-hyoglossal,medial-intrinsic and lateral-genioglossal reflex. Discharge areas of stimulation to medial branch were larger than that of stimulation to lateral branch,but discharge area of medial-genioglossal reflex was nearly as large as that of lateral-genioglossal reflex.

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MICRO STRUCTURE OF THE SCALP ELECTRIC FIELD. OZAKI, H[1], SUZUKI, H[1], KOIKE, T[2], KATADA, A[2] AND LEHMANN,D[3] Lab. Physiol., Ibarak Univ[1], Psychophysiol., Tokyo Gakugei Univ[2], Neurol., Zurich Univ[3]*

There are not only long-lasting, functional states of the brain such as sleep and wakefulness, but also shorter fluctuations lasting for seconds or less. These momentary states are manifestated in the EEG. We propose a procedure for adaptive EEG segmentation using spatial criteria of EEG data. 16-channel data are re-arranged into time series of maps of the field distributions. Global field power computed for each map assesses the momentary strength of map relief. During alpha, field power as function of time shows about 20 maxima per sec. At each moment of maximal field power, the location of the maximal and minimal (extreme) potential in the map are determined. A spatial window around each extreme value is set. If later, an extreme occurs outside of the set window, a new segment is started. Data during 2 min of resting from six volunteers were segmented after digital bandpassing to 8-12Hz. Mean segment duration over subjects was 210 msec. Over subjects, the most frequent type of segment covered 20% of total analysis time and constituted 12.5% of the incidence of all segments. The results show very short-lasting, different types of EEG activity when diagnosed by field configurations.

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THE TEMPORAL VARIABILITY OF THE FREQUENCY AND THE AMPLITUDE IN THE PEAK COMPONENTS OF CHILDREN'S EEGS. KOIKE,T.,KATADA,A. OZAKI,H.AND SUZUKI,H.Tokyo Gakugei Univ.,Ibaraki Univ.

The temporal variability of frequency components were investigated in EEGs of 30 normal children (3-6 years). EEGs were recorded monopolarly under the conditions of eye-closing and -opening. From EEGs of 3 minutes, the power spectrum array was calculated and the temporal variability of peak frequency and amplitude was measured. Theta and alpha components which had the the occipital-dominant distribution showed attenuated power under the condition of eye-opening. But in the same condition, theta components with the frontocentral-dominant distribution did not change markedly. These components showed higher temporal variability about the peak frequency and the amplitude, compared to the occipital-dominant components. It may be pointed out that the occipital-dominant alpha component of adults appears within the theta frequency band in the early developmental change of EEGs, and the generating mechanism of this component has different aspects from that of the theta components with the frontocentral-dominant distribution.

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EVENT RELATED POTENTIAL(CNV) IN SELF REGULATION METHOD.

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Psychological and physiological effects of Self-Regulation Method (SRM) are examined. SRM is a modification of autogenic training developed by Schultz. More than 100 subjects were used in this study. They have been informed about the method and trained themselves for five weeks according to the standard instructions. EEG, CNV and several psychological tests(STAI, YG, CMI) were examined before, during and after the course of the training schedules. Decreased anxiety and tention were shown by these psychological tests. EEG showed decrease of beta wave and increase of alpha and theta wave pattern. Negative shift of CNV between visual stimuli and imperative stimuli were decreased in amplitude during SRM without prolongation of the reaction times and increase of response errors. The results suggest that SRM induced a state of relaxed alertness.

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EFFECTS OF COMPRESSION AND DECOMPRESSION OF HYPERBARIC HELIUM-OXYGEN GAS IN SATURATION DIVES TO VARIOUS DEPTHS. TATSUNO, J., ASHIDA, H. AND OZAWA, K. Natl. Def. Med. Coll., Tokorozawa 359 and Undersea Med. Center Kurihama 239

During saturation dives in hyperbaric helium-oxygen gas of 7, 11 and 21 ATA, EEG was recorded from 12 locations to investigate the effects of compression and decompression by the gas to the theta and alpha activities through two-demensional isopotential map. The augmentation of theta component in frontopolar area is concluded that it is not EEG sign of high pressure nervous syndrome, because it was not accompanied by decrease of alpha activity. The theta increases were observed mainly on the way of compression or decompression in all the experiments and they are found to be different from frontal midline theta from the reason of topographical pattern. Even 21 ATA had not durable effects to the theta increase, therefore it is presumably due to the effect to emotion of the subjects during pressure change. Subtle differences in topographical patterns should be estimated by objective criteria and one method was introduced.

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DYNAMIC ASPECTS OF CORTICAL AUDITORY EVOKED POTENTIALS IN RELATION TO SLEEP-WAKING STAGES IN FREELY BEHAVING RATS. OKANO,Y., HONDA, K., and INOUE, S. Inst. for Med. and Dent. Eng., Tokyo Med. Dent. Univ., Chiyoda-ku, Tokyo 101

Auditory evoked potentials (AEPs) to continuous click stimuli at 1-s intervals from the cortex of freely behaving male rats were analyzed on their time-course variations in the peak-to-peak amplitude and latency of the middle and long components. Circadian variations in these parameters were also studied by comparing the results obtained from the first three hours of the light and the dark period. During slow wave sleep (SWS), AEPs were characterized by a marked increase in the amplitude and latency of the second negative (N2) and positive (P2) waves. This was clearly dependent on the depth of SWS as judged by increased EEG-delta activities. In contrast, AEPs were considerably stable during paradoxical sleep. During wakefulness, N2-P2 amplitudes occasionally tended to decrease presumably due to habituation or gating to the stumulation, although the latency of N2 and P2 components were rather unaffected. Significant differences were detected in parameters between diurnal and nocturnal AEPs.

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PHASE RELATIONS BETWEEN ELECTRICALLY INDUCED PAROXYSMAL DISCHARGES AND THE HIPPOCAMPAL NONPYRAMIDAL CELL FIRINGS. KOGURE, S. AND FUJII, N. Dept. of Physiol., Nippon Med. School, 1-1-5, Sendagi, Bunkyo-ku, Tokyo, 113

The depth profiles of evoked potentials (EPs) and electrically induced paroxysmal discharges (EPaDs), both elicited by contralateral stimulation, were recorded in the hippocampal CA1 region of lightly anesthetized and immobilized rabbits. Whereas the population spike of EP showed maximum amplitude in the pyramidal cell layer, the population spike component of EPaDs exhibited maximum amplitude in the apical dendrite layer. This suggests predominant excitation of the apical dendrites during EPaD.

TYPE II nonpyramidal cells that exhibited a sustained firing during EPaD, as previously reported, were classified into two subgroups according to their phase relations to individual paroxysmal spikes and waves. One group (N=12) showed a synchronous firing with individual ictal activity. It was therefore referred to as ictal type. The other group (N=14) exhibited a sustained firing with higher frequency during interictal periods than during ictal periods. It was therefore referred to as interictal type. An increase in the firing rate of ictal type cells during EPaD was particularly conspicuous. Namely the rate increased from 7.2±1.2 Hz in the spontaneous state to 43.0±3.7 Hz during EPaD. Consequently, it is suggested that ictal type cells are closely related to the mechanism for maintaining the paroxysmal discharges.

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THE EFFECT OF ANODAL DIRECT CURRENT ON CORTICAL EEG IN RABBIT. HAYASHI, Y., HORI, Y., ASAKI, H., HATTORI, Y. AND MORIWAKI, A. Dept. of Physiol., Okayama Univ. Med. Sch., Okayama 700

An anodal direct current was passed to the surface of the forelimb area in the motor cortex of awake or pentobarbital anesthetic rabbit. The current intensity was gradually raised from 10-20 μA to 500 μA by the step of 10-20 μA. The initial abnormal activities in EEG, which were often isolated spikes, appeared mostly from the frontal cortex at the intensity of about 40 or 130 μA in awake or anesthetic rabbit, respectively. For the stronger current, more frequent spikes and, in addition, augmentation of fast activities were observed. In awake rabbit, despite for severe seizure activity in EEG, behavioral alterlation was not recognized except for enhancement in the microvibration of the forelimb. When anodal current was turned off, abnormal activities in EEG and microvibration returned to nomal pattern in most cases. In several experiments, however, seizure activities or enhanced microvibrations continued even after the current was turned off. When the current was passed repeatedly , the threshold for the spike initiation was lowered. Therefore, anodal direct current may induce some plastic change in the cortex.

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MHBAA AND REM SLEEP. OKUDAIRA, N., HAGINO, K.*, KUDOH, K.*, OHSHIGE, H.*, KOIKE, H.*, INUBUSHI, S., YAMANE, M.* AND TORII, S. Dept. of Physiology, Toho University, School of Medicine and Dept. of Biochemistry, Tokyo Medical College, Ohta-ku, Tokyo 143

It is generally accepted that acetylcholine is the neurotransmitter which has the best established role in the initiation and maintenance of REM sleep and cholinergic mechanisms of the pontine reticular formation (PRF) underlies the generation of REM sleep. 1-methyl heptyl-γ-bromoacetoacetate (MHBAA), included endogenously in human cerebro-spinal fluid, was found to be a competitive inhibitor of the acetylcholinesterases. To determine the anticholinesterase action of MHBAA, 4 male cats, weighing 3 to 5 kg, were carried out the microinjection of MHBAA followed by a 48-hour continuous monitouring of surface EEG, EOG and neck EMG. MHBAA (683 nmol/250 nl) were injected at 10:00, through the chronically implanted bilateral guide tubes aimed at the rostral PRF. Control recordings were obtained following injection of 250 nl of sterile saline into the same site. MHBAA showed a significant decrease of the latency to onset of sleep, increase of the total aleep time during 24 hours and increase of the percentage of REM sleep during first 6 hours, compared to saline injection. The locations of the injection sites were grouped caudal to the ventral tegmental nucleus and rostral to the genu of the facial nerve and the abducens nucleus. These findings suggest that extrinsic MHBAA probably enhances REM sleep by driving cholinergic mechanisms.

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CHANGES IN CENTRAL NERVE ACTIVITY WITH DESTRUCTION OF THE INTERNAL CAPSULE, CAUDATE AND GLOVES PALLIDUS. SAKURAI, H., HASEGAWA, H., NAITO, H. AND YASUHARA, M. Dept. Physiol., Kansai Med. Univ., Osaka 570

The effect of destruction of the internal capsule(IC), caudate(C) and gloves pallidus(GP) of the rabbit on the threshold of the arousal reaction and evoked muscular discharge due to stimulation of the cerebral cortex or brain stem reticular formation, photo-evoked eyelid microvibration(MV) and photopalpebral reflex(PPR) was investigated.

The threshold increased markedly following IC destruction, slightly by GP destruction, but did not show pronounced change with C destruction. The changes in amplitude of MV following IC destruction could be divided into 2 groups, one in which the amplitude is decreased and the other in which the amplitude increased. The amplitude of the PPR components was decreased after IC destruction. The amplitude of MV and PPR components did not indicate marked changes with C and GP destruction.

The threshold decreased prominently by administration of CDP-choline after destruction of IC. The MV amplitude did not increase with CDP-choline after destruction of IC.

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FIRING PATTERNS IN MOTONEURONS INNERVATING THE PHARYNX 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 Aplysia buccal ganglia we identified a pair of motoneurons (PB neurons) innervating the ipsilateral posterior pharynx muscles (Px). Application of seaweed extract to the lips in semi-intact preparations induced rhythmic bursts of spikes in the PB neuron in almost antiphase with the retractor muscle activity (response-I). Even after cessation of the retractor muscle activity the rhythmic bursts in the PB neuron were still maintained (response-II). During the response-II, rhythmic change of inner pressure of the pharynx followed the burst activities in the PB neuron, and the sequential movements of the pharynx and esophagus were induced. The rhythmic change of membrane potential of the PB neuron during the response-II were completely ceased by steady hyperpolarization of the PB neuron. In addition, rhythmic bursts of spikes could be produced in the PB neuron by steady depolarization of the neuron. When the rhythmic bursts were produced in the PB neuron by steady depolarization, synchronized muscle potentials could be recorded in the ipsilateral anterior Px. These results suggest that the rhythmic activity in the PB neuron during the response-II is generated by the intrinsic properties of the PB neuron itself, and the PB neuron can also induce the movements of the ipsilateral anterior Px.

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CLASSICAL CONDITIONING OF THE CRAYFISH EYE-CUP WITHDRAWAL REFLEX. CHIBA, A., KOSAKA, M., MATSUSHITA, K. AND CHICHIBU, S. Dept. Physiol., Kinki Univ. Sch. Med., Sayama, Osaka 589

The classical conditioning of an eye-stalk withdrawal response was studied on crayfish (P. clarkii). A photic stimulus (CS) to the eye was paired with a tactile stimulus (UCS) applied to the ipsilateral cephalothorax. When the stimulations were paired, the CS became to evoke larger eye-stalk response progressively by trials. The CSs were divided into two groups; on and off of the illumination. The time needed for the learning of the light extinction as the CS was shorter than that for the illumination. The extinction process of the learning also showed the similar tendency. It was concluded that the light extinction was more important than the illumination. Comparing the adult and the young preparations, the former was gained learning and extinction of the photic stimuli faster than that of the latter. The associative learning in crayfish is possible to study at the behavioral and neuronal levels as a model of simpler neuronal circuitry.

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AFFERENT INPUT TO TELSON FLEXOR INHIBITORS IN THE CRAYFISH. TAKAHATA[1], M. AND WINE*, J.J. Dept. of Psychol., Stanford Univ., Stanford, CA 94305. [1] Zool. Inst., Fac. of Sci., Hokkaido Univ., Sapporo 060

Afferent input to telson flexor inhibitors (FI6 and FI7) in the terminal abdominal ganglion of crayfish was analysed by intracellular recording and staining (3% Lucifer yellow in 2.5M LiCl) techniques. Major findings are: 1) Electrical stimulation of the 4th or 5th root innervating telson mechanosensory hairs elicited a short-latency, fast-rising response that was often suprathreshold in FI7. The stimulus intensity for firing FI7 was weaker than that required to elicit spikes in the lateral giant (LG) which would act as the command neuron for escape behavior. 2) Stimulation of other roots which innervate mechanosensory hairs on other parts of abdomen than the telson elicited a long-latency, slow response in both FIs. 3) No laterality was observed between stimulation of any root on either side. The results support Dumont and Wine's hypothesis (1987) that sensory information is feedforwarded to motor pattern generator to cancel some of the LG output to form a final motor pattern of escape behavior. However, the weighted receptive field organization of telson FIs revealed in this study is not reflected in the actual escape behavior. Further interspecific and developmental studies will be necessary to clarify its functional meaning which at present remains inexplicable in terms of neuronal circuitry.

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A STUDY OF QNB BINDING SITES IN THE CHICK BRAIN AFTER IMPRINTING.
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The distribution of muscarinic cholinergic binding sites, with an affinity for (^{3}H)QNB, were studied in certain area of the chick brain, especially medial hyperstriatum ventrale (MHV) which has previously been implicated in imprinting process. QNB binding sites were present in relatively high concentration in visual projection area and low in cerebellum. The effects of imprinting stimulus on the concentration of QNB binding sites in MHV were investigated. Thirty minutes after imprinting stimulation, specific QNB binding sites in right MHV increased 30% compared with those of dark reared chicks. This increasement continued at 24 hours after the stimulation. But there was no such effect in left MHV. It was suggested that hemispheric asymmetries are present in MHV after imprinting and right MHV may play dominatly in imprinting process.

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Behavior analysis of myelin deficient mutant mice, shiverer and mld.
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Behavioral deficits of two genetical myelin deficient mutant mice, shiverer and myelin deficient (mld) were examined. The primary affect-ed site of shiverer has been proven to be myelin forming cells themselves. Mld is allelic mutant to shiverer and it has been clarified that the degree of biochemical and morphological abnormalities of mld is less severe than that of shiverer. Shiverer did not show any deficits in the radial maze performance which has been considered to be natural foraging behavior of rodents, but they did show deficits in successive reversal learning. Mld also did not show any deficits in the unlearned behavior in the radial maze, but showed less deficits in the learning performance than shiverer. This finding is compatible with the previous studies of biochemical and morphological studies of the mice. And in both tasks, they required more time to perform than their normal controls. The present study indicated that shiverer and mld showed not only motor impairement but also learning deficits.

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ANIMAL MODEL OF MEMORY IMPAIRMENT BY CHOLINERGIC NEUROTOXIN, AF64A.
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Learning behavior of rats in which a central cholinergic hypofunction was induced by a cholinergic neurotoxin, ethylcholine mustard aziridinium ion (AF64A) was studied as a potential animal model of aging-related memory disorder. The AF64A or vehicle was infused bilaterally into each lateral cerebral ventricle. Radial maze performance was significantly impaired in both groups of AF64A (3 and 6 nmoles) in training 2 weeks after dosing and in relearning 3 months after the original training. Also, the AF64A treated rats showed significant deficit in delayed alternation behavior which was tested in a T-maze apparatus. By contrast, they showed a less impairment in a passive avoidance training which was considered as a type of punishment learning. In the AF64A groups the activity of choline acetyltransferase was largerly reduced from 30 to 50% of control group in both dorsal and ventral hippocampus, whereas it was only decreased from 80 to 90% of control in the frontal cortex and showed no significant change in the striatum. These results indicated that hypofunction of the septo-hippocampal cholinergic system caused chronic impairment particularly in learning performance related with spatial memory.

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NEURAL RESPONSES IN AMYGDALA DURING TONE DISCRIMINATION BY THE RAT.

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Single neuron activity was recorded in the corticomedial (CoM) and basolateral (BL) nuclear groups of the rat amygdala (AM) during discrimination of cue tones that predicted glucose or rewarding intracranial self-stimulation (ICSS) to the lateral hypothalamic medial forebrain bundle (MFB). Each impending stimulus was signaled by a distinctive cue tone (CTS): 1200 Hz ($CTS1^+$) for glucose, 4300 Hz ($CTS2^+$) for ICSS and 2800 Hz for no reward. In the BL, more than half (57%) and in the CoM, two thirds (67%) of the neurons responded to either or both rewards. Excitation was dominant in the BL and inhibition was dominant in the CoM. About half of the neurons that responded to either or both rewards, also responded to CTSs. The CTS responses were usually in the same direction as the associated reward responses. Some neurons responded differentially to $CTS1^+$ and $CTS2^+$; more BL (11%) than CoM (6%) neurons responded in this way. The data suggest that AM neurons are related to the processing of sensory information; and BL neurons are more important in discrimination the significance of a stimulus.

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ANYLYSIS OF THE ROLE OF INTRINSIC NEURONS OF THE AMYGDALOID FIELD IN THE FORMATION OF CNDITIONED RESPONSES TO ACOUSTIC STIMULI.

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We have previously reported that projection from medial geniculate body(MG) to posterior caudate-putamen(CPu) and amygdala(AMG) mediate auditory aversive conditioning responses. In this study, we investigate whether intrinsic neurons in this field mediate conditioning responses, if so whether critical neurons are contained in the AMG or in the CPu. Selective neurotoxin, ibotenic acid, is injected into CPu and/or AMG. Contralaterally MG is damaged by electrical procedure. As a control group, unilateral MG is electrically lesioned and phosphate buffer is injected into contralateral CPu and AMG. After two weeks of recovery period, rats are subjected to calssical fear conditioning involving the pure tone in association with footshock. Conditioned changes in mean arterial pressure(MAP), heart rate and behavior(freezing) elicited by the tone were assessed during extinction test. Destruction of intrinsic neurons in the AMG but not in the CPu disrupted the associative learning responses in MAP and freezing. Histological and biochemical experiments showed that ibotenic acid damaged only neuronal cell bodies and spared sxons of passage. In conclusion, intrinsic neurons in the amygdala appear to be involved in mediating the emotional responses conditioned to acoustic stimuli.

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CHEMOSENSITIVITY OF LATERAL HYPOTHALAMUS NEURONS INVOLVED IN CUE TONE LEARNING BY RAT.

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Single unit activity of 125 neurons in the rat LHA was recorded during discrimination of cue tones (CTS) that predicted rewarding stimuli (glucose or ICSS) and aversive stimuli (electric shock or tail pinch). The catecholaminergic, cholinergic, and opioid systems in the LHA were investigated by electrophoretic application of noradrenaline (NE), dopamine (DA), ACh, morphine (Mor) and their antagonists (spiperone, phenoxybenzamine, atropine and naloxone). During CTS learning, 105 (84%) responded in one or more phases. NE inhibited firing in 41/79 and excited 3/79. DA inhibited 20/80 and excited 7/80, ACh excited 16/43 and inhibited 2/43, and Mor inhibited 5/17 and excited 1/17. DA sensitive neurons responded to rewarding stimuli and predicting CTS more often than DA insensitive neurons. Inhibitory responses to CTS were blocked by spiperone or naloxone and excitation was blocked by atropine or spiperone. Inhibitory responses during and after licking for glucose were blocked by naloxone and excitation was reduced by spiperone. Data suggest that afferent inputs to CTS learning related LHA neurons from dopaminergic, cholinergic and opioid systems are involved in CTS learning in different ways.

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AGE EFFECTS ON SCHEDULE CONTROLLED LEFT-RIGHT DISCRIMINATION LEARNING TEST IN FISCHER 344 RATS. NOMURA, M. Dept. of Physiol. School of Med. Fujita-Gakuen Health Univ., Toyoake, Aichi 470-11.

The decline of cognitive process in aging animals is clear. But it is still questionable whether the decline occurs in all phase of learning and memory. Young Fischer 344 rats 3 months old and aged 24 months old were studied for a left-right discrimination learning test. The method of operant type learning test in the Skinner box was tasked food reinforcement on Multiple Variable Interval 15 seconds extinction schedule. The left-right discrimination learning test was composed of S+ as a light on at the right side lamp on the front wall of the Skinner box, and S- was reverse light on and off. The response number to S+ and S-, R+ and R- were remarkably decreased in aged rats. And the correct response ratio ((R+)/ (R+)+(R-))x100, as an index of learning ability, also was shown to be less than those of young rats. The low level of left-right discrimination learning test in aged rats might be represented the disturbance of space recognition and memory.

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MARKOV PROPERTIES OF BEHAVIOR IN THE RABBITS DURING CONDITIONING ON A DRL SCHEDULE. FUJII H., AYA K.*, SHIMA K.*, YAMAMOTO M.*, NAKAHAMA H.**
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In order to describe the patterns of responding behavior in the rabbits on a DRL schedule, we use a measure "dependency" which can evaluate quantitatively the order and the values of Markov properties of time series of events. The Markov order of binary trains (reinforcement or non-reinforcement) was 1-3 in sessions where the reinforcement rate was more than about 30%. The value of dependency was also significantly large in the sessions. The changes in Markov order were similar to those in the value of dependency. It shows that the lever pressing is affected by one or more of its preceding reinforcements or non-reinforcements.

Thus, for understanding the behavior of animals, it is important to examine the observation from the viewpoint of the Markov properties of a behavioral sequences, where higher order statistics as well as first order statistics has substantial meanings.

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AREA TE IN THE INFEROTEMPORAL CORTEX OF THE MACAQUE AS A PRESUMED SITE FOR VISUAL MEMORY. Osawa, Y., Yukie, M., Watanabe, J., Yaginuma, S., Sato, T. and Iwai, E. Department of Behavioral Physiology, Tokyo Metropolitan Institute for Neurosciences, Tokyo 183

A concurrent learning task with many objects is considered to be an associative memory task, because it is required to achieve learning on the task against the proactive and retroactive interactions across various objects. Overtraining on a task after learning would make it to consolidate the memory of learned habit. The present study examined the effects of bilateral ablations of areas TE and TEO in the infero- temporal cortex on the concurrent learning task with 12 pairs of 48 junk objects that was overtrained by about 1000 trials. Monkeys with lesions of area TE showed severe impairment in the retention of the overtrained habits, whereas monkeys with lesions of area TEO did not. More importantly, the deficit of the retention on the preoperatively overtrained habits was almost the same as that of the retention on the preoperatively learned but non-overtrained habit. The present findings indicate that area TE is a presumed site for visual memory storage.

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HORMONAL MODIFICATION OF THE DURATION OF AN OLFACTORY MEMORY IN FEMALE MICE. KABA, H., ROSSER, A. E.* AND KEVERNE, E. B.* Dept. Physiol., Kochi Med. Sch., Nankoku, Kochi 781-51, *Dept. Anat., Univ. Cambridge, Cambridge, CB2 3DY, U.K.

Virgin female mice form an olfactory memory to the stud male which is essential to their reproductive success. Once formed, the memory lasts between 30 and 50 days post mating unless pregnancy ensures. The olfactory memory fades significantly faster in the event of pregnancy.

The mechanisms for this fading or loss of olfactory memory were further investigated by examining the influence of oestradiol, a hormone which is secreted during pregnancy. Female mice that were left for 27 days before testing for memory retention were shown to still recognise the familiar stud male, since his pheromones were not capable of blocking pregnancy. However, females left for around 27 days during which they received oestradiol implants for 12 days could no longer recognise the familiar male, since his pheromones were able to block pregnancy.

These data suggest that the elevation of oestradiol that normally occurs during pregnancy facilitates the extinction of olfactory memory.

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CORTICAL EVOKED RESPONSE TO ULTRASONIC SIGNALS DURING ESTROUS CYCLE IN THE RAT. INOUE, M.*, NAITO, H. AND TONOUE, T., Dept. Physiol. II, Azabu Univ., Sagamihara 229

Elucidation of ERP, a series of endogenous potentials related to the perceptual detection of relevant signals, would require a strategy identifying the homologous potentials in animals. The aim of this study is to demonstrate ERP like potentials in the female rat to ultrasonic signals used in intraspecific communication. The evoked responses to 100 ms tone signals of 8,22,50 or 70 kHz were recorded in the adult female rat during estrous cycle. The stimulus bound evoked potentials recorded from the cortex to audible and ultrasonic sounds did not vary with the estrous cycle. The cortical responses with the latency longer than 100 ms were not detectable in the response to audible and ultrasonic signals in diestrus, proestrus or metestrus rats. In the estrus rat, 50 kHz sounds which are emitted by mating males produced a negative potential peaking at 200-250 ms. Other sounds delivered failed to elicit any late potentials even in the estrus rat. The responses in the inferior colliculus did not vary either with the frequency of sounds or with estrous cycle. These findings suggest that ERPs are generated during the cognitive process of ultrasonic signals in the rat.

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NEURONAL ACTIVITY IN THE MIDBRAIN DORSOLATERAL TEGMENTUM DURING MALE COPULATORY BEHAVIOR OF RATS. SHIMURA,T., HORIO,T., AND SHIMOKOCHI,M. Dept. Behav. Physiol., Faculty of Human Sciences, Osaka Univ., Suita 565

Lesion studies have suggested that neural connections between the medial preoptic area (MPO) and the mesencephalic dorsolateral tegmentum (DLT) are essential for male sexual behavior. Since Horio et al. have already found the behavior-specific neuronal activity in the MPO during male sexual behavior, in this experiment we recorded neuronal activity in the DLT during free copulatory behavior of male rats. Neurons could be separated into five groups based on firing patterns around pursuit-mounting behavior: 1) The firing frequency increased concurrently with pursuit of female and it decreased just before intromission to the baseline level (n=6;22.2%). 2) It increased only during pelvic thrusting accompanied with intromission (n=3;11.1%). 3) It decreased only during pelvic thrusting (n=4;14.8%). 4) It increased during genital grooming (n=9;33.3%). 5) The other five neurons (18.5%) showed no specific change around pursuit-mounting behavior. These neuronal activities may suggest that the DLT is involved in processing sensory information necessary to the normal expression of male copulatory behavior.

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FEEDING MODULATED BY N-ACETYL AMINO SUGARS, IMPLICATIONS OF THEIR EFFECTS ON PERIPHERAL CHEMOSENSITIVE UNITS.
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Mechanisms of feeding modulation induced by physiologically active form of N-acetylglucosamine and its analogue of 1-deoxy-N-acetylglucosamine were investigated, and compared with those of glucosamine and 1-deoxyglucosamine. Administration of N-acetyl amino sugars at doses of 1200 μmol into the stomach potently increased or suppressed food intake, but their infusion into the third cerebroventricle could not affect feeding, drinking and ambulation.

Effects of glucosamine and its 1-deoxy analogues on feeding were completely reciprocal. Bilateral subphrenic vagotomy abolished feeding modulation induced by N-acetyl derivatives. Peripheral chemosensitive units were indicated to be involved in feeding modulation of N-acetyl amino sugars, in contrast to central feeding mediation of glucosamine and its 1-deoxy analogues.

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EFFECTS OF DSIP ANALOGUES ON NOCTURNAL SLEEP IN UNRESTRAINED RATS.
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Delta-sleep-inducing peptide (DSIP) is known as a putative endogenous sleep substance. Four different kinds of synthetic analogues of DSIP were tested by our standardized long-term nocturnal intracerebroventricular infusion technique in freely behaving rats. Their sleep-modulating effects were compared with those of a synthetic preparation of DSIP (2.5 nmol, the Peptide Institute, Osaka). P-DSIP (presented by Hoffmann-La Roche Co., Basel), in which the serine in position 7 is phosphorylated, induced a maximal excess sleep at a dose of 0.5 nmol. The increments of slow wave sleep (SWS) and paradoxical sleep (PS) in the 12-h dark period were respectively 39.1 min (21.5 % of the baseline) and 27.7 min (82.0 %). Lower and higher doses (0.025-0.25 and 2.5-25 nmol) were ineffective. Among D-Ala2-DSIP (2.5 nmol), D-Trp1-DSIP (2.5 nmol) and D-Ala2-DSIP(1-6) (1.7 nmol), presented by Dr. V.M. Kovalzon, Moscow, D-Ala2-DSIP exerted a marked sleep-inducing effect comparable to DSIP. The increments of SWS and PS in the dark period were respectively 59.8 min (31.8 %) and 42.9 min (102.0 %).

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ENHANCED OCULAR FOLLOWING RESPONSE OF MONKEY DURING SMOOTH PURSUIT EYE MOVEMENT.
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The effects of smooth pursuit eye movements on the ocular following responses to brief (40ms) ramp movements of the visual scene were studied. Monkeys faced a tangent screen which was partitioned into central and peripheral regions. Monkeys were trained to fixate a target spot projected on the central part of the screen (5° × 90°) and to pursue it as the spot moved horizontally. A random dot pattern was projected onto the remaining peripheral region. Unexpected movements of the visual stimulus in the peripheral region elicited ocular following responses even while the monkey pursued a visual target. Enhanced ocular following responses were observed only when the peripheral stimulus moved in the same direction as the smooth pursuit eye movement. The magnitude of the enhancement was dependent on 2 factors, the speed of the smooth pursuit (when the eyes moved faster (range: 5 - 30°/s), subsequent enhancement was larger), and on the speed of the peripheral stimulus (exceeding the speed of 80°/s reduced the enhancement). We suggest that an efference copy of the eye-velocity command of a smooth pursuit eye movement influences not only visual inputs from the central part of the retina, but also those from the surroundings.

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LATENT DEFECT IN MONOCULAR OPTOKINETIC NYSTAGMUS AFTER NEONATAL REMOVAL OF THE LATERAL SUPRASYLVIAN AREA IN THE CAT. HAMADA,T. Bionics Section, Electrotechnical Laboratory, Sakuramura, Niiharigun, Ibaraki, 305.

Three kittens underwent unilateral removal of the lateral suprasylvian area of cortex at the age of 1 month. After normal rearing for two years, their monocular optokinetic nystagmus was studied. During the experiment one eye was "seeing" the optokinetic stimulus, but the other eye was "covered"; by implanting scleral coils on both eyes we measured movements not only in the "seeing" eye, but also in the "covered" eye. The stimulus was moved at a velocity between 1 and 40 deg/sec. The results were compared with those of normal cats.

The gains (slow phase velocity/stimulus velocity) of the "seeing" eye were almost normal. However, the gains of the "covered" eye were significantly higher than the normal values when the stimulus was presented in the temporonasal direction, at a velocity between 1 and 40 deg/sec to the eye ipsilateral to the lesion and at a velocity of 40 deg/sec to the eye contralateral to the lesion; in other conditions of stimulation the gains were not significantly different from the normal values. (The experiment was performed at INSERM Unité 94, France)

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ACOUSTIC CHARACTERISTICS OF THE VELAR STOP SOUNDS [k, g] RELEASED LATERALLY IN THE ARTICULATORY CLOSURE. SIMADA, Z. Dept. of Physiol., Sch. of Med., Kitasato Univ., Sagamihara, Kanagawa 228

This study explored acoustic measures to characterize the lateral lisps involving the velar stop sounds [k, g]. Two adult females produced lateralized and non-lateralized tokens consisting of the mora [ki], [ke] or [gi]. Both subjects had shown distorted pronunciations in their childhood, but had been corrected to normal articulatory gestures with speech training. The measures examined were the root-mean-square (r.m.s.) amplitude and spectral properties of the consonantal burst. For the r.m.s. amplitude, an energy ratio was calculated for each token between the amplitude value in the onset of the vowel and the amplitude value in the burst. The r.m.s. amplitude of lateralized tokens was larger than that of non-lateralized tokens. Furthermore, it was suggested that the energy ratio could separate lateralized from non-lateralized tokens. In spectra, a local peak was noted consistently in the vicinity of 5.0 kHz for the lateralized tokens [ki] across both subjects.

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K^+ CHANNEL ACTIVITIES OF THE HERMISSENDA TYPE B PHOTORECEPTOR.
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Two microelectrodes voltage-clamp of the photoreceptor-soma in the Hermissenda crassicornis previously revealed three voltage-dependent outward K^+ currents: I_A, $I_{Ca^{2+}\text{-}K^+}$, and I_K (not appreciable at Vm < 0 mV, absolute). Light activates an inward Na^+ current, and $I_{Ca^{2+}\text{-}K^+}$ (via intracellular release of Ca^{2+}). Patch-clamp (cell-attached configuration) of somata revealed at least two populations of voltage-dependent outward channels (reversal potential of -60 to -70 mV, absolute), most likely I_A and $I_{Ca^{2+}\text{-}K^+}$, and no light-induced inward Na^+ channels. One type of outward channel (I_A) had a conductance of 2.0 $\pm$ 0.72 pS (n=5) , occurred with greater frequency at the onset of depolarization, was not activated from holding potentials $\geq$ -40 mV and was blocked by 10 μ M 4-AP. The other type ($I_{Ca^{2+}\text{-}K^+}$) could be activated at more positive holding potentials and had a conductance of 15.3 $\pm$ 4.4 pS (n=16). These latter channels, recorded with inside-out configurtion, showed increased amplitude and frequency when Ca^{2+} was elevated from 1.6 to 11.5 μM. In 0 Na^+-ASW, light elicited (only in the cell-attached configuration) outward channels with the same properties as the voltage-dependent latter channels ($I_{Ca^{2+}\text{-}K^+}$). Since at -60 to -40 mV in 0 Na^+-ASW light elicits no change of photoreceptor membrane potential, the light-elicited $I_{Ca^{2+}\text{-}K^+}$ cannot be a consequence of voltage-dependent $I_{Ca^{2+}}$ activation, and thus could result from diffusion of Ca^{2+} from the rhabdome to the soma.

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EFFECTS OF IP_3 ON THE cGMP-AND LIGHT-SENSITIVE K^+ CURRENT IN THE MOLLUSC, *Onchidium* EXTRAOCULAR PHOTORECEPTOR.
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Previous studies have shown that the depolarizing receptor potential(the photoresponse) in the *Onchidium* extraocular photoreceptor (A-P-1) results from the light-suppression of a cGMP-induced current which has electrical properties similar to those of the light sensitive K^+ current. The cGMP levels of the ganglion including the A-P-1 were decreased by exposure to light, but no change in cAMP levels was detected. Thus, these results support the idea that the light induced fall of cGMP levels mediates the photoresponse of A-P-1, similar to that proposed for vertebrate phototransduction. Furthermore, the effects of GDP-β-S, GTP-γ-S and inositol triphosphate (IP_3) injected into the A-P-1 by ionophoresis from microelectrodes were investigated. GDP-β-S reversibly inhibited the photoresponse, depending on its injection time, but no holding or dark current of A-P-1 under voltage clamp was influenced by GDP-β-S. Short-term injections of GTP-γ-S and IP_3 enhanced the photoresponse, respectively. However, the photoresponse was depressed by long-term injections of GTP-γ-S or IP_3. Both effects of GTP-γ-S or IP_3 were not also associated with changes in holding current under voltage clamp.

These results suggest that IP_3 may involved in modulation of the cGMP-mediated photoresponse of A-P-1 through the activation of a step, GTP-binding protein in the common phototrasnduction for both vertebrate and invertebrate.

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RESPONSE TO L-GLUTAMATE OF DISSOCIATED SOLITARY BIPOLAR CELLS OF GOLDFISH RETINA.
KANEKO, A. AND TACHIBANA, M. Natl. Inst. Physiol. Sci., Okazaki, 444.

Acidic amino acids, such as L-glutamate (L-glu), are the most likely candidates for the neurotransmitter substance released from photoreceptors. To study the synaptic mechanisms underlying light-evoked responses of bipolar cells, we studied the effect of L-glu on solitary bipolar cells. Of morphological subtypes, cells with a huge axon terminal were identified to be the rod-dominant on-center cells in reference to earlier works (Saito *et al.* 1982, 1984). Cells without the large terminal bulb are probably a mixture of cone-driven on-center cells and off-center cells. L-Glu was effective for most of the bipolar cells in a dose-dependent manner (the minimum effective concentration, *ca.* 10 μM). The acting sites were mainly the dendritic processes. L-Glu-induced an inward current at the resting potential accompanied by a conductance increase, thus a depolarization in these cells. The L-glu-induced current showed a strong inward rectification and its reversal potential was near E_{Cl}. Lowering Na_o strongly suppressed the response amplitude, but without a shift in the reversal potential. Aspartate was also effective, but other agonists, *e.g.*, kainate or 2-amino-4-phosphonobutyric acid (each at 100 μM) were ineffective. In the present study we were unable to find a cell in which L-glu application lowered the membrane conductance.

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SPATIAL AND CHROMATIC PROPERTIES OF VISUAL INTERNEURONS IN THE SWALLOWTAIL BUTTERFLY LARVA. ICHIKAWA, T., Dept. of Biol., Fac. of Sci. Kyushu Univ., Fukuoka 812

The butterfly larvae have three types of color receptors (UV, blue and green). Processing mechanisms of color signals in the optic lobe were examined by recording responses to illumination of individual stemmata (ommatidia) from the interneurons in the medulla.

There are many neurons exhibiting an antagonistic interaction between signals from one particular stemma (center) and neighboring stemmata (surround). Most of the neurons showed a color opponent interaction in the center and a non-color opponent one in the surround. These color opponent neurons belong to three families, according to the opponent colors: blue vs. green, UV vs. green, and blue vs. UV + green. Each family has two sets (or types) of neurons which show opposite color opponency. Each set consists of a few types of neurons which exhibit different degrees of color opponency mediated by the same combination of color receptors. Since similar restrictions (or preferences) of the color combinations and variation in the degree of color opponency have been reported in the vertebrate, these findings as well as spatially antagonistic interaction suggest common principles for the color coding mechanism in the vertebrate and invertebrate visual systems.

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DYNAMICS OF SPIKE RESPONSE OF SECOND-ORDER NEURONS OF COCKROACH OCELLI. MIZUNAMI, M. AND TATEDA, H. Dept. of Biol., Fac. of Sci., Kyushu Univ., Fukuoka 812

The relationship between slow potential and spikes of second-order ocellar neurons of the cockroach, Periplaneta americana, was studied using sinusoidally-modulated light with various mean illuminances. The slow-spike conversion process was bandpass at about 0.5-5 Hz. The spike threshold at the optimal frequencies (about 0.5-5 Hz) remained unchanged over a mean illuminance range of 3.6 log units. The slope of the low frequency cut-off was steeper under brighter illumination. Under brighter illumination, the voltage noise in the response was smaller and the mean membrane potential was more negative. The steady- or noise-current stimulation during light stimulation showed that the change in the slope of the low frequency cut-off by the mean illuminance change was due to the change in the noise magnitude. We concluded that the noise facilitates the spike initiation. The change in the mean potential level had little effects on the spike threshold.

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FORMATION OF VISUAL PIGMENT CHROMOPHORE DURING THE DEVELOPMENT OF XENOPUS LAEVIS. AZUMA,M.,SEKI,T. AND FUJISHITA,S.
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The amounts of retinoids were analyzed by HPLC method at several stages in the development of Xenopus laevis. Xenopus eggs contain almost equal amounts of all-trans retinal$_1$ and retinal$_2$ (total;about 50 pmol/egg). With the advance of development,the amount of all-trans retinal decreases and that of all-trans retinyl ester, mainly retinyl palmitate, increases in turn. The chromophores of visual pigment,11-cis retinal$_1$ and retinal$_2$, can be detected in the larval eyes at stage 40 and their amounts increase after that stage. The ratio of 11-cis retinal$_2$ to retinal$_1$ is about 1 at stages 40-42 and becomes larger and larger after stage 43. The ratio is about 20 at stage 46. The ratio of all-trans retinyl palmitate$_2$ to retinyl palmitate$_1$ begins to increase at stage 42. The conversion of A_1 to A_2 in all-trans retinyl ester leads to the increase in amount of 11-cis retinal$_2$. The chromophore 11-cis retinal is generated after stage 40 probably via retinol which is formed from all-trans retinal and retinyl ester.

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EVALUATION OF LIGHT-INDUCED Km INCREASE OF cGMP PHOSPHODIESTERASE IN FROG ROD OUTER SEGMENTS.
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Light-activation of cGMP phosphodiesterase (PDE) in rod photoreceptors is an intermediary process of phototransduction. On its activation, the Michaelis constant (Km) of this enzyme increases about 10-fold from the value in the dark (100 μM) to that in the light (1 mM). The in situ PDE activity is determined by the Michaelis-Menten equation, $V=Vmax\ S/(S+Km)$. When dark and light Km values and internal free cGMP concentration (S; several μM) are taken into account, 10-fold Km increase causes a net 10-fold decrease in the PDE activity in situ. Therefore, the light-induced Km increase counteracts the maximal PDE activity (Vmax) increase induced by light. The present study indicated that the Km increase is attained by PDE molecule itself and does not require other components. It was also found that the Km value increases as early as 200 msec after the onset of a light exposure. Though the Vmax recovery after a light flash is slower than the potential recovery, the rapid Km increase may compensate the slowness of the Vmax recovery to shape the waveform of the photoreceptor potential.

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EFFECTS OF ADAPTING LIGHT ON FAST PIII AND $[K^+]o$ OF FROG RETINA.
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Bullfrog retinas were superfused with the physiological solutions containing the chemicals which suppressed the slow component (slow PIII) of distal PIII. $[Ba^{++}]$ of 20 μM in the superfusate suppressed the slow PIII. A gliotoxin, L-α aminoadipate (L-αAA), abolished the b-wave and slow PIII components. Measurements of the fast PIII isolated by the chemicals and of the light-induced decrease of $[K^+]o$ were carried out with Ag/AgCl electrodes and K^+-selective microelectrodes, respectively. At 0.09 mM $[Ca^{++}]o$ (low Ca), the amplitude of fast PIII at 10 sec-dark after the offset of the light was larger than that in the initial dark (called hypersensitivity). The hypersensitivity observed at low Ca was markedly affected by reducing $[Na^+]o$. A decrease of $[K^+]o$ induced by a flash light was remarkable in the dark after the offset of the light at low Ca. It is discussed that hypersensitivity is caused by the increase of Na^+-gradient across rod membranes.

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SYNAPTIC MECHANISM OF THE SPREADING DEPRESSION IN THE FROG RETINA.
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In the low Cl^- media, the frog retina gives rise to spreading depression (SD) receptor side negative potential (SDP). The SD is thought be generated in the cells which have sysnaptic contact in the inner plexiform layer, such as bipolar, amacrine or ganglion cells. An identification of the original cell and the generating mechanism of the SD has been investigated in the retina of the frog, Rana catesbieana.

The membrane potential of some kind of the ganglion cell begins to be depolarized preceding to the SDP, which suggests that the ganglion cells have initiative role in the generation of the SD. Light, GABA and strychnine (one of the antagonists of glycine) decreased the generating frequency of the SD. On the contrary, dark, bicuculline (one of the antagonists of GABA), and glycine increased in the frequency the SD.

These results suggested that the SD might be initiated in the off type ganglion cell which might be innervated with GABergic synapse which is thought to be inhibitory synapses. The retinal SD is probably caused by the abnormal activity of these inhibitory synaptic transmission in the low Cl^-.

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SIGNAL TRANSMISSION IN THE CATFISH INNER RETINA. I. Sakai, H. M. National Institute for Basic Biology

To characterize the temporal dynamic responses of ganglion cells and to define the possible inputs giving rise to their responses in the catfish retina, we recorded the ganglion cell responses evoked by 1) a step of light given in the dark, 2) an incremental and decremental step from a backgroud illumination and 3) a white-noise modulated light. We found that bipolar cells are the major source of linear components of ganglion cell responses and that type-C and type-N amacrine cells are the major source of nonlinear components. These linear and nonlinear components were encoded into spike trains by ganglion cells without major transformation of the temporal dynamic response properties.

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SIGNAL TRANSMISSION IN THE CATFISH INNER RETINA. (II) Naka, K.-I. National Institute for Basic Biology

An extrinsic current, either sinusoidally modulated or white-noise modulated, was injected into an interneuron and examined its effects on the spike discharges from a nearby ganglion cell. A current injected into a type-C cell modulated spike discharges of both on-center and off-center ganglion cells. Transmission from a type C-cell to an on-center ganglion cell was sign inverting whereas to an off-center ganglion cell was sign non-inverting. Spike discharges of an on-center and an off-center ganglion cell were simultaneously modulated by a current injected into a type-N cell. Transmission from a type-N cell, either of depolarizing or of hyperpolarizing type, to an on-center ganglion cell was sign inverting whereas to an off-center ganglion cell was sign non-inverting. Analysis of second-order nonlinearity of evoked spike discharges suggests that a very small amount of nonlinearity is produced during the signal transmission from preganglionic cells to ganglion cells. The second-order nonlinearity involved may attributed to the rectification or saturation of the spike discharges.

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COMPARISON OF PHOTOPIGMENTS BETWEEN PINEAL ORGAN AND LATERAL EYE RETINA IN CYCLOSTOMES. TAMOTSU, S., UCHIDA, K. AND MORITA, Y. 1. Dept. Physiol., Hamamatsu Univ. Sch. Med., Hamamatsu 431-31

Photopigments of the lamprey pineal were examined in comparison with those of the retina. Both pineals and retinae were irradiated by orange and blue light and changes in isomeric composition of chromophore were observed with high-performance liquid chromatography. Orange light gave rise to significant cis to trans isomerization in the retina but not in the pineal, or rather, a little trans to cis isomerization. The blue light adaptation decreased 11-cis-isomers and increased all-trans-isomers in the pineal organs. The results show that pineal photopigment is different from that of retina in property and that blue sensitive pigments are present in the pineal organ. The photoreceptors which contain the blue sensitive pigment must be concerned in the chromatic response, in which longer wavelength light elicits and near UV light inhibits impulses of ganglion cells.

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REGIONAL DIFFERENCE OF DENDRITIC MORPHOLOGY OF DOPAMINE CELLS IN CARP RETINA. TERANISHI, T. AND NEGISHI, K. Dept. Neurophysiology, Neuroinformation Res. Inst., Sch. Med., Kanazawa Univ., Kanazawa 920

The dendritic morphology of dopamine (DA) cells in the inner plexiform layer of the retina of carp (body length, about 33 cm) was investigated by identifying their fluorescent cell bodies in isolated, aldehyde-fixed flatmounts and injecting them iontophoretically with Lucifer yellow CH under microscopic control. Attention was payed to clarify regional difference in their dendritic morphology. In the marginal zone within 0.25 mm from the retinal edge, the density of DA cells was extremely high (120 cells/mm^2), their dendrites tended to extend in parallel with the retinal circumference, and the dendritic area was small (2.5×10^{-2} mm^2). As the injection point was shifted centrally by steps, the dendrites tended to extend towards the optic disc and subsequently towards the margin, finally forming a round or oval dendritic field of each cell. Concomitantly with such changes in the dendritic field, the cell density sharpely decreased to about 30 cells/mm^2 and the dendritic area increased to 10×10^{-2} mm^2 in a zone 3 mm interior to the margin. However, the dendritic coverage factor was consistently about 3 all-over the retinal field. Such morphological changes observed sequentially from the retinal margin to the intermediate region represent a growing process of DA cells in the carp retina.

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EFFECT OF PUTATIVE TRANSMITTERS ON RETINAL AMACRINE CELLS. TOYODA, J., FUJIMOTO, M. AND KUJIRAOKA, T. Dept. of Physiol., St. Marianna Univ. Sch. of Med., Miyamae-ku, Kawasaki 213

Glutamate(Glu) and aspartate(Asp) show depolarizing effect on some amacrine cells when applied locally near the recorded cell. They are therefore considered as one of the candidates of the bipolar cell transmitter. In the present experiments, effects of these amino acids on amacrine cells were tested by applying them in a perfusing medium. The effect of drugs were tested after blocking the light responses by cobalt ions. In 2 mM cobalt solutions, however, the synaptic transmission from bipolar to amacrine cells was not blocked. Under such conditions, ON amacrine cells were hyperpolarized while OFF amacrine cells were depolarized by Glu and Asp. In 5 mM cobalt solutions, the effect of Glu and Asp on ON amacrine cells was hardly detectable. Kainic acid, a potent glutamate agonist, showed little effect or a slight depolarization on ON amacrine cells. These results are incompatible with the idea that Glu or Asp is the transmitter of bipolar cells, at least in an ON system.

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GABAERGIC INHIBITION ON DOPAMINE CELLS OF THE FISH RETINA. KATO, S., ISHITA, S. AND NEGISHI, K. Dept. Neurophysiology, Neuroinofrmation Res. Inst., Sch. Med., Kanazawa Univ., Kanazawa 920

Inner retinal cells containing dopamine (DA) cells were isolated and collected from the carp (Cyprinus carpio) retina by enzyme dissociation and metrizamide gradient centrifugation method. Using such a cell fraction, the effects of GABA antagonist on the release of ^{3}H-DA prelabeled were investigated. Bicuculline stimulated the release of ^{3}H-DA in a dose- and Ca^{2+}-dependent manner. The minimal effective concentration was about 0.5 μM. High K^+ also stimulated the release of ^{3}H-DA in the same fashion. In the presence of 2 mM of GABA, the stimulatory action of bicuculline and high K^+ on ^{3}H-DA release was completely abolished. After pretreatment of the cell fraction with GABAase, a GABA degradating enzyme, the bicuculline-induced ^{3}H-DA release disappeared whereas the high K^+-induced one remained responsive. The data suggest that GABA inhibits the DA release from retinal DA cells and bicuculline evokes the DA release by a disinhibition mechanism through GABA receptors on DA cell bodies.

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CONDUCTANCE DECREASING NEUROTRANSMITTER ACTION ON CARP L-TYPE HORIZONTAL CELLS ASSOCIATED WITH BLUE LIGHT

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Vertebrate photoreceptors of every kind as well as luminosity type horizontal cells (LHC) respond to light with graded hyperpolarization. This sign-conserving synaptic transmission has been explained by assuming that the light-induced photoreceptor hyperpolarization reduces the secretion of an excitatory neurotransmitter. The present experiment reveals, however, that the situation is not as simple as recapitulated above, and the result seems to advance the recently emerging notion that short-wavelength inputs and red light signals are mediated differently on their way to second-order retinal neurons. Treatment of the retina by dopamine enabled us to measure the membrane resistance (R_m) of LHC. Flashes of light increased R_m. This increase depended on the spectral content even when the intracellular voltage responses were equal in amplitude; the R_m values were such that red $\geq$ yellow > green > blue. Often, R_m even decreased with blue flashes. No single postsynaptic mechanism can accout for any constant-voltage R_m difference such as this. The synaptic spectral segregation is probably subserved by a dual scheme wherein the transmitter from blue- and/or green-sensitive cones acts to decrease the membrane conductance of LHC, whereas the synapse made by red cones is of a classical excitatory type.

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NEURAL MECHANISM OF CHROMATIC ADAPTATION OF L-TYPE EXTERNAL HORIZONTAL CELLS(LEHC) IN CARP RETINA.

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The response of LEHC to bluish-green test light is enhanced when the red background (BG) light is applied to the retina. With a prolonged BG illumination, however, LEHC shows a specific process of light adaptation (SPLA) in which the response amplitude to test light is decreased and reaches a steady state. The SPLA is prominent when monochromatic light around 500nm is used for the test light. Off-phase of responses to test lights starts earlier and earlier during red BG light, while the slope of on-phase is almost the same. Such results imply that the SPLA is produced by gradual advancement of the beginning of off-phase in each response to test light. The advancement of off-phase of test responses is eliminated in solution containing GABA, a putative transmitter of LEHC. The SPLA is also observed in the 6-hydroxydopamine(6-OHDA)-treated retina where interplexiform cells were destroyed. GABA eliminates the beginning of off-phase of test response in the 6-OHDA-treated retina. A small amount of Co^{2+}, which is reported to block the GABA-induced current, inhibits the advancement of off-phase. Dopamine, which is reported to inhibit the GABA release from LEHC, advances the beginning of off-phase. These results strongly suggest that the negative-feedback from LEHC to cones modifies the off-phase of response to test light.

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LENGTH CONSTANT OF HORIZONTAL CELL AXON TERMINALS IS LITTLE AFFECTED BY DOPAMINE.

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It has been reported that dopamine (DA) narrows the receptive field of cone-driven horizontal cells by suppressing electrical coupling between these cells. Spread of responses in the syncytium of the horizontal cells in the carp retina was measured by changing the distance between the slit of light (0.2mm x 4.2mm) and the recording electrode. In the fish retina, the response to the slit decayed with distance with a single exponential function when recorded from rod-driven horizontal cells (Tsukamoto et al.,1987), and with a double exponential function when recorded from the soma of L type horizontal cells (Yagi,1986). By applying 10 μM DA the length constant of rod horizontal cells was reduced by more than 50 % and the response amplitude in the center approximately doubled. When recorded from the L cells, DA also reduced the short length constant which can be ascribed to the soma syncytium. However, DA had no effect on the long length constant ascribed to the axon terminal syncytium. This suggests that the electrical coupling of the axon terminals has low sensitivity to DA in the carp retina.

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TELODENDRIAL CONTACTS OF CONE PHOTORECEPTORS IN THE TURTLE RETINA.

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In the turtle retina, the cones of identical chromatic sensitivity (homologous cones) were shown to be coupled. Recently, the coupling between the cones of different chromatic sensitivity (heterologous cones) was also found. We studied the pathways of such cone coupling in the freshwater turtle retinas by using intracellular injection of horseradish peroxidase (HRP) and electron microscopic analysis. The HRP-filled cones and neighboring photoreceptors, rods and three chromatic types of cones, were unequivocally identified by the presence and colors of the oil droplets. Eleven cones were studied; 5 red, 2 green, and 4 blue cones. The synaptic terminal (pedicle) of each HRP-filled cone radiated 7-10 main processes (telodendria) running in the outer plexiform layer. These telodendria penetrated into the invaginations of neighboring cone pedicles and they made basal junctions. No ribbon synaptic contacts were found. The telodendria arising from the red cones were found in the neighboring red and green cones, those from the green cones in the red and blue cones, and those from blue cones in the red and green cones. Thus, the homologous and heterologous cone couplings in the previous studies seems to be mediated directly by the telodendrial contacts and indirectly probably through the second-order neurons.

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SYNAPTIC CONTACTS BETWEEN PHOTORECEPTORS AND HRP-FILLED BIPOLAR CELLS IN THE TURTLE RETINA

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Synaptic contacts between photoreceptors and bipolar cells in the retina of the turtle (Geoclemys reevesii) were studied by the intracellular injection of HRP and subsequent electron microscopical analysis. ON- and OFF-bipolar cells were identified by the light responses and were filled with HRP, while rods and three chromatic types of cones were identified morphologically by the oil droplets. Synaptic contacts between these two groups of cells were studied by the serial ultrathin sections.

Both ON- and OFF-bipolar cells emanated 5-6 dendrites which invaginated into the pedicles of rods and three chromatic types of cones. The HRP-filled dendritic processes were found to make basal junctional contacts. The bipolar cell processes were not found in the central element of ribbon synapses as previously reported. However, we found another morphological type of bipolar cell, 'the displaced bipolar cell', whose soma locates in the outer nuclear layer, showing their dendritic processes in the ribbon synapses of both rods and cones. Thus, the bipolar cells in the turtle retina seemed to receive rod and cone signals by way of the basal junctional contacts, while the displaced bipolar cells by the ribbon synaptic contacts.

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THE INFLUENCE OF FUNCTIONS OF THE FROG LIVER ON THE REGENERATION OF RHODOPSIN.

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The regeneration of rhodopsin in the retina of a frog is influenced by several substances contained in the liver and the blood of the frog. The greater the content of vitamin A in the liver of a frog.the lower limit of the quantity of regenerated rhodopsin may be raised.Comparing the frogs possessing similar quantity of vitamin A in their livers, the quantity rhodopsin regenerated in each of these frogs' retinas is determined by the ratio of quantities of glucose to fatty acid in their blood. The greater the quantity of regenerated rhodopsin in 1 hr, the greater the ratio of glucose to fatty acid.

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THE EFFECT OF GLUCOSE DEPRIVATION ON THE SQUID RETINA.
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Concerning photoreception, we have previously reported that glucose deprivation causes a decline in heat generation by isolated slices of squid retina, in response to light.

In the present experiments we used the same squid retina preparation for measuring the effect of glucose deprivation on the electroretinogram (ERG) and photoreceptor ultrastructure. Excluding glucose from the physiological saline of the sliced retina of Loligo resulted in the disappearance of the ERG within 20 min. This change was reversible, with the ERG returning to normal on replacing the physiological saline with one containing 10 mM glucose. There were no obvious effects on the structure of the retina, until detailed measurement were taken of the mitochondria. Measurements of oblateness showed a tendency for the mitochondria to become shorter and fatter during glucose deficiency.

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EFFECT OF CONCENTRATION CHANGE IN Na^+, Cl^- OR K^+ ON C-WAVE OF ERG RECORDED FROM THE ISOLATED CHICK RETINA. SATO, T., ASAMIZU*, N., MATSUMOTO, N. AND SUZUKI, T.A. Dept. Oral Physiol., Sch. Dent., and *Dept. Ophthalmol., Sch. Med., Iwate Med. Univ. MORIOKA 020

Ion species involved to generate the electroretinogram (ERG) c-wave of the isolated chick retina were investigated by using a two-channel perfusing chamber. Concentration of Na^+, Cl^- or K^+ was varied only in the vitreous perfusing media. A photoemission diode of red color was used as a light source and stimulus duration was 10 sec.

Amplitude of the c-wave, whose crest time was about 5 sec, did not vary significantly, when concentration of Na^+ or Cl^- was reduced to 60% of the control value. On the other hand, it was reduced 2/3-1/4, when concentration of K^+ was increased 2- and 3-folds. Thus, it was generated predominantly by movement of K^+ as reported by other investigators.

In addition, the augmenting effect of GABA on the c-wave and polarity reversal of the c-wave by picrotoxin, observed in the in vivo studies, were reconfirmed in the present experiment. In the presence of 0.3-1.0 mM picrotoxin, the polarity reversal of the c-wave, whose peak time was between 1 and 3 sec, was demonstrated only in the range of lower stimulus intensity. GABA receptors sensitive to picrotoxin ,therefore, seem to be involved in generating the c-wave during its rising phase.

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CENTRIFUGAL EFFECTS FROM THE MPA TO THE RAT RETINA. TAKAHASHI, T., KITAGAWA, K., SAITO, H.* AND TAMAI, A., Dept. of Ophth. and Physiol*, Kochi Med. Sch., Nankoku, Kochi 781-51

We investigated centrifugal effects from the medial pretectal area (MPA) on the rat electroretinogram (ERG). Urethane anesthetized adult rats were placed on the stereotaxic apparatus. The ERG recording was made in a glass microlectrode inserted into the vitreous from the pars plana. Photic stimulation was made by the xenon flash lamp, and was guided to the cornea by optic fibers. A monopolar platinum electrode was used for the MPA lesions, and a coaxial bipolar stainless steel electrode was used for the stimulation of the MPA. Microinjection of lidocaine to the MPA was used for the transient block of the MPA. ERGs were recorded before and after the lesion, the stimulation, or the block of the MPA. The MPA lesions produced supernormal ERGs. Microinjection of lidocaine to the MPA also produced a transient supernormal ERG. The MPA stimulation, on the other hand, lengthened the peak latencies of the OPs.

These findings indicate that the MPA has some inhibitory effects on the rat ERG.

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EFFECTS OF EEG-SYNCHRONIZATION UPON THE VISUAL RESPONSE OF Y-, X- AND W-CELLS IN THE CAT LATERAL GENICULATE NUCLEUS. SAWAI, H.* MORIGIWA, K.* AND FUKUDA, Y., Dept. Neurophysiol., Osaka Univ. Med. Sch., Osaka, 530.

How the synchronization of cortical EEG affects visual responses of Y-, X- and W-type relay cells of the lateral geniculate nucleus was studied in chronically prepared cats. The cat's head was restrained to a stereotaxic apparatus, the eye was immobilized with i.v. injection of Flaxedil and the respiration was maintained artificially. N_2O/O_2 (70:30) was continuously administered to relieve possible pain or unpleasantness. To induce EEG-synchronization the animals were occasionally anesthetized with Halothane (1 to 3%) or thiopental (i.v., 10-25 mg/kg); to desynchronize the EEG, various auditory or somatosensory stimuli were applied. Visual responses to an on-and-off light spot flashed at the receptive field center was continuously recorded for each of the Y-, X- or W-cells. Degradation of the visual response during EEG-synchronization was most marked in W-cells (N=4), intermediate in X-cells (N= 9) and the weakest in Y-cells (N=14). In most Y-cells the phasic component of the visual response was well preserved even when the cortical EEG showed a highly synchronized pattern. This characteristic of Y-cell's behavior could be ascribed to their being unaffected by the feedforward inhibition of intrageniculate interneurons which are active during EEG-synchronization.

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SYNAPTIC POTENTIALS EVOKED IN STRIATE CELLS OF SLICE PREPARATIONS OF ADULT CATS BY STIMULATION OF THE WHITE MATTER AND LAYER I. NAKAJIMA, S., KOMATSU, Y., HAMAZAKI, T. AND TOYAMA K. Depts. Psychiat., Physiol. and Neurosurg. Kyoto Prefectural Sch. Med. Kyoto, 602.

Layer I (LI) in the striate cortex contains abundant fibers the functional significance of which still remains unknown. The synaptic potentials produced by LI stimulation was studied by intracellular recording from striate cells in slice preparations of adult cats in comparison with those by stimulation of white matter (WM). WM stimulation evoked a sequence of excitatory (EPSP) and inhibitory postsynaptic potentials (IPSP) in almost all striate cells. Latency analysis indicated that the EPSPs were monosynaptically produced in almost all cells in layer IV-VI while they were transferred polysynaptically to many cells in layers II and III. By contrast, LI stimulation produced a sequence of EPSP and IPSP or EPSP alone in layer II, III and V cells but never in layer IV and VI cells, while IPSP were commonly produced in layer II-VI cells. In addition there was a significant number of cells unresponsive to LI stimulation. There was a strong tendency in layers IV and VI that cells monosynaptically excited by WM receive IPSP or no input from LI, while no such tendency in layers II, III and V. These findings indicate that excitatory influence from WM and LI is mutually exclusive in layer IV and VI cells.

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TYPES OF EXCITATORY AMINO ACID RECEPTORS OPERATING AT GENICULO-CORTICAL SYNAPSES IN THE VISUAL CORTEX OF KITTENS AND ADULT CATS. HAGIHARA, K.*, TSUMOTO, T., SATO, H., and HATA, Y.* Dept. of Neurophysiology, Inst. of Higher Nervous Activity, Osaka University Medical School, Kitaku, Osaka, 530

To explore which type of glutamate (Glu)/aspartate (Asp) receptors is operating at geniculo-cortical synapses in the kitten visual cortex and further to study their functional development, we studied effects of microionophoretic application of Glu/Asp antagonists on responses of visual cortical neurons to afferent electrical and visual stimulations. The antagonists used were kynurenic acid (KYNA), a non-selective antagonist for the Glu/Asp receptors, and 2-amino-5-phosphonovaleric acid (APV), a selective antagonist for N-methyl-D-aspartate (NMDA)-preferring receptors. The kittens ranged in age between 4 and 8 weeks. During recordings the animals were anesthetized with N_2O and O_2 in addition of Halothane when necessary. In the adult, an application of KYNA suppressed responses elicited by electrical and visual stimulations in most of the cells tested while APV did not suppress the responses. This indicates that Glu/Asp receptors of non-NMDA type may be involved in afferent synaptic transmission in the matured visual cortex. In the kittens, however, APV could effectively block the responses in most of the cells tested, suggesting that NMDA receptors may participate in synaptic responses of neurons in the developing visual cortex.

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MUSCIMOL AND BACLOFEN RESPONSES OF VISUAL CORTICAL NEURONS IN IN VITRO CAT'S BRAIN SLICE PREPARATIONS. ITO, S., KATSUTA, Y. AND OGAWA, T. Dept. Physiol., Akita Univ. Sch. Med., Akita 010

By intracellular recordings from visual cortical neurons located in layer III of cat's brain slice preparations we obtained the following results.
1) Stimulation of the white matter produced an EPSP followed by a long-lasting hyperpolarization consisting of two components. The early component of the hyperpolarization (peak latency, ca. 10 ms) had a reversal potential of ca. -70 mV in normal Ringer solution which was proportionately shifted toward depolarization in a Cl^- deficient medium. The late component (peak latency, ca. 130 ms) had a reversal potential of ca. -100 mV.
2) Muscimol (bath applied), an agonist of $GABA_A$ receptor, produced potential changes resembling the early component in that the reversal potential was in ca. -70 mV in normal Ringer. Baclofen, an agonist of $GABA_B$ receptor, produced a hyperpolarization resembling the late component in that the reversal potential was in ca. -100 mV and that the amplitude decreased with a decrease in concentration of Ca^{2+} in a bathing medium.

These findings suggest that the muscimol response and the early component are Cl^- dependent and that the baclofen response and the late component are related to Ca^{2+}-dependent K channel.

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RESPONSIVENESS OF PRESTRIATE VISUAL AREAS. (AREA 21A) OF THE CAT. TOYAMA, K., ITOI, M., MIZOBE, K. AND KAIHARA, T. Depts. Physiol. and Ophthalm. Kyoto Prefectural Sch Med. Kyoto, 602.

Neuronal responsiveness was studied in prestriate visual area (area 21a) of the cat. The area was identified in later histological examination as the cortical area where labeled cells were absent after injection of horse radish peroxidase in the border region between areas 17 and 18, bounded medially with area 19 and laterally with Clare-Bishop (CB) cortex containing many labeled cells. Area 21a cells preferred long slits and and stripe patterns, and exhibited sharp orientation selectivity, but lacked directional selectivity. These response patterns were rather similar to those of area 19 cells and were in strong contrast to those of the CB cells which preferred short slits and visual noise patterns and exhibited strong directional selectivity but no orientation selectivity. However, Fourier analysis of response patterns indicated that area 21a cells ignore phase information while area 19 cells encode that information. These findings indicate that area 21a cells enconde information for form vision ignoring positional information.

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CORTICAL UNITS SYNCHRONIZED WITH LENS ACCOMMODATION AND/OR PUPILLARY CONSTRICTION IN THE LATERAL SUPRASYLVIAN AREA IN CAT
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Units were sought in the medial bank of middle suprasylvain sulcus, corresponding to a part of lateral suprasylvian area (LSA) in 11 cats, anesthetized with -chloralose and urethane, and immobilized. Lens accommodation of the right eye was monitored by an infrared optometer, and pupillary area of the left eye was monitored by an infrared pupillo-meter. Total of 19 units were classified in three groups based on the effect of microstimulation through the recording microelectrode: group A&P, from which both accommodation and pupillary constriction were evoked by microstimulation; group A, from which only accommodation response were evoked; and group D, from which pupillary dilation was evoked. Four out of 9 units in group A&P were discharged in synchrony with spontaneously-occurring lens accommodation; another 4, with spontaneously-occurring pupillo-constriction; and one with both. Seven out of 8 units in group A discharged in synchrony with lens accommodation but not with pupillary responses; and one with both. All of 2 units in group D discharged in synchrony with spontaneously-occurring pupillodilation. The results were in agreement with the map of LSA on the evoked lens and pupillary responses made by systematic microstimulation in LSA.

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INTEGRATION OF VISUAL STIMULI IN THE RECEPTIVE FIELD OF MONKEY INFERIOR TEMPORAL CORTICAL NEURONS. Sato, T. and Kawamura, T. Dept. of Behav. Physiol., Tokyo Metropolitan Inst. for Neurosci., Fuchu, Tokyo 183

Macaque monkey was trained to perform a fixation task and visual discrimination task. During the fixation task, one or two task-irrelevant light stimuli were presented at fixed locations in the receptive filed of inferior temporal (IT) neurons. During the discrimination task, the monkey was required to release the lever quickly if there was a positive stimulus in one or two presented stimuli, which were a pair of colors or of patterns. Even when the neurons showed excitatory response to each of the two stimuli, the response of IT neurons to simultaneously combined stimulus of the two stimuli did not increase further but the responses of some neurons became rather smaller than the stronger one of the responses to the individual stimulus. This was consistent for the both behavioral paradigms. The decrease in response intensity to the combined stimulus was more prominent during the discrimination task than the fixation task. When the two stimuli were applied separately in both visual hemifield, the responses of most neurons to the ipsilateral stimulus were neglected by the response to the contralateral stimulus. These suggest that the activity or the response to visual stimuli in a large receptive field of IT neuron is controlled well by the inhibitory circuits.

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RELATIVE IMPORTANCE OF VARIOUS STIMULUS PARAMETERS FOR RESPONSES OF SIZE-CHANGE CELLS AND ROTATION CELLS IN A DORSAL PART OF THE MACAQUE MEDIAL SUPERIOR TEMPORAL AREA. SAITO, H., TANAKA, K., FUKADA, Y., SAITO, S.*# and FUKUMOTO, M.*$, NHK Sci. & Tech. Res. Labs., Setagaya-ku, #Dept. of Inform. Sci. & Comm. Technol., Faculty of Engng., Tamagawa Univ., Machida, $Dept. of Physiol., Faculty of Medicine, Tokyo Univ., Bunkyo-ku; Tokyo

In the medial superior temporal (MST) area of the macaque, there are two unique types of directionally selective cells: S cells respond to an expansion or contraction and R cells to a clockwise or counter-clockwise rotation of a visual pattern. In this study, we examined a relative importance of several stimulus parameters for the responses of these cells to make an inference on their functional roles. Recordings were made on Japanese monkeys anesthetized with nitrous-oxide and immobilized with gallamine triethiodide. Most of S and R cells were quite insensitive to the shape of the texture components, whereas the areal extent of the stimulus pattern was crucial. A movement field larger than 40° in diameter was required to maximally activate some cells, and even a field as large as 80° was required for the other cells. Though the tunings were broad, the response magnitude changed as the speed of the movement changed. The optimal speed was different for different cells. Since a movement of such a wide visual field generally occurs when the animal itself moves its eyes, head, and body, we believe that these properties of MST cells are best suited for analyzing the visual flow caused by such self movements.

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UNDERLYING MECHANISMS OF THE DISCRIMINATION OF SIZE CHANGE AND ROTATION OF VISUAL PATTERNS BY CELLS IN A DORSAL PART OF THE MACAQUE MEDIAL SUPERIOR TEMPORAL (MST) AREA. TANAKA, K., SAITO, H., FUKADA, Y., SAITO, S.*$ AND FUKUMOTO, M.*¥ NHK Science and Technical Research Laboratories, $Tamagawa University and ¥Tokyo University.

The MST area has two unique types of cells which selectively respond to special motion patterns of a wide visual field. S cells respond to an expansion or contraction of patterns and R cells respond to a clockwise or counterclockwise rotation of patterns. In this study, we asked what are the essential factors by which they discriminate the motion patterns. Recordings were made in monkeys anesthetized with N_2O and immobilized with gallamine triethiodide. A size change and rotation of a dot pattern as well as artificial motion patterns with some factors off from the real size change or rotation were realized on 16mm movie film by the animation technique. Elimination of the size change of individual dots (for S cells), the inward accerelation of movements of dots (for R cells) and the gradient of the speed of local movements (for both) from the original motion patterns reduced responses of S and R cells only slightly. The remaining factor, i.e., the unique spatial combination of the direction of local movements, was thus proved to be essential for activating S and R cells. Their response magnitude increased as the number of directions combined in the stimulus increased, although the number of directions that was required to evoke submaximal responses ranged from 2 to 8.

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NEURON ACTIVITIES IN THE MACAQUE SUPERIOR TEMPORAL SULCUS DURING THE SEQUENTIAL DISCRIMINATION OF FACES. AKICHIKA MIKAMI, Dept. Neurophysiol., Primate Res. Inst., Kyoto Univ., Inuyama 484, JAPAN

In order to understand the neuronal mechanisms underling the face recognition, neuron activities were recorded from the superior temporal sulcus (STS) of a macaque monkey during the performance of a sequential discrimination task. With pressing a lever, the first sample picture was presented onto a TV screen for 1 sec. Then, after 1 sec of diffuse gray display, a picture appeared again for 1 sec. This sequence was repeated several times. The monkey was trained to keep pressing the lever when the picture was same as the first sample picture and release the lever when different. 80 pictures (32 human faces, 32 monkeys, 16 foods and other objects) or computer graphics were used as a sample or a test stimulus. About 16 % of tested STS neurons showed selective and/or differential responses to the picture of human faces. In about two thirds of them, neuron activities were increased when the same picture was appeared again as a test stimulus, or used as the picture to release a lever. The result suggested that this area might be involved in the recognition of faces.

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POSITRON EMISSION TOMOGRAPHIC STUDIES OF THE CENTRAL VISUAL SYSTEM IN THE NORMAL AND BLIND SUBJECTS. TASAKI, K., SUZUKI, H., SUGITA, Y., TAMAI, M., TSUKAHARA, Y., UEMURA, K., KANNO, I., SHISHIDO, F., MURAKAMI, M. AND FUKADA, Y. Depts. of Physiol. and Ophtal., Tohoku Univ. Sch. of Med., Res. Centr. for Appl. Inf. Sci., Tohoku Univ., Sendai, Akita Res. Inst. of Brain and Blood Vessels, Akita, NHK Sci. and Tech. Res. Labs., Setagaya, Tokyo

Regional cerebral metabolism for glucose, rCMRGl, was measured using ^{18}F-fluorodeoxyglucose and a positron emission tomograph, and rCMRGl in the primary and association cortex was compared between the normal and blind subjects. In the occipital cortex of the two types of subjects the areas 17, 18 and 19 are clearly distinguishable under any stimulus condition, either sensory deprived or illuminated state. In the normal subjects the area 17 shows the highest glucose metabolism and very low rCMRGl is found in the area 18, the area 19 having a slightly higher value than the area 19. In the blind man, on the contrary, very much lower rCMRGl is found in the area 17 which receives no direct visual input from the eyes, and the areas 18 and 19, the association visual area, show markedly increased metabolism of glucose. Preliminary study on the right-left asymmetry in the auditory cortex was carried out by binaural stimulation of language and music.

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ON THE PRESENCE OF NEGATIVE WAXING. TSUKEDA, K., Sch. Med., Tokyo Univ., Tokyo 113

Like negative after-image, negative waxing takes place in the retinal area where the cones and rods co-exist. Contiguous long and short fan-shaped holes were bored in a rotating disk so that the stimuli would end simultaneously. Iso-energy monochromatic lights through these holes were gazed through a slit, the visual angle of which was about 30'. The color sensation of 0.1 sec up to the maximum of waxing was set as the standard. Color sensation of durations shorter than this was investigated by peripheral vision at 2-3° and 5-6° in complete dark adaptation. Since the color sensation which appeared with stimulus duration under 0.005 sec was always light blue independent of the color of the stimulus, it was referred to as "negative waxing". The color sensation with duration of 0.005-0.01 sec ranged from light blue to the color of the stimulus itself. Light blue negative waxing never appeared in the fovea in complete dark adaptation. These experiments on negative waxing are considered to support the dualism of color sensation that the cones are sensitive to long wave-length light and the rods for short wave-length light.

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FUNCTIONAL CHARACTERISTICS OF GABA RECEPTORS INDUCED BY RETINAL mRNA INJECTION.
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Using current and voltage clamp analysis the synaptic receptors translated from retinal mRNA in the Xenopus oocyte were studied after mRNA injection. They were incorporated into the oocyte's plasma membrane within 1-3 days. Compared with extracts from goldfish, rabbit and rat, mRNA from chick retinas was most effective in producing inhibitory synaptic receptors. They appeared in greater number than receptors activated by excitatory transmitters. Among agonists, GABA was 100X more effective than beta alanine and 1000X more than taurine. Muscimol was several times more effective than GABA. Bicuculline and picrotoxin are potent antagonist but strychnine is also an antagonist of the GABA receptor. Pentbarbiturate and Flurazepam potentiate the GABA action. As a result of desensitization the GABA actions decline to 1/20 of the initial magnitude when GABA is applied continuously. The receptors translated in the oocyte are a rich source of information because they are studied in a well defined single cell system.

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A COMPARATIVE STUDY OF IMMUNOREACTIVE CELLS IN COLD-BLOODED VERTEBRATE RETINAS.
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The retinas of river lamprey, fish, frog and turtle were studied by an indirect immunohistochemical method with various antibodies against some polypeptides, GABA, 5-HT and tyrosin hydroxylase (TH). Throughout the four species, many immunoreactive amacrine cells were commonly found, although dendritic distribution of a certain class of cells was different in the inner plexiform layer of different species. GABA immunoreactivity was found also in external horizontal cells of fish, frog and turtle, and 5-HT was seen also in a small population of bipoalr cells of frog and turtle. Although fish TH-like immunoreactive cells have been known as typical interplexiform cells, a few dendritic fibers were observed in the outer plexiform or inner nuclear layer, which were reactive to substance P in lamprey, somatostatin in fish, glucagon and somatostatin in frog and neuropeptide Y in turtle, respectively. In retinal flatmounts, the cell density and dendritic arborization were seen to be various in different classes of cell of the same species as well as in a given class of cells of different species. No firm evidence was found to indicate coexistence of two immunoreactivities in one cell, with regard to substance P and glucagon, neuropeptide Y or somatostatin in the four species.

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A SELECTIVE LABELING OF THE DISPLACED BIPOLAR CELLS IN THE TURTLE RETINA.
TAUCHI, M. Natl. Inst. Physiol. Sci., Okazaki, 444.

Despite of a ubiquitous presence in the turtle retina, displaced bipolar cells (bipolar cells with their somata in the outer nuclear layer, OPL) are still not well understood for their population and function. In the present study the distribution of displaced bipolar cells were studied by a selectively labeling by intravitreally injected 4,6-diamidino-2-phenylindole (DAPI, 100ng in 5 μl distilled water, one day survival). The labeled retinas were fixed, embedded in 5 % agar and sectioned on a Vibratome. The retinal slices were examined under the fluorescent microscope to count DAPI labeled cells. The labeled cells were further injected with lucifer yellow under a direct visual control. The dye-injected DAPI-labeled cells in the ONL were identified as displaced bipolar cells. The density of the displaced bipolar cells ranged from 1,500 (at the superior margin) to 7,000 (in the central retina) cells/mm^2. The displaced bipolar cells did not take up serotonin or its derivatives which could be taken up by a population of bipolar cells of conventional shape. In conclusion, the displaced bipolar cells is considered to constitute a major subpopulation of the bipolar subset in the turtle retina, since their density is as high as one third of the receptor cell density at the corresponding retinal locations.

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DISPLACED BIPOLAR CELL RESPONSES OF THE TURTLE RETINA.
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The somata of 'ordinary' bipolar cells in the vertebrate retinas locate in the inner nuclear layer. In some vertebrates, however, some bipolar cell somata are also found in the outer nuclear layer. These 'displaced' bipolar cells in the turtle retina occupy 1/3 of somata of the outer nuclear layer. In spite of such high population, their light-evoked responses were not known. Thus, by using intracellular injection of Lucifer yellow, the responses of displaced bipolar cells identified morphologically under a fluorescent microscope were analyzed. In total, 25 displaced bipolar cells were studied. To a white spot illumination (spot; diam. 0.25mm), 24 cells were hyperpolarized (OFF type) and one cell was depolarized (ON type). Of 24 OFF types, 4 cells showed antagonistic depolarization to a white annular illumination (annulus; inner diam. 0.3mm, outer diam. 10mm), 9 cells showed also depolarization only to the presence of the spot prior to the annulus, and 11 cells were hyperpolarized to the annulus. The former two groups showed single color opponency to the combination of red (or green) spot and green (or red) annulus. The ON cell was hyperpolarized to the annulus. These responses were the same as the ordinary bipolar cells in the previous studies. Thus, the turtle retina comprises two morphological types of bipolar cells which transmit photoreceptor signals to the proximal retina.

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RECEPTIVE FIELD PROFILES OF CHROMATICITY TYPE HORIZONTAL CELLS IN THE CARP RETINA.
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The spatial decline of the peak amplitude of L type horizontal cells to the slit stimulus was described by a single or double exponential functions which decayed with distance from the center (Yagi,1986). Red and green responses from R/G type horizontal cell somata had two spatial components (steep and wide). Whereas, the responses from the axon terminal of the R/G type cells had a single wide spatial component. These results were similar to those of the L type cells. The receptive field became larger by increasing the light intensity. The red response of R/G cells was slightly smaller in the center compared with that at the lateral sides when light intensity was higher. Green background light, however, regained the central red response, which shows the central response depression is induced by shorter wavelength inputs from green or blue cones. Receptive field profiles of the depolarizing responses in the R/G cells and R/Y/B cells were larger than those of hyperpolarizing responses. This result is suggesting that each chromatic component could be composed through different synaptic pathways between the cones and the horizontal cells.

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PHOTORECEPTOR TYPES CONNECTING TO THE HORIZONTAL CELLS AND THEIR DISTRIBUTION IN THE DACE RETINA.
UEKI, K. AND HASHIMOTO, Y. Dept. of Physiol., Tokyo Wom. Med. Coll., Tokyo 162

The dace retina contained two kinds of photorecetor terminals. One was large in size and the other was small. Recently, we got a conclusion that the large terminal was cone and the small one was rod. The cone terminals were further divided into two types based on their size and numbers of ribbons. The large cone terminals contained 8-17 ribbons and the small one had 5-7 ribbons. We studied the cone types connecting to the horizontal cells and their distribution in the dendritic fields. L-type horizontal cells made contact with 12-15 large cone terminals, the majority was double cones, either both members or long members, that was red and green cones, and distributed in evenly in the dendritic fields. On the other hand, C-type horizontal cells made contact with several small cone terminals in a different ratio among bi- and triphasic types. The majority of cone terminals was single cones, it might be green, blue and/or UV cones, and distributed in peripheral zone of the dendritic fields. Additionally, the C-type horizontal cells made contact with numerous rods occupied in central area of the dendritic fields.

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SYNAPTIC MECHANISMS FROM PHOTORECEPTORS TO HORIZONTAL CELLS IN THE CARP RETINA.
TAKAHASHI, K.-I. and MURAKAMI, M., Dept. Physiol., Keio Univ. Sch. Med., Tokyo 160.

In electrically coupled horizontal cells, the conventional technique of intracellular current injection is not available for measurement of reversal potential, since a functional syncytium cannot be uniformly polarized. We reported a newly developed technique together with the results that, in cone horizontal cells of the carp retina, reversal potentials of light responses and electrically evoked EPSP's coincided well with that of amino acid-induced responses, and that glutamate and aspartate are leading candidates for the transmitter released from cones*. Here we report similar results obtained in rod horizontal cells. In a solution containing high Ca, Ba, and K channel blockers, the cell produced a Ca action potential. During its overshoot, light responses and electrically evoked EPSP's appeared with polarities reversed to those elicited at the resting state. Their reversal potentials coincided well with the maximal depolarization of amino acid responses. As this maximal level was necessarily the reversal potential of amino acid responses*, it is suggested that the synaptic mechanisms from rods to horizontal cells is identical to those of the cone system including the neurotransmitter.

*Murakami & Takahashi (1987) J. Physiol., 386 (in press)

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PUSH-PULL EFFECT OF LIGHT STIMULATION ON EXCITATORY AND INHIBITORY INPUTS TO GANGLION CELLS IN THE MUDPUPPY RETINA.
MIYACHI, E.-I., Department of Physiology, Keio University School of Medicine, Tokyo 160

Illumination of the receptive field center caused a sustained depolarization with an increase in conductance in ON-center ganglion cells, and a sustained hyperpolarization with an increase in conductance in OFF-center ganglion cells. Addition of surround illumination during this response caused a membrane potential change of the opposite polarity and a decrease in conductance. Surround illumination alone could give responses which were opposite in polarity to center responses but associated with an increase in conductance. These results suggest that illumination of the receptive field surround can affect both sustained excitatory and sustained inhibitory synaptic inputs to ON- and OFF-center ganglion cells in a "push-pull" manner, by decreasing the synaptic input that was increased by center illumination and by increasing the synaptic input of opposite sign inputs.

Supported by NIH Research Grant EY01653 to J. S. McReynolds, Department of Physiology, the University of Michigan.

Reference: E.-I. Miyachi, J. S. McReynolds, J. H. Belgum & D. R. Dvorak (1986) Invest. Ophthalmol. Vis. Sci. Suppl. 27, 173.

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SIMULATION STUDY OF COLOR SIGNAL PROCESSING IN THE CONE-HORIZONTAL CELL CIRCUITRY OF THE VERTEBRATE RETINA.
USUI, S., KAMIYAMA, Y., AND OHTSUKA, T.+ Toyohashi Univ. Tech., Toyohashi 440 and +Natl. Inst. Physiol. Sci., Okazaki 444

Horizontal cells in the vertebrate retina reveal three different spectral responses; luminosity, biphasic chromaticity, and triphasic chromaticity horizontal cells(LHC, BHC, and THC). These three types of responses have been thought to be made by the different cone inputs. The depolarizations of BHC and THC were believed to be produced by the negative feedback signals from horizontal cells to cones. Recently, however, the BHC and THC of the turtle retina were found to make ribbon synaptic contacts directly with red-sensitive cones. Based on this new morphological evidence, we investigated the color signal processing of cone-horizontal cell circuitry by using a computer simulation, 'SIGMA', a continuous system simulator.

Spectral responses of cones were simulated by the Gaussian distribution function and horizontal cell responses were expressed by the linear summation of these inputs. We found 1) that the ratios of weighting factor of inputs were similar to those of cones found in the morphological studies and 2) that the neutral points of spectral responses of the BHC and THC were determined by the cone and horizontal cell inputs. Thus, previous negative feedback hypothesis seems not to be essential to the different spectral responses of horizontal cells.

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FUNCTIONAL DEVELOPMENT OF NEURONAL CIRCUITS IN THE KITTEN STRIATE CORTEX STUDIED BY CROSS-CORRELATION ANALYSIS. HATA, Y.*, TSUMOTO, T., SATO, H. AND HAGIHARA, K.* Dept. of Neurophysiology, Inst. of Higher Nervous Activity, Osaka Univ. Med. Sch., Kitaku, Osaka, 530

Interactions between activities recorded simultaneously from a pair of cells were studied by cross-correlation analysis, in kittens ranging in age from the 2nd to 9th weeks. Even at the 2nd week of age when the eyes were just opened, correlated firings indicating common inputs to each of the pairs or excitatory connections from one to the other were detected. During the 2nd and 3rd weeks, significant correlations were most frequently observed between relatively matured cells with orientation selectivity and immature cells with no selectivity or very weak visual responses. Excitatory connections were found in the direction from the selective cells to immature cells. Also, the significant correlations were observed between a pair of matured cells with similar orientation preference. During the 4th to 6th weeks, the proportion of selective cells increased and the significant correlations were most frequently found between these cells. At the 7th week and thereafter, the significant correlations were found only between cells with the same or similar orientation preference except for a few cases. These results suggest that functional interactions may already exist between immature cells and selective cells just after the time of eye opening.

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EXTRAOCULAR PHOTORECEPTION IN THE ENTRAINMENT OF THE CIRCADIAN LOCOMOTOR RHYTHM IN THE TOAD. OGASAWARA, T. AND TASAKI, K. Dept. of Physiol. Tohoku Univ. Sch. of Med., Sendai 980

Entrainment and phase shifting of the circadian locomotor rhythms in the toad, Bufo bufo japonicus, were examined by a running wheel method. Three types of the entrained patterns of the rhythms were revealed in L (300 lux)D(0)12:12 cycles: bimodal activity in the dark, monomodal activity in the first half of the dark and splitted activity in the first halves of the dark and the light. Similar three patterns of activity were observed in the LD cycles in bilaterally blinded toads. The activity rhythms were able to follow a 6 hr phase advance shift of the LD cycle with a few transient cycles, accompanied by splitting and lengthening of the activity time. Splitted activity could follow the phase shift of the LD cycle in 1-2 days. Hibernated toads showed light-on activity once a day even under LD6:6 cycles, suggesting the activity depends on both exogenous light and endogenous rhythm.

These results suggest the presence of extraocular entrainment of the circadian locomotor rhythms in the toad.

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ANALYSIS OF THE AIR-CURRENT SENSORY SYSTEM OF CRICKET BY A RANDOM SIGNAL STIMULUS. SHIMOZAWA, T., Zool. Inst., Fac. Sci., Hokkaido Univ., Sapporo 060

Key features of air motion which activate the cercal sensory interneurons (INs) of the cricket, Gryllus bimaculatus, were studied. White noise contains all possible combinations of stimulus features. The white noise stimuli given prior to neuronal responses must commonly contain a key feature. Summation of the stimulus wave forms given before the neuronal responses shows up the common feature.

The white noise was generated by a shift register sequence program in an 8-bits microcomputer. The frequency bandwidth of the stimulus noise was 100 Hz. The noise was fed into a miniature wind tunnel for air-current stimulation. The noise signal was delayed and summated with the trigger of the neuronal response.

The key features extracted by large INs 8-1,9-1,9-2, and 9-3 were deceleration of air motion. INs 10-2 and 10-3 extracted flows of air to a direction with high sensitivity.

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VIBRATION OF THE SENSING MEMBRANE IN THE FROG AMPHIBIAN PAPILLA. YANO, J., OOYAMA, H., SUGAI, T. AND SUGITANI, M. Dept. Physiol., Kanazawa Medical Univ., Ishikawa 920-02

In the bullfrog amphibian papilla (AP), the macula is on the under surface of the ceiling, and a sensing membrane (SM) extends therefrom to the floor. Anteromedially, the SM attaches to the tectorial membrane hanging at the rostral part of the macula, and posterolaterally, to the column of the AP branch of the eighth nerve. previous study suggested the frequency selectivity of this structure, that is, anteromedial and posterolateral region of the SM mechanically tuning to low and high frequency, respectively. To elucidate this point, the observation of the SM vibration was carried out. Mica powders were sprinkled on the surface of the SM. Pure tones(200-1200 Hz) were applied into the perilymph. The frequency of the stroboscopic illumination was slightly detuned to the driving tone, so that the SM appeared to vibrate slowly (1-2 per second). The flickering reflection from one of the mica particles was taken as the threshold of vibration, and the vibration tuning curve(TC) was obtained to that portion of the SM. The vibration thresholds were high and the TC's were flat compared to those in the AP unit activities. The best frequencies (BF's), however, were still discernible. The BF's were low(300-500 Hz) for the anteromedial and high(600-800 Hz) for the posterolateral region of the SM. Results indicate that the SM shows place frequency selectivity, which may contribute to the tonotopic organization in the AP.

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KANAMYCIN OTOTOXICITY IN THE BUDGERIGAR (*Melopsittacus undulatus*) HASHINO, E. AND *SOKABE, M. Tokyo Woman's Christian Univ., Tokyo 181, *Dept. Physiol., Nagoya Univ. Sch. Med., Nagoya 466

The chronic effects of kanamycin (KM) on the budgerigar hearing were investigated by behavioral audiometry. The birds were received a daily intramuscular injection of KM (200 mg/kg) for successive 10 days and comparison of absolute thresholds between pre- and post KM treatment were performed. As a result, KM induced low frequency selective transient and permanent hearing loss, i.e., the disorder at lower frequencies less than 1 kHz was considerably larger than at higher frequencies. The low frequency selective effect of KM in the present study is contrary to the high frequency selectivity of the well documented aminoglycoside ototoxicity in mammals. To check the change in frequency difference limen, critical ratios were estimated in the pathological birds and the low frequency selective shifts were observed again. There also existed a rigid linear relationship between the shifts of critical ratio and those of absolute threshold suggesting KM did not deteriorate the spectral resolving power of the birds.

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STIMULATED OTO-ACOUSTIC EMISSIONS FROM THE EARS WITH UNILATERAL SENSORINEURAL HEARING LOSS. TANAKA, Y. Dept. Otolaryngol., Koshigaya Hosp., Sch. Med., Dokkyo Univ., Saitama 343

A study of stimulated oto-acoustic emission (OAE) was made of various cases of unilateral sensorineural hearing loss. The OAE pseudothresholds of peripheral losses such as inner ear anomaly, mumps deafness, or sudden deafness elevated in the affected side. Those of central losses did not elevate even in their affected side. As to the interaural difference in each cases of peripheral losses, there was a correlation between the psychoacoustic hearing threshold and the OAE pseudothreshold. The correlation coefficient between them in the cases of sudden deafness was 0.77. The results support the hypothesis that the OAE originates from the cochlear micromechanics related to hair cell function. The OAE can be instrumental in evaluating inner ear damages.

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AFTER-HYPERPOLARIZATION FOLLOWING A Ca-DEPENDENT RECEPTOR POTENTIAL IN THE AMPULLARY ELECTRORECEPTORS. SUGAWARA, Y., Dept. of Physiol., Teikyo Univ., Sch. Med., Tokyo 173

The sensory epithelium (ampulla) of Plotosus electroreceptors shows two kind of hyperpolarizing responses: one due to Na/K pump activity (1986) and the other that is an after-hyperpolarization (AH) following the regenerative receptor potential (RP). Under I-clamp the AH amplitude was dependent on RP duration, and under V-clamp the corresponding outward current on the receptor Ca current; both of which suggested a contribution of Ca influx. Since the decay of AH showed more than one phase, the AH amplitude was tentatively measured at 1 s (early AH) and at 20 s (late AH) from the end of RP. On hyperpolarizing the DC-level of the ampulla, both AH's were linearly decreased, with the extrapolation for the early AH intersecting at -68 mV in 4 mM K. K-blockers (4-AP and TEA) suppressed the early AH, but little affected the late AH. Ouabain (0.5 mM) or KCN (0.25 - 1 mM) suppressed the early AH, but only partially the late AH. In contrast, the hyperpolarization due to the Na/K pump activity is V-independent, and completely inhibited by Ouabain at 5 uM. The early and late AH's, however, seem to differ slightly from each other in their relative dependence such as on K-conductance or on metabolic processes.

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THE EFFECTS OF THE STIMULATION OF THE EFFERENT FIBERS ON THE SACCULAR NERVE ACTIVITY IN RESPONSE TO VIBRATION. SUGAI, T., OOYAMA, H., YANO, J. AND SUGITANI, M. Dept. Physiol., Kanazawa Med. Univ., Ishikawa 920-02

Some of the efferent fibers bifurcate in the eighth nerve of the toad and innervate two or more vestibular organs. Thus, stimulation of one branch affects the afferent activities in other branches. The effects of the electrical stimulation of the lagenar nerve, on the vibration stimulated saccular afferent activities were studied. Electrical conditioning stimulation(ECS), train of 31 pulses at 100/s, was applied to the lagenar nerve disconnected from its end-organ. With 50 ms latency, vibration test stimuli(30-100 Hz) were applied to the wall of the sacculus. Afferent single unit activities were recorded in saccular nerve. Electrical stimulation caused an elevation of the vibration threshold. Firing rate-intensity curves obtained with the test stimuli and ECS, had similar shape to that obtained with the test stimuli alone but was shifted to the higher intensity levels. The shift between the two curves ranged from 3 to 26dB(11.9±4.9dB). Thus, an activation of efferent fibers to the sacculus may shift the range of the afferent sensitivity to match with large vibration amplitude. The time course of the inhibition on the activity in response to 2 cycles of vibration was studied. Inhibition appeared with a delay of about 20 ms after the first pulse in the train, and reached its peak at about 50 ms. Complete recovery took from 200 to 300 ms.

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SOUND-INDUCED COMPONENT OF INTRACOCHLEAR CURRENT FLOW.
HASHIMOTO, T. and TANIGUCHI, I. Inst. Med. Dent. Engin., Tokyo Med. Dent. Univ., Tokyo 101; Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo 113.

The intracochlear current flow was measured by applying the voltage clamp technique to the scala media of the first cochlear turn of the guinea pig under sodium pentobarbital anesthesia. By an enamel-coated wire electrode the potential signal in the scala media was recorded and by the other glass micropipette electrode was injected the feedback current through a voltage control amplifier. The cochlear transduction current across the basilar membrane, which was induced by the sound reception, could be measured. This current might be named the cochlear microphonic current, which would be produced from the same origin with the cochlear microphonic potential. The cochlear microphonic current would be spatial summation of the transduction current of the ionic channel on the stereocilia of the cohlear hair cell. The sound-induced conductance change of the basilar membrane was estimated from the cochlear microphonic current and potential record.

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IMMUNOELECTRON MICROSCOPIC LOCALIZATION (NA^+, K^+)ATPASE IN THE LATERAL WALL OF THE RAT COCHLEAR DUCT.
IWANO, T.*, YAMAMOTO, A., OMORI, K., KUMAZAWA, T.*, AND TASHIRO, Y. Dept. Physiol., and Otolaryngology,* Kansai Med. Univ., Moriguchi 570

Lateral wall of rat cochlear duct was fixed by perfusion with 4% paraformaldehyde and embedded in LR-GOLD. The ultrathin sections were incubated with antibody against holo(Na^+, K^+)ATPase purified from rat kidney, subsequently with protein A gold complex and the electron micrographs were quantitatively analysed. In the stria vascularis, many gold particles were found over the basolateral membrane of the marginal cell and hardly found over the endolymphatic surface. Numerous gold particles were also found over the plasma membrane of the spiral prominence stromal cell and over the intercellular microvilli of the external sulcus cell. These results suggest (Na^+, K^+)ATPase on the lateral wall of the cochlear duct plays important roles for maintaining endolymphatic cation gradients and generation of the endocochlear potential.

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DISCHARGE PATTERNS FROM ANTERIOR AMPULLAR NERVE IN CARP.
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The anterior ampullar nerve in carp generates the action potentials spontaneously, when the carp is placed at the horizontal position. The spontaneous discharge frequencies varied among nerve fibers and the patterns of serial potential recordings were divided into three groups, e.g. regular, irregular and burst types. The discharge frequencies were mostly the range between 10 and 100 Hz and sometimes beyond this range. The analysis of patterns showed that the discharges from the anterior ampullar nerve fiber with efferent innervation to the hair cell were scattered with wide range of frequencies,comparing with the discharges from the primary afferent fiber. (The vestibular nerve bundle was cut off near the medulla, to delete the efferent effect.)

We can conclude that the efferent fibers are modifying the vestibular activities and the excitabilities of hair cells with efferent innervation are more variable. All hair cells in the crista cannot be arranged with the same manner and cannot excite at the same time with the same degree of excitability. This is thought to be one of the reasons why three types of discharge patterns were appeared.

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Ca-ACTIVATED K CHANNELS OF DIFFERENT UNITARY CONDUCTANCES IN THE GOLDFISH HAIR CELL MEMBRANE. SUGIHARA, I. and FURUKAWA, T. Dept. of Physiol. Tokyo Med. and Dent. Univ. Sch. of Med., Yushima, Bunkyo-ku, Tokyo 113.

Ca-activated K channels were studied with inside-out mode of the patch clamp method in the basolateral membrane of enzymatically isolated goldfish saccular hair cells. We identified 145 Ca-activated K channels on 90 hair cells. Upon measuring unitary conductances in symmetrical 125 mM KCl, we found that they are composed of four distinct groups which gathered around the mean of 150, 200, 250 and 300 pS. A test of the sensitivity to apamine indicated that all of these channels would belong to the large conductance group of Ca-activated K channels. Gating properties also differed; the 150 and 200 pS groups had shorter mean open time (0.08-0.25 ms when measured at 50 mV of membrane potential and 10 uM of inside Ca) than the 250 or 300 pS groups (0.2-1.1 ms under the same condition). Observed differences in the properties of Ca-activated K channels would be attributable to some unknown variations in the composition of channel protein.

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ON THE SITE OF MECHANO-ELECTRICAL TRANSDUCTION OF THE HAIR CELL. H.Ohmori, National Institute for Physiological Sciences, Okazaki.

Ca ion is one of the most permeable ion through the mechano-electrical transduction (m-e.t.) channel of the hair cell, despite of its very low concentration in the endolymph in which the hair bundle is bathed and the transduction proccess is likely to be operated.By the use of Fura-2,a Ca indicator dye, the distribution of Ca^{2+} within the hair cell was studied. Without stimulation,the nucleus,the cuticle and the hair bundle demonstrated lower $[Ca]_i$ than the other part of the cell body.With depolarizing mechanical stimulation $[Ca]_i$ increased, while it decreased with hyperpolarizing stimulation. By the stimulus of 1 kHz tone,marked increases of $[Ca]_i$ were demonstrated about the hair bundle's insertion to the cuticle. Mn is the another divalent cation which is permeable through the m-e.t. channel and quenches the fluorescence of Fura-2. Direct puff of 2 mM Mn saline quenched the fluorescence at the hair bundle. With limited puff towards the hair bundle the fluorescence intensity decreased about the hair bundle's insertion to the cuticle. These observations suggest that the insertion of the hair bundle to the cuticle could be a site of the mechano-electrical transduction.

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PHYSIOLOGIES AND MORPHOLOGIES OF SYNAPSES BETWEEN VESTIBULAR PRIMARY AFFERENTS AND HAIR CELLS OF THE CHICK CRISTAE AMPULLARES. YAMASHITA, M. Nat. Inst. Physiol. Sci., Okazaki 444.

Intracellular recordings and stainings were made from vestibular primary afferents and hair cells in cristae ampullares of the posterior canal of the chick with glass micropipettes filled with Lucifer Yellow CH. Mechanical stimulation was applied to the sensory hair by a fine glass rod vibrated at 200-300 Hz adjacent to the hair bundle. Hair cells showed transduction potentials with depolarizing DC and AC responses, of which frequencies were the same to the stimuli. The primary afferents showed two kinds of responses to the mechanical stimulation: One with DC and AC responses similar to the hair cells, the other with transient responses of rapid rise and slow decay. The latter occurred synchronously to the start of the mechanical stimulation and at random intervals during stimulation. The former primary afferents had calyceal terminals, and the latter had only bouton-type terminals.

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EFFECTS OF CROSSED OLIVOCOCHLEAR BUNDLE ON ALTANATING CURRENT-INDUCED OTO-ACOUSTIC EMISSION IN GUINEA PIGS. HOSOKAWA, Y., MORIYAMA, T., MINAMI, S., AND MURATA, K. Dept. of Neurophysiol., Med. Res. Inst., Tokyo Med. & Dent. Univ., Tokyo 101

An alternating current at a frequency of Fc was injected through a platinum microelectrode into the scala media of the cochlea of guinea pigs anesthetized with urethane (120mg/kg). During simultaneous application of the current and a pure tone at a frequency of Ft to the closed ear canal, the frequency spectrum analysis of sounds in the ear canal showed emission of tones at Fc and Ft±Fc. Selective block of the crossed olivocochlear bundle (COCB) by mechanical incision or cooling of COCB increased the emission at Ft±Fc and stimulation of COCB decreased them, although the emission at Fc remained unchanged. COCB stimulation became ineffective during COCB cooling and the effect revived reversibly after recovery of COCB temperature. These results imply that COCB suppressed the emission of Ft±Fc continuously and that the suppression was enhanced by COCB activation.

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INTRACELLULAR RECORDINGS FROM RAT COCHLEAR NUCLEUS NEURONS Ito,S., *Katayama,Y. and Murata,K. Dept. of Neurophysiol. and *Dept. of Autonomic physiol., Med. Res. Inst., Med. and Dent. Univ., Tokyo 101

Intracellular recordings were made from dorsal cochlear nucleus neurons in sliced brainstems of rats in vitro. Three types of response to intracellular depolarizing current pulses were observed; i.e. a regularly firing type (R type), an on-transient single-firing type (S type) and a burst firing type (B type). In neurons showing the B type response, a slowly developing depolarization together with increasing firing rate was caused during constant depolarizing currents. Focal stimulation evoked membrane depolarizations. Since they were reversiblly abolished in Ca^{++} free/high Mg^{++} solution, they are thought to be excitatory postsynaptic potentials (EPSPs). With strong focal stimulation, B type response neurons evoked a large EPSP, eliciting burst discharges, and then the EPSP terminated abruptly. A facilitation or an adaptation of EPSPs was observed in some cells with repetitive stimulation. The superfusion of glutamate (up to 1mM) caused a membrane depolarization associated with an increased membrane resistance in a small proportion of neurons, while aspartate showed no detectable effects.

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DISTRIBUTION OF BEST FREQUENCIES AND RESPONSE LATENCIES IN THE RAT AUDITORY CORTEX. HORIKAWA, J., ITO, S., HOSOKAWA, Y., AND MURATA, K. Dept. of Neurophysiol., Med. Res. Inst., Med. & Dent. Univ., Tokyo 101.

Distributions of best frequencies (BFs) and response latencies of auditory cortical neurons in rats (Wistar strain) were studied with tungsten microelectrodes under Nembutal anesthesia (5 mg/kg/hr). Responses of single neurons to pure tones were found to be localized in a temporal region (corresponding to area 41 in Krieg's cortical map of albino rats (1946)). In the region, the BFs were concentrically distributed: 50-55 kHz area was located in the center and the BF decreased gradually to 0.7-1.0 kHz toward the periphery. Anteroventral to this area, another 40-50 kHz area was found with lower BFs in the periphery. The response latencies were 7-12 ms in the former area and 14-20 ms in the latter area, suggesting that the former was the primary auditory area and the latter was the secondary one or higher than that. Electrode penetrations oblique to the cortical surface showed gradual change of the BFs, but those perpendicular to the surface showed almost constant BFs. This suggests that the columnar organization in BF in the rat auditory cortex exists which is similar to the other animals.

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THE RESPONSES OF THE AUDITORY CORTEX OF JAPANESE MONKEY TO VARIOUS SOUNDS, SPECIES-SPECIFIC CALLS, AND THE HARMONIC COMPONENTS OF CALLS. KAMADA, T., KAMEDA, K. AND KOJIMA, S.* Dept. of Oral Physiol., Hokkaido Univ. Sch. of Dent., Sapporo 060 and *Dept. of Neurophysiol., Primate Res. Inst., Kyoto Univ., Inuyama, Aichi 484

The responses of neurons from auditory cortex (AC) of two unanesthetized Japanese monkeys (*Macaca fuscata*) to pure tone pips, white noise and species-specific calls were examined. More than half units (131 out of 204) were tuned to narrow frequency range of pure tone, while others (73) responded to such a wide range of frequency that the best frequency (BF) of them could not be determined. The former located mainly in AI area, the latter did in surrounding areas. The AI units with high BF located more posteriorly than those with low BF. Seventy five units out of 197 responded to all, and 170 responded to more than one, of 8 monkey calls. The neurons from AC of two other monkeys were tested with regard to two types of "coo" sounds: smooth early high and smooth late high. Each one and some pairs of harmonic components of these sounds, simulated with a voltage-controlled oscillator, were also given. Seventeen neurons out of 98 responded with different temporal patterns to two calls. Some responses might simply be the sum of the responses to harmonics. However, other neurons did not respond to any one or a pair of harmonics, which suggests that they are not passive frequency filter networks, but are active recognition units.

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RESPONSES OF RHYTHMICAL CLICK DETECTORS AND BAND OF NOISE RECEIVERS TO PERIODIC AMPLITUDE FLUCTUATING TONES. MARUYAMA, N., KUDOH, M., FURUKAWARA, M. AND SHINZAWA, H. Dept. Neurophysiol., Brain Research Inst., Niigata Univ., Niigata 951

We have been able to elicit a sustained response in about 75% of the cat's AI neurons using various complex sound stimuli. Based upon the level of selectivity for the effective stimuli, auditory cortical neurons were classified into 3 groups: the highly selective neurons (consonant detectors, formant detectors, vowel detectors, etc.), the poorly selective neurons (amplitude-fluctuation receivers, band of noise receivers, pure tone receivers), and the non-selective neurons (general sound receivers). The amplitude-fluctuation receivers and the band of noise receivers responded to stimuli varying with time. In the present experiment, we tried to find what parameter does express the effectiveness well for the stimulus varying with time in these receivers. We found a few neurons which responded exclusively to a click train of about 10 Hz repetition. These neurons showed high selectivity for the shape of the wave envelpe and the frequency of repetition. Therefore, these neurons were considered to be rhythmical click detectors.

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AXONAL REGENERATION AFTER TRANSECTION OF THE COMMISSURE OF THE INFERIOR COLLICULUS. TANIGUCHI, I. Med. Res. Inst., Tokyo Med. & Dent. Univ. Tokyo 113

Axonal regeneration in the commissure of the inferior colliculus (CIC) of mice following its transection was studied morphologically by the horseradish peroxidase method and electrophysiologically by recording the neuronal discharges in the inferior colliculus (IC). The auditory responses of the IC neurons were modified by the electric stimulation to the contralateral IC one month after the CIC transection. Many IC neurons which showed a good response to the auditory stimulation were inhibitted by the electric stimulation. A few neurons showed summational or facilitative responses to a combination of auditory and electric stimuli. These results suggest that the regenerating fibers reestablished synaptic connections with the IC neurons.

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PROJECTION OF THE ANTENNULAR NERVE TO THE CEREBRAL GANGLION OF THE CRAYFISH.
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Structure of the cerebral ganglion of American crayfish, Procambarus clarkii, was studied by the reconstruction schema from 10μm serial sections with relations to the input from the mechanoreceptive neurons belonging to the antennular setae. The basic stain used were the Holmes-Blest silver impregnation. Specimens used were the adult male having the cephalothorax length of 45 mm. The antennular nerve comining from the first antenna entered the cerebral ganglion at the paracentral ventral surface. The nerve bundle gave branches which form the ventral median antennular I neuropile, and then passed posterodorsally, which in turn form the dorsal m. ann. I neuropile. Both neuropiles contain several small subdivisions. The subdivisions were encircled by nerve bundles, and were filled with finely branched nerve fibers with varicose-like formations.

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DIRECTIONAL SELECTIVITY AND EXCITABILITY OF PERIODONTAL MECHANORECEPTORS.
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Slowly adapting units of periodontal mechanoreceptors show directional selectivity with vigorous response when stimulated in the most sensitive direction and with no response when stimulation is in the opposite direction. For the purpose of examining excitability change in relation to stimulus direction, the threshold level of receptors during the conditioning mechanical stimulus was measured by electrical test pulses (5-50 msec) applied through electrodes set at the pulpal cavity after a pulpectomy and on the gingival tissue of the maxillary canine and/or by mechanical test pulses (5msec) applied to the tooth. Unitary discharges were recorded from the superior alveolar nerve in cats anesthetized with pentobarbital sodium (40mg/kg,ip). When subliminal mechanical stimulation was applied to the tooth in the most sensitive direction, the excitability of receptors increased. With stimulation in the opposite direction, however, excitability decreased in proportion to the stimulus intensity. These results suggested that there was not only an excitatory but an inhibitory process in the periodontal mechanoreceptors.

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MONOCLONAL ANTIBODIES AGAINST CARBOHYDRATE DIFFERENTIATION ANTIGENS RECOGNIZE TYPES OR SUBTYPES OF SENSORY RECEPTOR CELLS IN THE RABBIT OLFACTORY SYSTEM.
MORI, K. Dept. Physiol., Gunma Univ. Sch. Med., Maebashi, Gunma 371

Several monoclonal antibodies (MAbs) against carbohydrate differentiation antigens were used to study immunohistochemically the cell surface carbohydrate expressions by types or subtypes of sensory receptor cells in the rabbit main and accessory olfactory systems. MAbs-SSEA-3 and -SSEA-4, both of which bind to certain globo-series carbohydrates, labeled all vomeronasal receptor cells in the accessory olfactory system, but did not stain olfactory receptor cells in the main olfactory epithelium. MAb 2C5, which binds to certain lacto-series carbohydrates, recognized a subset of olfactory receptor cells. The 2C5-positive receptor cells were widely distributed over the olfactory epithelium and were intermingled with 2C5-negative receptor cells. MAb 2C5 also labeled the majority of vomeronasal receptor cells. MAb 4C9, which binds to fucosyl-poly-N-acetyllactosamine, did not label olfactory receptor cells but stained a subset of vomeronasal receptor cells. MAbs 2C5 and 4C9 also labeled the axons of these chemosensory receptor cells and thus revealed their axonal projection sites in the main and accessory olfactory bulbs.

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EXAMINATION OF THE OUTPUT OF A NEW OLFACTOMETER. MOTOKIZAWA, F. AND SHIMOMURA, F.
Dept. Physiol., Nara Med. Coll., Kashihara, Nara 634

In order to perform a well-controlled odor stimulation, an output from a new olfactometer which is equipped with a plastic bag was monitored with a F. I. D. or a CO_2 analyzer. A concentration-time relation of the output was trapezoid. This waveform was measured over 6 items; (1) time from the beginning of the output to the start of the rising phase of the waveform(Td), (2) time from the end of the output to the start of the falling phase of the waveform(T'd), (3) time from the start of the rising phase to attain to 90% of a peak amplitude(T_{90}), (4) time from the start of the falling phase to decline to 10% of a peak amplitude(T_{10}), (5) time from the start of the rising phase to reach a peak amplitude(T_p), (6) peak amplitude(A_p). Reproducibility of the waveform was very good; measured values of the 6 items were nearly constant for a week. The sizes of the plastic bag(3L, 5L and 10L) have no effects on the waveform. As the diameter and length of a tube connecting the olfactometer with the monitor increase in size, the waveform was gradually changed except a peak amplitude. The volume flow rates for delivery of an output of the olfactometer to the monitor and for exhaust from the monitor are controlled independently. It was found that these two volume flow rates must be adjusted to be equal and to be over 300mL/min.

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Microstimulation of single afferent nerves in man. TOMA,S.,NAKAJIMA,Y. AND HOMMA,S. Dept. of Physiol., Sch. of Med., Chiba Univ., Chiba 280.

In 22 human subjects, the single afferent activities from mechanoreceptors of the hand were recorded by tungsten microelectrode inserted into the median nerve and identified by unit type (RA,PC,SAI,SAII) in determining receptive field. Through the recording electrode, electric short pulse trains were delivered at successively increasing current intensity, until the subject reported the sensation noticed in the hand. When stimulated by positive pulse, the location, size and shape of the perceptive fields were spatially matched with their receptive fields, suggesting that the sensation could be accounted for by the recorded unit that had been selectively activated by the current pulses. RA unit stimulation evoked the tapping sensation and developed the vibration sensation with the stimulation pulse of 20-100Hz. PC unit stimulation did vibration sensation which was perceivable over 300Hz. SAI unit did sensation of continuous indentation. SAII unit stimulation could not evoke any sensation. On the other hand, negative pulse stimulation almost always provoked paresthesia associated with tingling sensation in the large perceptive field beyond it's receptive field. These experiments indicated that positive pulses were most effective in stimulating single nerve fibers and the specific percepts were often elicited. The results of negative pulse stimulation endicated that several myelinated and non-myelinated fibers adjacent to the electrode tip were affected by stimulation, producing fused sensation as tingling paresthesia.

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SOMATOSENSORY EVOKED POTENTIALS CORRELATES OF MAGNITUDE ESTIMATIONS FOR AIR-PUFF STIMULATION OF HAND IN MAN. HASHIMOTO, I., YOSHIKAWA, K. AND SASAKI, M.
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Six levels of sharp-fronted air-puff stimulation were applied to the base of the right index finger in man to elicit somatosensory evoked potentials (SEPs) and also to obtain psychophysical magnitude estimations. The relationship between magnitude estimations and air-puff intensities was appropriately expressed by a power function. Six components (N23, P29, N40, P48, N57 and P72) were consistently recorded from the contralateral hand sensory area and the amplitudes of the components systematically increased and the latencies decreased with increasing air-puff intensities. The amplitudes of all components except the late N57-P72 component correlated with stimulus intensity when the effect of subjective magnitude was controlled. In contrast, the amplitudes of later N40-P48 and N52-P72 components were significantly associated with subjective magnitude when the effect of stimulus intensity was partialed out. The data suggest that earlier SEP components may reflect physical parameters of sensory stimuli while later components reflect subjective evaluation of sensory stimuli.

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FUNCTION AND MORPHOLOGY OF THE SENSORY AXON TERMINAL IN FROG MUSCLE SPINDLE AFTER TREATMENT OF COLLAGENASE. INABA, H., FUJITSUKA, N., KORI, A. A. and ITO, F. Depart.Physiol., Nagoya Univ. Sch. Med., Nagoya 466

A condition to remove the capsule of frog muscle spindle without any damage on the sensory axon terminal was established in order to direct application of ions or drugs to the terminal. Muscle spindles were isolated from semitendinosus muscles of the frog Rana catesbeiana. The optimum condition was obtained by incubating the isolated muscle spindle in a calcium-free Ringer's solution containing 0.2 % collagenase at 34°C for 30 min. In this condition the response pattern of the spindle during stretch could not be distinguished from that of intact spindles, although the duration of individual afferent spikes was prolonged about 4 times that of the intact spindle. A partial disruption of the outer and inner capsules, and an invasion of HRP into the intrafusal muscle fibers in the decapsulated spindles were observed. No significant change was observed of the size and density of intramembrane particles in the freeze fracture replica of the decapsulated spindles.

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DISTRIBUTION AND CLASSIFICATION OF THE MUSCLE SPINDLES IN FROG SEMITENDINOSUS MUSCLE BASED ON MORPHOLOGICAL AND PHYSIOLOGICAL CHARACTERISTICS FUJITSUKA,N., FUJITSUKA,C. and ITO,F. Depat.Physiol.,Nagoya Univ. Sch. Med., Nagoya 466

Muscle spindles isolated from semitendinosus muscle of the frog Rana catesbeiana were classified into complex and simple type muscle spindles, based on the branching of the sensory axon terminal and the number of intrafusal muscle fibers. The freeze fracture replica revealed intramembrane particles in protoplasmic face along the sensory axon terminals. The mean densities of particles in the complex and simple type spindles were 970 $\pm$ 16/μm^2 and 420 $\pm$ 13/μm^2, respectively, although no significant difference between the sizes of the particles in the two types of spindles was observed. Tonic and phasic discharges in the complex and simple spindles, respectively, in response to stretch may be explained by the difference of the particle density, in addition to the difference in mechanical properties which is due to dissimilarity in the number of intrafusal fibers between those two kinds of spindles.

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COMPARISON BETWEEN ELECTRICAL RESPONSES IN FROG TASTE AND SUPPORTING CELLS. SATA, O. AND SATO, T. Dept. Physiol., Nagasaki Univ. Sch. Dent., Nagasaki 852

The electrical responses of taste cells and supporting cells in bullfrogs were compared. The mean resting potential of taste cells was at -23.4 mV, and that of supporting cells was at -17.8 mV. In both cells, the depolarizing or hyperpolarizing responses were elicited by the four basic taste stimuli (NaCl, acetic acid, quinine-HCl and sucrose) and deionized water. The response profiles in both cells were similar. The rise times of the supporting cell responses for all the stimuli tended to be shorter than those of the taste cell responses. The membrane resistances of supporting cells and taste cells were decreased by NaCl, acetic acid and sucrose, but were increased by Q-HCl and water. With all stimuli except for Q-HCl no difference was found between the resistance changes in the supporting and taste cells. The reversal potential for the depolarizing responses of supporting cells in response to 0.5 M NaCl was at +3.8 mV. These results suggest that the response characteristics of the supporting and taste cells are similar to each other.

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MECHANISM OF SALT TASTE RECEPTION IN THE FROG GLOSSOPHARYNGEAL NERVE.
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The present study was undertaken to investigate whether or not changes in the surface potential are involved in salt taste reception of the frog glossopharyngeal nerve. The surface potential is a function both of the charge density of the membrane surface and of the ionic strength of the medium.

Unitary discharges were recorded from single water fibers of the frog glossopharyngeal nerve. $CaCl_2$, $MgCl_2$ and NaCl were effective stimuli. However, $LaCl_3$ which changes the charge density of the membrane surface had no excitatory effect. Increase of the ionic strength was done by addition of a certain amount of other salts to the stimulating solution. The $MgCl_2$ response and the NaCl response were not affected by the increase of the ionic strength. The $CaCl_2$ response was inhibited by other salts. However, the cause of the inhibition of the $CaCl_2$ response was not due to the ionic strength. It is concluded that changes in the surface potential are not involved in salt taste reception of the frog glossopharyngeal nerve.

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SODIUM PERMEATION THROUGH THE FROG TONGUE EPITHELIUM
SOEDA, H., SAKUDO, F., KAJIYA, H. AND NODA, K. Dept. of Physiol., Fukuoka Dent. Coll., Sawara-ku, Fukuoka

Stimulation of the frog tongue with NaCl produces a transepithelial potential change, associated with a decrease in resistance across the isolated dorsal epithelium. This suggests that the tissue permits permeation of some ions responsible for this response. Flame-photometrically, we attempted to measure sodium ions penetrating through the tissue. After replacing all ions of the tissue with isotonic sucrose solution on both sides, addition of NaCl to the mucosal solution elicited a transepithelial sodium permeation to the serosal side. This was dependent upon the amount of added NaCl, and the ions appeared faster and more as compared with the case in the opposite direction. Potassium and lithium ions also permeated through the tissue from the mucosa to the serosa, when their equimolar chlorides were respectively added to the mucosal solution. The order of easiness of permeation was sodium = potassium > lithium. Ouabain had no significant effect on sodium permeation, while tetracaine suppressed it. The sodium permeation of the dorsal epithelium was considerably larger than that of the palatine mucosa or the abdominal skin. The results indicate that the sodium permeation of the dorsal epithelium produces the transepithelial response which is able to influence taste reception.

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THE EFFECT OF INTRACELLULAR INJECTIONS OF C-GMP INTO THE MOUSE TASTE CELLS.
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The mouse taste cells were morphologically and electrophysiologically classified into two types, H- and D-type, according to their sucrose responses. It is natural that there are several complex intracellular taste transduction mechanisms in the taste cell. Since c-GMP and c-AMP might be postulated as a candidate for an intracellular transmitter in a variety of cells. In the present experiments, in order to examine the possibility that c-GMP is an internal transmitter in the process of taste transduction of H-type taste cell. C-GMP was iontophoretically injected into a mouse taste cell from one barrell of a double-barrelled microelectrode with the other barrell monitoring membrane potential and resistance changes. C-GMP induced a depolarization membrane potential accompanied by an increase in membrane resistance. The depolarization potential change was also caused by c-AMP injection, though it was always smaller than that by c-GMP. The results suggest that c-GMP is involved in the taste transduction process in the mouse taste cell.

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NEURAL CONNECTIONS OF THE SUPERIOR SECONDARY GUSTATORY NUCLEUS OF THE JAPANESE SEA CATFISH. LAMB, C. F. IV*, MARUI, T. AND KASAHARA, Y. DEPT. ORAL PHYSIOL., KAGOSHIMA UNIV. DENT. SCH., KAGOSHIMA 890

The superior secondary gustatory nucleus (nGS) of teleost fishes receives afferent fibers from the facial (FL) and vagal (VL) lobes of the medulla, and projects to the inferior lobe (LI) of the ventral diencephalon. We studied electrophysiological responses of nGS neurons in gonzui to chemical and mechanical stimulation of the external body surface and oropharyngeal cavity by glass microelectrodes. HRP was injected into the nGS, VL, and FL to determine the connections of the nGS. Responses of nGS neurons generally involved large receptive fields (RFs), including the whole body surface and oropharyngeal cavity. Restricted RFs were observed including only the ipsilateral barbels, but these neurons did not appear to be topographically arranged within the nGS. HRP-labelled efferents from the nGS projected to the nucleus lobobulbaris (nLB) and nucleus diffusus (nDLI) of the LI along with VL and FL fibers, and reciprocal projections were seen from neurons of the nLB to the VL, FL, and nGS. This provides an anatomical basis for a feedback system between the diencephalon and the primary and secondary gustatory nuclei, and possibly for the incorporation of telencephalic input in feeding behavior.

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Cross-correlated activity of two taste neurons in the solitary tract nucleus (STN). ADACHI, M., YAMADA, S., OHSHIMA*, T. and SATOH, T. Dept. Physiol. Aichigakuin Univ. Dent. Sch., Nagoya 464

Multiple microelectrodes were inserted into the rat STN to record simultaneously from two taste neurons. Of 22 simultaneously recorded pairs, eleven had no detectable peak in their cross-correlograms. From these negative pairs the probability to encounter by chance two neurons having the same taste quality to which the response is most strong (best taste) was calculated to be 0.376. Other 11 pairs had a narrow peak at the center of the cross-correlograms for one to four kinds of taste quality. The ratio for the paired neurons to have the same best taste was 0.727. The ratio for the best taste of one of the paired neurons to be identical with that of the common pace-maker neuron was 0.727. The ratio for a set of three neurons to have the same best taste was 0.636. Synchronous discharges occurred more often during stimulation with NaCl or HCl, but rarely during sucrose or quinine. However, the weight of the synchronous discharge in the total output of neuron was in some cases much heavier during stimulation with sucrose or quinine. It may follow that informations on salt and sour are signaled mainly through the channels of higher activity, while sweet and bitter are handled in a different way where both sporadic, highly synchronous activity and disappearance of synchronization are the significant output from the STN.

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DISTRIBUTION OF TASTE NEURONS IN RAT CEREBRAL CORTEX. OGAWA, H., ITO, S., MIKI, K., and MURAYAMA, N. Dept. of Physiol., Kumamoto Univ. Med. Sch., Honjo 2-2-1, Kumamoto 860

While stimulating the entire oral cavity with four basic taste solutions, we recorded taste neurons at the cerebral cortex of SD rats (250-350g) anesthetized with urethane. A vast majority of taste neurons were located at the granular insular cortex, area I of Rose (1929), and a few at the agranular insular cortex, area AI. Tactile neurons as well as thermoreceptive neurons were also found in these two areas. When the frontal plane of the cortex was reffered to the bed nucleus of the anterior commissure, the rostro-caudal extent of the taste responsive area was ca. 2 mm, and the maximum dorso-ventral extent was ca. 2 mm. Taste neurons in area I showed different features in comparison with those in area AI. Taste neurons in area I produced inhibitory responses more frequentry than in area AI, and most of taste neurons in area AI were excited by HCl.

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Response features of solitary tract nucleus neurons to taste, mechanical and thermal stimulation of oral cavity in rats. Y. Yamashita, H. Ogawa and T.Hayama. Dept. of Physiol., Kumamoto University Medical School, Honjo 2-2-1, Kumamoto 860

While applying taste, thermal and mechanical stimulation to the entire oral cavity, we studied receptive properties of solitary tract nucleus (NTS) neurons of anesthetized rats. We identified 3 types of neurons; taste (55%), mechanoreceptive (30%) and cold units (15%). A majority of taste neurons (75%) responded phasically to either cooling (40-20°C) or warming (20-40°C) or both. Receptive fields (RFs) for thermal stim., were found on the RFs for taste. Among them, taste neurons, most excited by sucrose, responded to warming and mostly had the RF on the nasoincisor duct. A high correlation was found between sucrose and warming but not between HCl and cooling, in contrast to previous findings on the chorda tympani fibers (Ogawa et al. 1968). A half the mechanoreceptive neurons observed responded phasically to cooling and their RFs for cooling were located on regions similar to that for mechanical stim. Cold neurons gave rise to both phasic and tonic discharges to cooling, but were entirely inhibited by warming.

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RECEPTOR MECHANISMS FOR "ELECTRIC TASTE". NINOMIYA, Y., MIZUKOSHI, T., AND FUNAKOSHI, M. Sch. Dent., Asahi Univ., Gifu 501-02

Receptor mechanisms for "electric taste" were studied by examining responses of the rat chorda tympani nerve to chemical and electrical tongue stimulations. The application of 1% procaine, 1μM TTX, 30mM $MnCl_2$ or the mixture of TTX and $MnCl_2$ for 10min to the tongue reduced responses to anodal current at 15μA of intensity by 43, 65, 64 or 45%, respectively, but only slightly if at all those to chemical stimuli such as NaCl, HCl, sucrose or quinine. The reduction of responses to anodal current by the drugs increased with increasing intensity of the applied current from 2.5 to 30μA, and was greater when current was applied with a dilute NaCl solution than a dilute KCl, $CaCl_2$ or HCl solution. The suppression of responses observed when procaine was injected into the lingual artery was not selective. The selective suppression of responses to electrical stimulation by the drugs was observed in a single chorda tympani fiber. These results suggest that the site of action of the drugs is in taste receptor cells but not in taste nerve fibers. Therefore, it is probable that specific receptor mechanisms for "electric taste"(procaine-, TTX- or Mn-sensitive) exist in the taste cell membrane.

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DIURESIS AND ANTIDIURESIS PRODUCED BY THE SUPERIOR LARYNGEAL AND GLOSSOPHARYNGEAL NERVES IN THE RABBIT. SHINGAI, T., TAKAHASHI, Y.*, AND MIYAOKA, Y. Dept. Physiol., Niigata Univ. Sch. Dent., Niigata 951

Functional differences between the superior laryngeal nerve (SLN) and the glossopharyngeal nerve (GPN) in urine regulation were studied using urethane anesthetized rabbits. Electrical stimulation (40 Hz) was applied to these nerves for 1 min. Urinary flow was increased by stimulation of the SLN. Usually the diuretic effect appeared as early as the first 10 min after the start of stimulation and reached its maximum 20-40 min after stimulation. On the contrary, GPN stimulation decreased urine flow. The antidiuretic effect peaked around 30 min after stimulation. Effects of water and NaCl stimulation were also examined. Water administration to the larynx produced a diuresis, whereas NaCl injection to the oral cavity and pharynx innervated by the GPN provoked an antidiuresis. These results and electrophysiological findings for the SLN and GPN reported previously suggest that water fibers contained in the SLN produce a diuresis, while Na-fibers in the GPN provoke an antidiuresis.

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RESPONSES OF THE LINGUAL NERVE AFFERENTS TO THERMAL, MECHANICAL AND CHEMICAL STIMULATION ON THE CAT TONGUE Kimisato Naito,Naoki Hanashima, Koko Kagaya, Koichi Iwata, Hiroyuki Kamogawa and Rhyuji Sumino.
Department of Physiology,School of Dentistry, Nihon University Kandasurugadai Chiyoda-ku 1-8-13 Tokyo 101 Japan.

Experiments were performed on cat anesthetized with ketamine-HCL(50mg/Kg) and maintained with a pentobarbital(5mg/Kg/h). At the recording sessions, the animals were immobilized with pancronium bromide (5mg/Kg/h). A total of 120 functionally identified single fibers isolated from the lingual nerve were studied. About 13% of fibers responded to heat stimulation (Hs-units). Hs-receptors were distributed marginal region of the tongue, while insensitive receptors were in the wide region of the tongue. About 30% of Hs-units responded to low threshold mechanical stimulation (< 2.0 gw) and about 70% of those units responded to high threshold mechanical stimulation (>4.0 gw). Conduction velocity of those units were arranged in two populations (the Aδ and the C units). Almost all mechanical high threshold Hs-units were increasing in firing frequency following perfusion of the algesic agents via the lingual artery.

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EFFECTS OF PROSTAGLANDIN-E_2 ON THE RESPONSE TO HEAT STIMULATION OF THE CANINE VISCERAL POLYMODAL RECEPTORS. SATO, J., MIZUMURA, K., AND KUMAZAWA, T. Dept. Nervous & Sensory Functions. Res. Inst. Environ. Med., Nagoya Univ., Nagoya 464

Polymodal receptors are characterized by their responses to noxious heat stimulation. In particular, these receptors have been shown to exhibit augmented responses to repetitively applied heat stimulations (heat sensitization). Although the mechanism of heat sensitization is not yet fully understood, prostaglandin (PG)-E_2 has been noted as a possible agent in heat sensitization. Single polymodal receptor discharges were recorded in vitro using testis-superior spermatic nerve preparations excised from deeply anesthetized dogs. Heat stimulation was applied by replacing the bathing Krebs solution with pre-warmed solution. After heat stimulation at 55°C, responses to heat stimulation just above the threshold temperature (40-48°C) were strongly augmented. Acetylsalicylic acid (aspirin), an inhibitor of PGs synthesis, was not able to abolish these augmented responses to repetitive heat stimulation. In addition, PG-E_2 up to 1.4×10^{-6} M (for 2-3 min), had only a weak augmenting effect, if any, on the responses to heat just above the threshold temperature. These results suggest that PG-E_2 might not be a principal agent in heat sensitization.

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GUSTATORY NERVE RESPONSES TO FOUR BASIC TASTE STIMULI IN MICE EXPOSED TO SUCROSE DURING THE VARIOUS POSTNATAL PERIODS. YAMADA, T., UMEZU, M. AND HUKUSHIMA, Y.* Physiol. Lab., Japan Women's Univ., Bunkyo-ku, Tokyo 112

We applied to the tongues of mice a filter paper soaked either with 40% sucrose solution (suc. group) or with distilled water (D.W. group) during the period of 2-21, 8-21, 8-35 and 71-89 postnatal days. Then we recorded the integrated responses of the chorda tympani nerve to 0.0001-0.5M NaCl, 0.01-1M sucrose, 0.0001-0.003M HCl and 0.0001-0.03M quinine hydrochloride.

The magnitude of responses in ratios 0.1-1Msucrose/0.003MHCl and 0.1-0.5MNaCl/0.003MHCl was larger in mice exposed to sucrose during the period before 35 days old. In mice exposed to sucrose before 35 days old, increase of nerve responses to sucrose and NaCl was found at higher concentration in according with the length of exposure period. In adult mice exposed to sucrose during 71-89 days old, there were not significant differences in responses of two groups at any taste stimuli of various concentration ranges.

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RAPID AND VOLUNTARY EYE MOVEMENT TRIGGERS CHANGE IN TONUS RECORDED FROM THE ANTERIOR VERTEBRAL MUSCLES. Watanabe,K., Liao,T.J., Takeyama,K., Suzuki,H. and Tasaki,K. Dept. of Physiol., Tohoku Univ. Sch. of Med., Sendai 980

Our needling experience for more than ten years has suggested that the anterior vertebral muscles such as M.longus colli and M.scalenus anterior increase their tonus, triggered by the eye movement, with latency between 3 to 6 seconds. This phenomenon was not observed in healthy subjects but in patients suffering from neural disorders. In order to find an objective measure to analyse a neural mechanism causing this reflex-like phnomenon, we recorded local EMGs and an electric impedance as an alternative of the muscle tonus. Adequacy of our measurement was confirmed by recording them using an insulated acupunctureneedle with a non-insulated tip from the anterior tibial muscle and from the flexor digitorum profundus. Increase in the amplitude of integrated spike discharges as well as the impedance was in proportion to the amount of the isometric contraction. The isotonic contraction caused proportional decrease in the impedance. Rapid and voluntary contraction induced decrease in the impedance of the anterior vertebral muscle, the latency of which ranged from 2 to 8 seconds. No impedance change was recorded from that muscle of healthy subjects. These are in agreement with the previous experience. We conclude that recording of the impedance is an objective measure to detect local change in the muscle tonus around the cervical vertebrae.

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OBJECTIVE AND QUANTITATIVE MEASURE FOR THE INTENSITY OF THE "HIBIKI" SENSATION CAUSED BY THE ACUPUNCTURE STIMULATION. Liao,T.J., Suzuki,H and Tasaki,K. Dept. of Physiol., Tohoku Univ. Sch. of Med., Sendai 980

Hand manipulation of an acupuncture needle causes a sustained and characteristic sensation, "hibiki", which is a prerequisite for the effectiveness of acupuncture treatment. We attempted to measure this sensation both subjectively, using a hand dynamometer with a strain gauge, and objectively, by measuring the electrical impedance change of the muscle around the tip of the acupuncture needle. To confirm the validity of the objective measurement, we applied the technique of cross modality matching (CMM). Subjects were asked to press the hand dynamometer in response to the brightness of light and to the loudness of sound. The results were in agreement with those reported by Stevens (1961). Furthermore, we found that hand pressure followed continuously changing loudness and that the relation between them also obeyed Stevens' power low. This means that CMM can be applied to expressthe intensity of the "hibiki" sensation. The relationship between the amplitude of electrical impedance change at any moment were linear. From this we conclude that muscle impedance change at the site of needle stimulation gives a good objective measure of the subjective acupuncture sensation.

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RESPONSE OF RAT A1 REGION NEURONS TO STIMULATION OF PERIAQUEDUCTAL GRAY MATTER AND ADJACENT MIDBRAIN RETICULAR FORMATION. TODA,K., Dept. Physiol., Fac. Dent., Tokyo Med. Dent. Univ., Tokyo 113 JAPAN.

Single unit activity was recorded from neurons in the A1 region to clarify the functional role in the descending inhibitory mechanisms in stimulation-produced analgesia from the periaqueductal gray matter (PAG) and midbrain reticular formation (MRF).

After chemical stimulation of the PAG by glutamate injection, a clear facilitation was observed in a majority of TYPE II neurons which projected to the spinal cord,however,the activity of TYPE I neurons which projected to the raphe magnus was scarcely changed. In contrast, naloxone-reversible glutamate-induced suppression was obtained in about 60% of TYPE I neurons after electrical and chemical stimulation of MRF. In TYPE II neurons, naloxone-nonreversible facilitation was observed after both stimulation of MRF. The effective sites for chemical stimulation was within the caudal midbrain,however,those of electrical one extended over almost the whole midbrain level.

These results suggest that at least two types of descending information are transmitted from the so-called analgesic center in the midbrain to A1 region.

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THE EFFECTS OF BRAINSTEM STIMULATIONS UPON THALAMIC NOXIOUS NEURONS.
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Many previous reports demonstrated that electrical stimulation of various sites in the brainstem modulate pain transmission at spinal cord dorsal horn, but their effects on thalamic neurons are still unclear. We studied with extracellular recording the effects of stimulation in nucl. raphe magnus (NRM) simulations and nucl. reticularis gigantocellularis (NGC) upon thalmic noxious neurons in 32 cats.

Under light anesthesia, noxious neurons were identified by contralateral sural nerve electrical stimulations with intensities strong enough to activate C-fibers. NRM stimulation inhibited 41 of 69 noxious and 40 of 111 non-noxious neurons. This difference was statistically significant ($p<0.01$). NGC stimulation also inhibited 28 of 45 noxious and 12 of 51 non-noxious neurons, but did not coincide with effects of NRM stimulation. In 5 cases influences of dorsal lateral funiculus (DLF) lesions in the cervical spinal cord did not significantly affect these inhibitions. These data suggest that NRM and NGC stimulations modulate sensory transmissions at the medial thalamus through some ascending systems besides the raphe spinal desending system.

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INDIVIDUAL VARIATION OF EFFECTIVENESS OF ACUPUNCTURE ANALGESIA EVALUATED BY EVOKED POTENTIAL IN THE DORSAL PERIAQUEDUCTAL CENTRALGRAY.
HISHIDA, H., HUANG, X. F., LUO, C. P., AND TAKESIGE, C. Dept. Phisiol., Sch. Med., Showa Univ., Shinagawa, Tokyo. 142

Evoked potential in the dorsal part of the periaqueductal central gray (D-PAG) caused by acupuncture point (tibial muscle) stimulation was abolished by intraperitonial 1mg/kg naloxone, while that in the lateral part of the PAG caused by non-acupancture point (abdominal muscles) was not influenced.

The stimulus threshold to produce D-PAG evoked potential is always about 1volt lower in 0.05msec recutangular pulse in the responder than in the non-responder.

The amplitude of the D-PAG evoked potential is always heigher in the responder for each stimulus strength than that of in non-responder and the maximal height of it in the non-responder animals did not reach to that in the responder.

After treatment of intra-peritonial 250mg/kg D-phenylalanine (DPA), the threshold strength to cause D-PAG evoked potential in the non-responder decreased to that of the responder and height of it in non-responder also increased to that of the responder.

It was concluded that the individual variaton of effectiveness in acupancture analgesia might be originated in the spinal transmition involved the opioate receptor and DPA act on this transmission to abolish individual variation.

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THE DISTRIBUTION OF PAIN THRESHOLD IN DEEP TISSUES IN MAN.
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Experiments were performed on healthy volunteers. The insulated needle was used as a monopolar electrode (cathode), a surface EEG electrode was used as an anode. The intensity of stimulus pulse (3 train pulses, 2Hz) was automatically increased by the ramp wave at 0.01Hz. The current of stimulus was monitored, integrated and then recorded contineously. The threshold current of perception, pain and pain tolerance, and nature of pain sensation were recorded using pain charts. The order of pain threshold was as follows; nerve<artery<periosteum<fascia<tendon. The sensations elicited by the stimulation were varied but showed tissue-depended characteristics. When the needle inserted stepwisely, the threshold and the nature of sensation were changed remarkably. In the tender point, the threshold of fascia was significantly lower than that of non-tender point ($p<0.05$). These results indicate that the present method for pain measure is very useful for its reproducibility and restricted stimulation of deep tissue, and suggest that the tender points are the loci where the pain threshold in the fascia was tend to reduce.

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CLASSIFICATION OF INTRAFUSAL MUSCLE FIBERS IN FROG MUSCLE SPINDLE

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It has been found that some muscle spindles in a restricted region (red area) in semitendinosus muscle of the frog (Rana catesbeiana) are innervated by a fusimotor axon. To gain further insight into the structural similarity between the frog and mammalian muscle spindles, the enzyme-histochemical and morphological characteristics of the intrafusal muscle fibers and end-plates in the frog spindles were studied. Seven types of intrafusal fibers were classified on the basis of ATPase reactions following preincubation at alkaline (pH 10.38) or acid (pH 5.00). Four to seven intrafusal fibers in a muscle spindle, of which the number is equivalent to that of mammalian spindles, consist of slow and intermediate type fibers, without fast type fibers, in accordance with the definition of Smith & Ovalle (1972). Type T (trail) and type P (plate) end-plates were found around 500 and 750 μm, respectively, in the distance from the equator of spindles. The slow (thin) type intrafusal fibers appeared to be innervated preferably by type T end-plates.

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MECHANICAL RELATIONSHIPS BETWEEN RING- AND STRIP-SHAPED CORONARY ARTERIES.
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To examine the mechanical differences between ring- and strip-shaped vessels, adjacent canine coronary arteries were excised and mounted as a ring or as a transversal strip in an organ baths and connected to force-length transducers. For the static properties, active and passive length-tension relationships were studied by load steps followed by isometric activation of K^+ 125mM solution. Calculating mechanical conversion factors from ring- to strip-shaped vessels, least-square-error method was used. Length conversion factor was found as 1 if it is normalized to Lmax(length at maximal force development). The tension conversion factor from strip to ring was 1.6 (expected value is 2). For the dynamic properties, force-velocity relationship was determined by isotonic quick release 2 or 3 minutes after the onset of activation. The dynamic conversion factor from strip to ring at Vmax(unloaded shortening velocity) was 0.6 (expected value is 0.5).

Therefore these results showed that larger velocity and smaller force are required for ring-shaped vessels compared with strip-shaped vessels. This properties cannot be explained by the friction between wires of ring-shaped vessels.

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CALCIUM ACTIVATED SINGLE POTASSIUM CHANNEL OF CULTURED SMOOTH MUSCLE CELLS IN RAT AORTIC MEDIA.
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Electrical properties of Ca-activated K ($I_{K(Ca)}$) channel in primary cultured smooth muscle cells of the rat aorta were studied by patch-clamp method. In inside-out configuration with internal 142 mM-K, slope conductances were 69 ± 15, 86 ± 11 and 136 ± 5 (± S.E.) pS with 6.2, 20, 142 mM-K in the pipette near 0 mV, respectively. The E_r measured at pipette containing various K agreed well with E_K. Ionic permeability of K : Rb : Cs = Na was in the ratio 1 : 0.7 : <0.01. The channel opening was blocked by adding either external TEA (10-30 mM) or internal Ba (1-5 mM). The probability of channel opening (P_o) increased at $[Ca]_i$ over 10^{-7} M and further increased with depolarization in the presence of $[Ca]_i$. The channel activities were chracterized by burst-like openings. The probability density of the open time fitted well with an exponential distribution (time constant of 0.7 ms at -10 mV and 10^{-7} $[Ca]_i$), while that for the closed time was consisted of fast and slow components (the time constants of 0.6 and 154 ms, respectively). The slow component was decreased with either depolarization or increase of $[Ca]_i$. The results suggested that $I_{K(Ca)}$ channel was highly selective for K ion and that the activation depended on not only $[Ca]_i$ increase over 10^{-7} M but also membrane depolarization.

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TWO TYPES OF CA CHANNEL CURRENTS WITH DIFFERENT INACTIVATION KINETICS IN SMOOTH MUSCLE CELLS OF GUINEA-PIG TAENIA COLI.
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Ca channel currents were recorded in Cs-loaded cells in guinea-pig taenia coli smooth muscle using whole-cell clamp technique. Two types of Ca channel currents were observed with 1.8 mM Ca outside:one type inactivated rapidly and another inactivated relatively slowly. Most cells had both rapidly and slowly inactivating components. In these cells, both component could be separated by holding potential (h.p.):the rapidly inactivating component was abolished when the h.p. was set to -30 mV while the slowly one was still remained. Both components could also be separated pharmacologically:the slow component was inhibited by 0.2 μM nifedipine while the fast one was unaffected. The double pulse experiment showed that inactivation of the fast component was mediated by both voltage and current dependent processes while the slow one was purely voltage dependent process. These results suggest that there exsist two types of Ca channels having different inactivation process and dihydropyridine sensitivity.

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CALCIUM MOBILIZATION AND PHOSPHATIDYLINOSITOL TURNOVER IN SMOOTH MUSCLE OF DIABETIC RATS. SAKAI, Y., HONDA, H.* and AIHARA, K.* Dept. of Physiol, Showa Univ. Sch. of Med., Tokyo 142

We have already reported hyperactive responses of vasa deferentia smooth muscle isolated from 6-week streptozotocin(STZ)-treated rats to various agonists (Jpn. J. Smooth Muscle Res. 22,1986). In this study, voltage-dependent Ca channel and receptor-operated Ca channel mediating hyperactivity in STZ-treated diabetic rats, as well as their mediatory responses, such as Ca influx and phosphatidylinositol(PI) turnover was investigated. Strips from diabetics had greater Ca influx induced by 20mM KCl than controls. But no difference was seen in Ca influx increase induced by 10^{-5}M norepinephrine(NE) between diabetics and controls. 10^{-5}M NE increased the accumulation of [^{3}H]inositol phosphates by 3-fold in controls and 7-fold in diabetics. This increase was completely inhibited by 10^{-6}M prazosin but not by 10^{-6}M yohimbine. 10^{-5}M NE also increased the incorporation of [^{3}H]myo-inositol into lipids. There was no difference in the increase between diabetics and controls. Increased incorporation was completely inhibited by 10^{-6}M prazosin but not by 10^{-6}M yohimbine in both groups. These data suggest that vasa deferentia smooth muscle hyperactivity in diabetics is due to increse in Ca influx through voltage-dependent and receptor-operated channels and to increase in PI turnover mediated by α1-adrenoceptor.

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ACTIONS OF BETA ADRENERGIC AGONISTS ON IONIC CURRENTS OF THE GUINEA-PIG TAENIA COLI IN TEA MEDIUM. INOMATA, H. Sch. Med., Tohoku Univ.,Sendai 980

The beta actions on the smooth muscle of the guinea-pig taenia coli was studied by observing the effects of dibutyryl cyclic AMP (DBcAMP) (1.5 x 10^{-4} g/ml). DBcAMP hastens the rising phase of the action potential, decreases its amplitude without detectable change in the resting potential in a Na^+-free tetraethylammonium (TEA) medium. The underlying ionic mechanisms have been analyzed in voltage-clamped preparations. On calcium currents (I_{Ca}), DBcAMP reduces the maximum current and shifts the reversal potential to less positive voltage. The slope conductance is increased appreciably in voltage up to the maximum I_{Ca}, while the maximum conductance is not affected. The activation of the I_{Ca} is hastened slightly, but the inactivation is not changed. On I_b, the steady state outward current due to potassium ions, DBcAMP does not alter the reversal potential or the slope and maximum conductances. As a result, it may be suggested that a reduction in Ca influx during exposure to DBcAMP might be due to decreased driving force for Ca ions resulting from excessive intracellular accumulation by lowering a Ca extrusion pump induced by DBcAMP with less Na-Ca exchange in the Na^+-free solution.

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ON THE PROPERTIES OF AFTER RESPONSE IN THE CIRCULAR SMOOTH MUSCLE OF GUINEA-PIG VAS DEFERENS. FUKUSHI, Y. AND WAKUI, M. Sch. Med. Tohoku Univ., Sendai 980

Field stimulation of the circular smooth muscle of the guinea-pig vas deferens produces a contraction consisting of three phases: initial and second phases during the stimulation, and the third phase (after-response) after cessation of stimulation. For stimulation with a variety of duration used, the magnitude of the initial phase was roughly constant. The peak magnitude of the second phase increased with increasing stimulation length. On the other hand, the magnitude of after-response was dependent on stimulation length up to 10 sec, whilst it was smaller for stimulation longer than 10 sec with smaller contraction at the end of stimulation. TTX, atropine or prazosin added to the bath immediately after cessation of stimulation, did not affect the after-response. Cobalt ions or a Ca^{2+} -free solution, employed to the bath at the termination of the stimulation, strongly reduced the after-response.

In conclusion, the after-response may be myogenic in origin, which is probably induced by the re-excitation of the smooth muscle membrane with Ca^{2+} -spikes in the process of recovery of the preceding excitation (second phase).

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ON THE IONIC MECHANISM OF ATP-INDUCED DEPOLARIZATION OF SMOOTH MUSCLE OF GUINEA-PIG VAS DEFERENS. WAKUI, M., FUKUSHI, Y. AND NAKAI, Y.* Dept. Appl. Physiol., Sch. Med., Tohoku Univ., Sendai 980

On smooth muscle of guinea-pig vas deferens, the double sucrose-gap method was used to investigate the ionic mechanism of ATP-induced depolarization of which reversal potential was already proposed to be about 27 mV positive to the resting membrane potential by the method used. In a Ca-free medium, the membrane was depolarized and ATP further depolarized the membrane. The reversal potential of ATP depolarization in the medium was quite similar to that in the control medium. This suggests that a Ca conductance change is not involved in the ATP depolarization. In a Cl-deficient medium, the membrane conductance was decreased and excitability of the membrane, increased. In the medium, ATP induced a depolarization of which reversal potential was about 10 mV positive to the expected membrane potential in the given medium. In a Na-free medium, the membrane conductance was increased. In the medium, ATP still induced a depolarization associated with an increase in membrane conductance, but the size of depolarization was very small. Since the change in external ionic composition including Na and Cl provides a large change in liquid junction potential, the change in membrane potential by either Cl-deficient or Na-free environments is not clear in this study. However, the results may suggest that Na conductance change is the best candidate for ATP depolarization.

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RESPONSES OF ISOLATED MONKEY IRIS TO BIOLOGICAL ACTIVE SUBSTANCES. FUKUNAGA, H.*, OHHASHI, T.** AND SAKAGUCHI, M.*** Dept. *Ophtalmol. and **Physiol., Shinshu Univ. Sch. Med., Matsumoto 390 and ***Dept. Elect. Eng. Nagano Tech. Coll. Nagano 380

Responses of isolated monkey irides to biological active substances were investigated in vitro. Changes in the pupil area were measured by means of a domestic-made area measuring gauge utilizing an area image sensor. Adrenaline (AD), noradrenaline (NA), dopamine and histamine produced dose-dependent increase in the pupil area (mydriasis). The decreasing order of the responses was as follows: AD>NA>dopamine>histamine. The threshold concentration for the AD-induced mydriasis was about 3×10^{-9}M. On the other hand, prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), 5-hydroxytryptamine (5-HT), acetylcholine (ACh), ATP, ADP, AMP and adenosine caused dose-dependent decreases in the pupil area (miosis). The decreasing order of the responses was as follows: $PGF_{2\alpha}$>5-HT>ACh>ATP>ADP>adenosine>AMP. The threshold concentration for the $PGF_{2\alpha}$-induced miosis was about 10^{-9}M. We also studied the effects of the substances on the punched irides in which the pupillary sphincter muscles were removed by means of an ophthalmic trepan after an addition of 10^{-3}M acetylcholine. On the contrary, 5-HT and ACh caused a dose-dependent increase of the pupil area in the punched preparations. We have also discussed cooperational roles of the sphincter muscles and dilator muscles in the regulation of pupil area.

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LACK OF EQUILIBRIUM BETWEEN PHOSPHOCREATINE (PCr) AND ATP IN SMOOTH MUSCLES DURING HYPOXIA AND REOXYGENATION. Yukisato Ishida, Michio Hashimoto and Richard J. Paul* Mitsubishi-Kasei Inst. of Life Sci., Machida, Tokyo 194, Japan and Dept. of Physiol., Coll. of Med., Univ. of Cincinnati, Cincinnati, OH 45267-0576, USA.

Guinea pig taenia caeci contained 2.2μmol/g PCr and 1.1μmol/g ATP in the presence of 45.4mM KCl (high-K) under aerobic conditions. When the taenia caeci were exposed to hypoxic conditions (95% N_2,5% CO_2 bubbling instead of 95% O_2) in the presence of high-K PCr rapidly decreased concomitant with a parallel decrease in tension. However, ATP content did not significantly decrease during the relaxation phase and decreased by half. After the muscle was equlibrated under hypoxia, increasing media glucose increased ATP content but did not increase PCr significantly. When oxygen was readmitted after hypoxia, PCr rapidly increased beyond normal levels. ATP increased gradually and attained 75% of normal levels after the reoxygenation. In the hog coronary artery, hypoxic conditions and increasing media glucose in the presence of high-K under hypoxia did not alter PCr and ATP contents (0.2μmol/g for both PCr and ATP in control). These results suggest that PCr and ATP in the cell of the taenia do not distribute in a simple Lohmann reaction equilibrium. PCr production of the taenia is dependent on the oxidative metabolism, presumably through the "mitochondrial PCr shuttle." In the hog coronary artery, evidence for the line of PCr production to oxidative metabolism is obscure.

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THA ROLE OF ENDOTHELIUM IN THE CONTRACTILE RESPONSE TO CLONIDINE IN STRIPS OF MESENTERIC ARTERIES ISOLATED FROM SPONTANEOUSLY HYPERTENSIVE RATS. KOJIMA, M., ASANO, M., MASUZAWA, K.*, MATSUDA, T.* AND AOKI, K.*+ Dept. Pharmacol. and 2nd Dept. Int. Med.+, Nagoya City Univ. Med. Sch., Nagoya 467

In strips of mesenteric arteries isolated from 13-week-old spontaneously hypertensive rats (SHR), clonidine (Clo), norepinephrine (NE) and phenylephrine (PE) induced a contraction by acting on α_1-adrenoceptors (α_1-Rs). Contractile responses to Clo were more markedly enhanced than those to NE and PE by removal of the endothelium. When the strips with endothelium were contracted with PE, Clo induced a relaxation in many cases, but induced a contraction in a few cases, whereas, acetylcholine (Ach) induced a relaxation in all cases. After removal of the endothelium, Clo-induced relaxation was partialy inhibited, whereas, Ach-induced relaxation was disappeared. When the strips were contracted with either prostaglandin$F_{2\alpha}$ or 5-hydroxytryptamine, Clo induced only a contraction even in the presence of endothelium. Contractile responses to PE were competitively antagonized by Clo. These results suggest that Clo has at least three pharmacological actions in the SHR mesenteric artery; (1) the contractile effect by acting on α_1-Rs of arterial smooth muscle, (2) the antagonism of α_1-Rs, and (3) the relaxing effect through the release of relaxing factor by acting on endothelial α-Rs. It is likely that the final response is expressed as a combination of the three actions.

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FUNCTIONAL ALTERATION OF THE VOLTAGE-DEPENDENT CALCIUM CHANNELS IN FEMORAL ARTERIS OF SPONTANEOUSLY HYPERTENSIVE RATS. ASANO, M., MATSUDA, T.* AND AOKI, K.*+ Dept. Pharmacol. and 2nd Dept. Int. Med.+, Nagoya City Univ. Med. Sch., Nagoya 467

Vasoconstrictor effects of Bay k 8644, a dihydropyridine calcium (Ca^{2+}) channel agonist and vasorelaxant effects of nifedipine were compared between the femoral arteries isolated from 6-week-old spontaneously hypertensive rats (SHR), animals that are in an early stage of hypertension, and age-matched normotensive Wistar-Kyoto rats (WKY). Bay k 8644 elicited a dose-dependent contraction in SHR arteries with a pD_2 value of 8.55. The maximum contraction induced by this agonist was comparable to the maximum developed by KCl (K^+)-depolarization. Bay k 8644 was less effective in eliciting a contraction in WKY arteries. Increased sensitivity to K^+ was also observed in SHR arteries. An elevation in the concentration of extracellular K^+ eliminated the difference between the responses to Bay k 8644 in the SHR and WKY arteries. SHR arteries, but not WKY arteries, relaxed when placed in a Ca^{2+}-free solution. The addition of nifedipine to an unstimulated strip produced a dose-dependent relaxation in femoral arteries of SHR, but not of WKY. When the arteries were contracted by 60 mM K^+, nifedipine produced similar relaxations in both strains. These results suggest that the voltage-dependent Ca^{2+} channels in SHR femoral arteries are more activated than those in WKY femoral arteries.

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Ca-INDUCED Ca RELEASE MECHANSIM IN INTACT VASCULAR SMOOTH MUSCLE AS EVIDENCED BY THE ACTION OF RYANODINE. ITO, K. Dept. of Veterinary Pharmacology, Fac. of Agriculture, Miyazaki Univ., Miyazaki 889-21

Ryanodine inhibits the release of Ca from intracellular stores without affecting the transmembrane Ca influx in guinea-pig aortic smooth muscle (Circ. Res. 58, 370, 1986). It suppressed the contraction induced by Ca at below 1 mM in K-depolarized aorta. To assess whether transmembrane Ca influx can release the stored Ca the action of ryanodine on Ca-induced contraction of aorta depolarized by isotonic K was analyzed. 1) When the intracellular store was preloaded with Ca, 0.1 mM Ca induced a faster and greater contraction than in the muscle of which store had been depleted of Ca. Ryanodine (30 μM) exhibited a greater inhibition on the Ca-loaded muscle. Ryanodine did not affect the ^{45}Ca uptake in both muscles. 2) Low temperature (27° C) or Mg^{2+} removal enhanced the contraction due to 0.1 mM Ca, while the former suppressed or the latter did not affect the contraction due to 5 mM Ca. 3) When the Ca influx was augmented by CGP 28392 or decreased by nifedipine, verapamil or Cd^{2+}, the inhibitory potency of ryanodine was decreased or enhanced, respectively. 4) The inhibitory potency of ryanodine on Ca-contraction was inversely correlated with either the concentration of Ca added or ^{45}Ca uptake. The data suggest that when the Ca influx is small the Ca-induced Ca release mechanism operates in a contraction but when the influx is too much the mechanism does not operate.

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Single voltage-dependent chloride channel and its ion selectivity in cultured smooth muscle cells of rat aorta. KOKUBUN,S., SOEJIMA,M*, II Dept of Physiol., II Dept of Int. Med*, Jikei Univ. Sch. Med., 3-25-8 Nishi-shinbashi, Minato-ku, Tokyo, 105

It has been suggested that large Cl conductance plays an important role in membrane excitability in vascular smooth muscle cells. In this study we describe the properties of voltage-gated Cl channel in the plasma membrane of cultured smooth muscle cells prepared from embryonic rat aorta. The channel activity was barely observed in the cell-attached manner. In the exercised patch, however, we frequently observed channel openings. The channel is selective to anions over cations, and has a large single-channel conductance of ~340 pS in symmetrical 150 mM TEA-Cl. The channel is active at around 0 mV. The shift of the membrane potential to either positive or negative direction closes the channel to an apparent inactivated state. The permeability sequence of halides was F<Cl<Br<I, whereas the conductance sequence was Cl>Br>F>I. The internal dimensions of the channel was estimated by measuring the permeability of various anions with different size of molecular cross section. We showed the smallest cross section of the channel pore was about 33 $Å^2$.

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ABNORMAL FUNCTION OF THE β-ADRENOCEPTOR·ADENYLATE CYCLASE SYSTEM IN FEMORAL ARTERIES OF SPONTANEOUSLY HYPERTENSIVE RATS. MASUZAWA, K.*, ASANO, M., MATSUDA, T.* AND AOKI, K.*+ Dept. Pharmacol. and 2nd Dept. Int. Med.+, Nagoya City Univ. Med. Sch., Nagoya 467

Vascular relaxing responses to β-adrenoceptor (β-R) agonists are decreased in spontaneously hypertensive rats (SHR) when compared with normotensive Wistar-Kyoto rats (WKY). To determine the possibility that the abnormality in cyclic AMP metabolism is involved in this decreased β-R function, effects of several drugs which interact with the β-R·adenylate cyclase (AC) system on the contractile responses to norepinephrine (NE) were compared between the femoral arteries isolated from 13-week-old SHR and age-matched WKY. In the absence of timolol, a β-R antagonist, contractile responses to NE were significantly greater in SHR than in WKY. Timolol augmented the contractile responses to NE to a greater extent in WKY than in SHR. After the blockade of β-Rs by timolol, contractile responses to NE were not significantly different between the SHR and WKY. Cholera toxin, an activator of stimulatory GTP-binding protein of AC (Gs), inhibited the contractile responses to NE (+timolol) much greater in WKY than in SHR. Forskolin, an activator of AC, and dibutyryl cyclic AMP also inhibited the contractile responses to NE (+timolol). However, these inhibitions were not significantly different between the SHR and WKY. These results suggest that the reduced function of Gs is mainly involved in the abnormality of β-R·AC system seen in the SHR femoral arteries.

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THEORETICAL STUDY ON PRESSURE-VOLUME RELATION OF UTERINE CERVIX. KAWANO, K., MATSUDA, H. AND SHINAGAWA, Y. INFORMATION PROC. CENTER OF MED. SCI., NIPPON MEDICAL SCHOOL, SENDAGI, BUNKYO-KU, TOKYO 113

One of bicornis of the rat uterine was cut from the cervix on the middle stage of pregnancy. Effects of the large contraction during the terminal stage for the ripening of cervix were examined (previously reported[1)2)]). The volume of Kreb's solution, V(μℓ), which was injected in the cervix lumen by mycrometer-syringe and the inner pressure, P(mmHg), are represented as the following differential equation; $dV/dP = \Sigma(a_n/(P+d)^n)+c$. When the solution is injected, n=1 i.e. $V=a_1\log(P+d)+cP+K$; while dejected, n=2, $V=a_1\log(P+d)+a_2/(P+d)+cP+K$, where, a_1, a_2, c, K and d are tentatively named as elastic volume, dissipative coefficient, linear compliance, initial volume factor and hysteretic pressure constant, respectively. By means of nonlinear least squares method, each parameter was calculated by a personal computer. The grade of ripening of cervix is represented by the value of a_1(=8.80±1.35 at separated side cervix; 12.1±1.50 at non-separated side(16 examples)); the difference is significant ($p<0.01$).

1),2) Acta Obst. Gynaec. Jpn.(Kanagawa) 19 (1983), id. 21 (1984)

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VOLTAGE-CURRENT CHARACTERISTICS OF THE SINGLE Ca-ACTIVATED K CHANNEL IN THE GUINEA-PIG TAENIA CAECI. TOKUNO, H., TOMITA, T. AND KIHIRA, M.* Dept. Physiol. and Dept. Obst. Gynaecol.*, Sch. Med., Nagoya Univ., Nagoya 466

Ionic channels in the plasma membrane activated by low concentrations of Ca (0.01-1 μM) at a cytoplasmic side were found in the smooth muscle cells obtained from the guinea-pig taenia caeci. This channel was highly selective to K ions and has a high open-state conductance of about 200 pS in symmetrical 144 mM K medium (35°C). The amplitude of inward currents recorded in the inside-out membrane patch at 144 mM K outside and 6 mM K (138 mM Na) inside was dependent on the membrane potential and this relationship agreed well with the Goldman's constant field theory with a K permeability constant of about 4.5×10^{-13} cm/sec. When internal Na concentrations were reduced by replacing with sucrose, choline or TEA, keeping the K concentrations constant, the voltage-current relationship was modified depending on the substitute, but the reversal potential remained the same at 84 mV. The results can be explained by alteration of the membrane surface charge.

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EFFECTS OF Mg-FREE SOLUTION ON THE TAENIA OF GUINEA-PIG CAECUM. NAKAYAMA, S., CHIHARA, S., TOMITA, T., SEO, Y.* AND WATARI, H.* Dept. Physiol., Sch. Med., Nagoya Univ., Nagoya 466 and Natl. Inst. Physiol. Sci.*, Okazaki 444

The intracellular concentration of free Mg ions ($[Mg]_i$) was estimated from the chemical shift of a β-peak of ATP using the ^{31}P-NMR. In the taenia dissected from the guinea-pig caecum, $[Mg]_i$ was 0.29 mM (n = 14) at 32°C. This concentration remained the same in Mg-free solution for more than 100 min. When both Mg and Ca were removed and 1 mM EDTA was added, however, $[Mg]_i$ was gradually reduced to 6.3 μM (n = 5) in 100 min and recovered to the initial level in 50 min by readmitting Mg (1.2 mM). In Ca-free solution, the rate of oxygen consumption of the tissue was 0.33 μmoles/min/g wet weight and increased to 0.60 by an additional removal of Mg (n = 8). This increase was readily abolished by ouabain and not observed in a low (20 mM) Na solution. These results suggest that removal of both Ca and Mg increases the membrane permeability to Na as well as Mg, and that this leads to an increase in $[Na]_i$, which in turn stimulates the Na-pump, and a decrease in $[Mg]_i$.

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EFFECTS OF Mg-REMOVAL ON THE CARBACHOL-INDUCED CONTRACTION. UNO, Y., NAKAYAMA, S. AND TOMITA, T. Dept. Physiol., Sch. Med., Nagoya Univ., Nagoya 466

In the circular muscle of guinea-pig stomach, carbachol-induced contraction was markedly reduced by removing external Ca, but a small tonic contraction could be repeatedly produced without decay for more than 50 hrs in Ca-free solution containing 2 mM EGTA. Removal of Mg, in the presence of Ca, produced only a weak reduction of the response. On the other hand, when Mg was omitted from Ca-free solution, the carbachol-contraction was slowly reduced to less than 20% of the control in the presence of Mg (1.2 mM) within 2 hrs. The rate of decrease in response was roughly in parallel with that of intracellular free Mg concentrations separately estimated from the chemical shift of ATP measured with ^{31}P-NMR. The response to carbachol was recovered by readmission of either Mg or Ca. The Mg-dependent contraction was more resistant to agents which antagonize calmodulin than the Ca-dependent contraction of a similar size. The results suggest that a Ca-independent (Mg-dependent) component is partly involved in the carbachol response.

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COMPARATIVE STUDIES ON Ca-ACTIVATED K CHANNELS IN THE GUINEA-PIG TAENIA CAECI AND RAT MYOMETRIUM. KIHIRA, M., TOKUNO, H. AND TOMITA, T. Dept. Obst. Gynaecol. and Dept. Physiol., Sch. Med., Nagoya Univ., Nagoya 466

In the inside-out patch membrane, the threshold concentration of internal Ca for activation of the K-channel was slightly lower in the guinea-pig taenia than in the non-pregnant rat myometrium, but the fraction of time spent in the open state was much more steeply increased with increasing Ca concentrations in myometrium than in taenia. The single channel conductance was 199.8 ± 18.1 pS in taenia and 170.1 ± 24.7 pS in myometrium in symmetrical 144 mM K media at 35°C (n = 12). When the distribution of open and closed times of single channel activity was analysed, no clear difference in the kinetics was found between these tissues. Using electrodes of a similar size (about 1 μm in diameter), the average number of channels contained in a patch activated in the presence of 1 μM Ca was 3.6 and 2.1 in taenia and myometrium, respectively. The Ca-activated K channels seems to have stonger effects on the electrical activity of the taenia than the myometrium under the physiological condition.

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EFFECTS OF VERAPAMIL ON K- AND CARBACHOL-INDUCED CONTRACTION IN THE GUINEA-PIG TRACHEAL MUSCLE. GONDA, H. AND TOMITA, T. The 2nd Dept. Int. Med. and Dept. Physiol., Sch. Med., Nagoya Univ. Nagoya 466

In the guinea-pig tracheal muscle, verapamil was very potent in inhibiting the contraction induced by excess K compared with that induced by carbachol in the presence of 2.4 mM Ca. When the Ca concentration was reduced, however, the carbachol-induced contraction became very susceptible to verapamil. When the concentration-tension curve of Ca was studied in the presence of 40 mM K or carbachol (0.03-1 μM), the ED_{50} was much lower in the presence of carbachol than in high K solution containing no carbachol, and the Hill number of the curve was increased from 1.4 to 2.0 as the carbachol concentration was increased, independent of K concentrations. The dissociation constant of verapamil, calculated from the shift of Ca-tension curve and the change in Hill number, was the same with and without carbachol. The results suggest that carbachol increases the affinity of the channel to Ca (but not to verapamil), rather than activating receptor-operated Ca-channels separately, and that this produces an apparent reduction in the potency of verapamil.

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Changes of muscle protein components in disused atrophied muscle (2) Effects of stretching and denervation. ATOMI, Y., YAMADA, S., HATTA, H., YAMAMOTO, Y., SHINOHARA, S. Uni. Tokyo, Komaba, Meguroku, Tokyo 153

Muscle atrophy induced by tail suspension in rats specifically decreased 24 kilo dalton (24K) protein in soluble fraction of soleus muscle. This protein is rich in soleus muscle but not EDL or plantaris muscle. The effects of denervation and stretch on 24K protein component were investigated for 3 groups of control (C), suspension (S) and suspension with scietic nerve denervation (DS) treatment. In all rats of S and DS one leg was fixed in dorsiflexed and the other in plantarflexed conditions. Denervation detriorated the atrophy in all muscles of hindlimb, especially in soleus muscle. Stretched muscles decreased the atrophy induced by suspension, however, and maintained 24K protein in soleus muscle and increased it in EDL muscle, with and without denervation. From these results, possible functional relationship between 24k protein and stretching was suggested.

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PURIFICATION AND PROPERTIES OF ALKALINE PROTEASE IN MURINE MUSCULAR DYSTROPHY, C57BL/10-mdx. KUSUMOTO, S., DOI, Y., SAWADA, H. AND TSUJI, S. Dept. Physiol., Wakayama Medical College, 9-bancho, Wakayama-shi, Wakayama 640

An alkaline protease was purified from hind-limb muscle in the mouse of C57BL/10-mdx strain, a murine muscular dystrophy, on Phenyl-Sepharose and Lima bean trypsin inhibitor-Sepharose. Molecular weight was estimated as 25000 by gel filtration on Sephacryl S-300 and polyacrylamide gel electrophoresis in the presence of sodium dodecyl sulfate.
The isoelectric point was estimated as 7.7. The purified enzyme had a pH optimum between 8.0 and 9.5. The enzyme was inhibited by diisopropyl fluorophosphate, phenylmethylsulfonyl fluoride, chymostatin, soybean trypsin inhibitor, lima bean trypsin inhibitor and tosylphenylalanine chloromethyl ketone, suggesting that it is a chymotrypsin-like serine protease. This result indicates that the biochemical properties of this purified enzyme resemble that of chymase which had been reported in mast cell granules. On the purification procedure, we found a potent inhibitor(s) containing in unabsorbed fractions to Lima bean trypsin inhibitor-Sepharose.

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TWITCH POTENTIATION OF SKELETAL MUSCLE BY ANTIPYRINE. FUJISHIRO, N., KAWATA, H. Dept. Physiol., Fukuoka Univ., Sch. Med., Fukuoka 814-01

The effects of antipyrine were studied on isolated single muscle fibres of the frog Rana japonica. Antipyrine potentiated the twitch amplitude without significantly affecting the tetanus response and inducing any contracture by itself. Both the time to peak tension and half time for relaxation of twitch increased at 5 mM antipyrine. Antipyrine produced no change of resting membrane potential at 5mM. At this concentration, the maximum rate of decay of action potential fell so that its duration at -50 mV was prolonged. The mechanical threshold was determined by measuring the contracture response by various concentrations of potassium. The threshold was not affected by antipyrine. Verapamil and nifedipine did not affect on the twitch potentiation by antipyrine. It is concluded that antipyrine potentiates the twitch response by increasing the release of Ca from sarcoplasmic reticulum by prolongation of the action potential.

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ACTIVATING MECHANISM OF CONTRACTURES IN INSECT SKELETAL MUSCLE.
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To clarify the activating mechanism of contractures in insect skeletal muscle, $4X10^{-4}$ M L-glutamate- and 100 mM potassium-induced contractures were examined in the retractor unguis muscle of the cockroach in the presence of 10mM Mn, 1mM procaine and 1μM nifedipine. Manganese ions reduced L-glutamate contracture by about 73% while they reduced potassium contracture by about half. Procaine reduced L-glutamate contracture only by 12% while it reduced potassium contracture by half. 5min pretreatment of nifedipine reduced potassium contracture only by 10% while 10 min pretreatment of the drug reduced it to 34%.Recovery from 5 min pretreatment was conspicuous and contracture increased to almost twice of the control in about 1 hour after washing out of the drug. L-glutamate contractures were reduced by half with both 5 and 10 min's pretreatments of nifedipine. The recovery from the drug was small. These results may suggest that there are different processes of utilizing Ca ions through which contractures are induced by L-glutamate and potassium,respectively.

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INFLUENCE OF PICROTOXIN ON BIREFRINGENCE SIGNAL AND TWITCH TENSION IN SINGLE FROG SKELETAL MUSCLE FIBRES.
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The early large birefringence signal, BS, (Baylor and Oetliker, J. Physiol. 1977) was suggested to reflect dynamic changes in myoplasmic calcium concentration (Oetliker, J. Physiol. 1980). In single skeletal muscle fibres of Rana temporaria, picrotoxin (5 mM in Hepes Ringer) increased twitch tension by a factor of 1.5 to 1.8 while it increased twitch duration (measured at half maximal tension) by a factor of about 2. The amplitude of the BS was increased by a factor of up to 3.5 when fibres were singly stimulated at intervals of 2 min. When fibres were stimulated with trains of eight pulses at 2 Hz the effect on relaxation was progressive. The tension changes and the changes in the amplitude of the optical could be reversed by prolonged soaking in normal Ringer. The fact that the early large birefringence signal is increased in amplitude already 8 ms after stimulation and before any changes in the rising phase of the tension record can be seen as compared with controls suggests that the twitch potentiation by picrotoxin involves an increased release of calcium in addition to other possible actions.

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ON THE INFLUENCE OF INTRACELLULAR Mn^{2+} INJECTED ON THE MECHANICAL THRESHOLD OF FROG SKELETAL MUSCLE FIBRES.
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It was undertaken to examine some influences of Mn^{2+} injected into muscle fibres on the mechanical threshold by one-point voltage clamp method similar to that reported by Costantin in 1968. With respect to the intracellular microinjection of salt solutions,ultrapure water obtained by Milli Q II system (Millipore Co.) is of great use,but it is still necessary to remove Ca^{2+} due to impurities of $MnCl_2$ crystal from the salt solutions containing Mn. The author reported a method of microinjection driven by gas pressure. The tip of glas micropipette was abraised until the electrical resistance of micropipette filled with 3M KCl was decreased to 10 megohms. Microinjection was driven by gas pressure of 7 Kg per square centimeter with such abraised micropipettes. The microinjection was controlled by two solenoid valves connected each other with a suitable minipower relay.

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A ROLE OF CALCIUM CURRENTS IN EXCITATION-CONTRACTION COUPLING DURING POTASSIUM CONTRACTURES IN FROG SINGLE TWITCH MUSCLE FIBERS.
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In intact single twitch muscle fibers of the frog, a monophasic contracture was induced with an 80 mM K^+ solution containing a physiological concentration of Ca^{++}, when the conditions were such that only Ca ions carry current through the muscle fiber membrane. The amplitude of this K contracture tension depended on the concentrations of K^+ and Ca^{++} in the external solutions. Its peak tension was only slightly affected by 1 - 5 μM dantrolene (DAN) [DAN-resistant phase], while the rate of rise and the early part of the area under the tension curve were markedly reduced by DAN [DAN-sensitive phase]. The tension of the DAN-resistant phase was completely inhibited by lowering external Ca^{++} and greatly reduced by Ca^{++} channel blockers (0.5 - 2 μM nifedipine, 1 - 50 μM verapamil, 1 μM nicardipine, 1 mM Cd^{++}, 5 mM Co^{++} and 1 mM Ni^{++}), whereas it was potentiated by the Ca^{++} channel activator (0.5 - 2 μM Bay K 8644). These results clearly indicate that in frog twitch fibers K contracture can be produced under such conditions that only Ca^{++} is the carrier of current, and that contracture consists of a DAN-sensitive phase and a DAN-resistant phase. In addition, these results suggest that the DAN-resistant phase is clearly correlated with Ca^{++} currents flowing through dihydropyridine sensitive and voltage dependent Ca^{++} channels.

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EFFECT OF ADDITIONAL TN-I ON THE TENSION DEVELOPMENT OF GLYCERINATED FIBER IN SKELETAL MUSCLE.
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It was examined the effect of additional TN-I on the tension development of glycerinated fiber in skeletal muscle. After treatment with TN-I for 24 h at 0°C under a buffer A solution (120 mM KCl, 2 mM $MgCl_2$, 4 mM EGTA and 20 mM Tris-maleate pH 6.8), the treated fiber depressed the latent period, the rate of rise and maximum tension development in contraction at keeping the Ca^{2+}-dependent regulation. At this time, the peptides having 26 K and 28 K daltons were found on SDS-PAGE patterns from the buffer A solution after treatment of the fiber with TN-I. But, these peptides could not be found at the treatment of the fiber together with TN-I and -T. On the other hand, 26 K and 28 K peptides were also observed from the reaction mixture of myosin or heavy meromyosin with TN-I. These facts indicate that these peptides isolated from myosin head by a proteolytic action of TN-I, which was completely inactivated with TN-T.

From these results, it was suggested that TN-I treated fiber depressed the latent period, the rate of rise and the tension development in muscle contraction according to the damage of some myosin heads on the thick filaments in contractile unit.

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MECHANISM OF REFRACTORINESS OF SKELETAL MUSCLE SARCOPLASMIC RETICULUM TO REPEATED ADDITION OF CAFFEINE.
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Caffeine induced Ca^{2+} release from Ca^{2+}-loaded sarcoplasmic reticulum (SR) isolated from frog skeletal muscle. The Ca^{2+} released was almost completely taken up again. However, repeated addition of caffeine hardly induced Ca^{2+} release from the SR. The SR was layered on a discontinuous sucrose density gradient, and centrifugated at 90.000 x g for 30 min. After centrifugation, a main band was observed at 40-42.5%(W/V) boundary, irrespective of Ca^{2+}-loading. When Ca^{2+}-loaded SR to which caffeine had been added was applied on the centrifugal analysis, two main bands were found at 40-42.5% and 42.5-45% boundaries, while if A23187 was added with caffeine, only 40-42.5% band was found. A new band at 42.5-45% is probably due to the increase of the amount of Ca^{2+} in the SR. These results suggest that there is an SR population which takes up more Ca^{2+} after the addition of caffeine. The refractoriness of the isolated SR to the repeated addition of caffeine may be explained by the reuptake of the Ca^{2+} released from caffeine-sensitive SR by caffeine-insensitive SR.

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EFFECTS OF DANTROLENE AND TETRACAINE ON TWITCH AND SILVER ION-INDUCED TENSION IN FROG SKELETAL MUSCLE. OBA,T. AND HOTTA,K. Dept.Physiol.,Nagoya City Univ.Med.Sch.,Nagoya 467

Dantorolene sodium and tetracaine are known to block the twitch tension. The probable site of actions of these drugs is located on the T/SR junction. In frog skeletal muscle, we found that chemical binding of Ag to proteins on the T membrane produced an irreversible transient contracture (Ag contracture). Therefore, effects of dantrolene and tetracaine on the tension induced by electrical stimulation or Ag were compared in single fibers. One μM dantrolene inhibits the twitch tension to 62% of controls (38% inhibition). Increase in concentrations of dantrolene to 2,5 or 10 μM led to 45,48 or 50% inhibition. Action of dantrolene on the Ag contracture was much the same as that on the twitch tension (37,44,45 or 41% inhibition in 1,2,5 or 10 μM dantrolene, respectively). On the other hand, effect of tetracaine on the Ag contracture was quiet different from that on the twitch. Tetracaine in a range of 20 to 200 μM inhibited dose-dependently the Ag contracture, while the twitch tension was completely blocked, even in the presence of 20 μM. The difference is probably due to the blockade of Na channel by tetracaine, as evidenced by no occurrence of action potential in the presence of tetracaine in all doses used. These results suggest that Ag produces the contracture via the site(s) underlying the development of twitch tension.

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ASYMMETRICAL A-BAND ORGANIZATION DURING CAFFEINE CONTRACTURE AS REVEALED BY HIGH VOLTAGE ELECTRON MICROSCOPE (HVEM). YOSHIOKA,T., TAMAKI,T., TAKEKURA,H. AND NAKANO,S., Dept. of Physiol., Tokai Univ. Sch. of Med., Isehara, Kanagawa 259-11, Japan

The asymmetrical A-band organization in the sarcomere during 5mM caffeine contractures was studied. The frog skeletal muscles were incubated in caffeine solution for 5 min, and chemically fixed, and were taken to wash several times with K-dichromate and silver nitrate solutions (Golgi procedure). The stereo pairs of micrographs were made in the HVEM (tilt; 16°, accelerating voltage; 1,000 kV) from the thick sections. The "staining" is variable. The precipitates can be seen in the T-tubules, but not in whole fiber. The sarcomere length and organization could be recognized from the images of the successive T-tubule running arround of the myofibril. The drift (shift) of A-band was obtained from the measuring of displacement of M-band in the upper and lower layers of myofibrils. The shift was very small in the resting fiber. The rate of shift was 2.4±1.39% (Mean±S.D., n=37) in the sarcomere which was adjusted to 2.5μm by measuring distances of Z- to Z-bands. In the muscle incubated with caffeine, the rate was 6.6±3.54% (n=54) and was significantly ($p<0.001$) larger than the control. The shift of A-band may produce a typical tension development which has several peaks before ending in a maintained plateau.

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FUNCTIONAL SIGNIFICANCE OF TRIADIC JUNCTION IN ACTIVATION OF CONTRACTILE MACHINERY OF SKELETAL MUSCLE FIBERS OF FROG, RANA JAPONICA. M. FUJINO, T. ARIMA, Y. SATO, K. SHINOHARA, K. HARANO*, K. TOKUNAGA*. 1. Dep. of Physiol., Natl. Def. Med. Coll., Tokorozawa.

1. Under the condition of immersion in Ringer at pH 9.0 containing several mM of NH_4Cl, which do not yet bring about an uncoupling of excitation contraction (E-C) coupling, stretching to about one hundred and several teen % rest length evokes an intense tension development of about 70% of tetanus tension (Po), which is accompanied by a remarkable morphological change in especially triadic junction. 2. Under the similar condition further containing 400mM glycerol, removal of glycerol evokes also an intense tension development to the above; in contrast, addition of 400mM glycerol cannot do any sign of the development. Conclusion: Triadic junction morphology has an functional relationship in activation of contractile machinery, suggesting that an essential part of triadic junction in E-C coupling is mechanical in nature.

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INHIBION OF EXCITATION CONTRACTION (E-C) COUPLING BY CONCANAVALIN A (CON A) IN SINGLE SKELETAL MUSCLE FIBERS OF FROG, RANA JAPONICA. M. FUJINO, T. ARIMA, K. SHINOHARA, K. HARANO*, K. TOKUNAGA*. 1. Dep. of Physiol., Natl. Def. Med. Coll., Tokorozawa.

1. Con A and succinyl Con A of several ten μM inhibits E-C coupling (shift of tension-K concentration-relation curve, increase of peak time). 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. Peak frequency of the binding sites with respect to width of feet moves depending on depolarization, duration of depolarization, and repolarization. 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 the structure changes depending on membrane potentials.

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TEMPERATURE DEPENDENCE OF NICARDIPINE ACTION ON EXCITATION-CONTRACTION COUPLING IN FROG TWITCH FIBERS. FUJINO, M. AND SATO, Y. 1st Dept. of Physiol., Natl. Def. Med. Coll., Tokorozawa 359.

A calcium channel blocker nicardipine evoked an intense excitation-contraction (E-C) uncoupling in the frog (Rana japonica) twitch fibers at low temperature: The treatment with 20-30 μM nicardipine at 5-6°C for about 30 min completely inhibited both twitch response and potassium (190K) contracture despite the retention of both normal action potential and caffeine (3 mM) contracture. By contrast, the treatment under similar condition at 25°C only evoked a reversible twitch potentiation. Temperature-dependence curves obtained from the date on the treatment with 20 μM nicardipine for 30 min at various temperatures consisted of a sigmoidal shape with half maximum inhibition at 15 °C for twitch and at 12°C for potassium contracture. When the fiber treated previously with 20 μM nicardipine at 26°C was cooled to 6°C, the uncoupling developed gradually in the normal Ringer without nicardipine. On rewarming, the fiber completely recoverd twitch responses. The results suggest that a nicardipine target protein (= calcium channel) at the transverse tubule membrane is a subsidiary for E-C coupling and takes a "deformation" state only on cooling. This deformation restricts the function of another key component responsible for E-C coupling.

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LATERAL ELASTIC PROPERTIES IN SKINNED FIBERS OF SKELETAL MUSCLE: EFFECTS OF IONIC STRENGTH AND MAGNESIUM ION. UMAZUME, Y. Dept. of Physiol., Sch. Med., Jikei Univ., Minatoku Tokyo 105

The 1,0 lattice spacing (d) of mechanically skinned fibers of frog semitendinosus muscle was measured at various osmotic pressure exhibited by polyvinylpyrrolidone K-30 (PVP). With increasing osmotic pressure in standard relaxing solution, d decreased steeply until a definite 'break point' was reached (at about 35 nm). From the geometrical consideration, it has been considered that there is contact of myosin heads with thin filaments at the break point. Although d in 0% PVP increased from 40 to 43 nm with increasing ionic strength from 0.06 to 0.2 M, the break point was not affected. The position of myosin head would be independent of ionic strength. The swelling may be due to the decrease in attractive force in M-line and/or lateral elastic elements. With increasing Mg ion from 1 to 30 mM, d did not decrease in 0% PVP but did by 10% in 6% PVP. This Mg effect in PVP was observed at d less than 35 nm. The myosin heads would move to the thick filament backbone with Mg ion. In 30 mM Mg containing rigor solution, d decreased from 38 to 36 nm even in 0% PVP.

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CHANGES IN CONTRACTILE PROPERTIES WITH SELECTIVE DIGESTION OF ELASTIC FILAMENT IN SKINNED FIBERS OF FROG MUSCLE.

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Changes in contractile properties during trypsin (0.25 μg/ml) treatment in mechanically skinned sigle fibers was examined. The resting tension was decreased by trypsin treatment but the stiffness of rigor fibers was not. Futhermore, SDS-PAGE (Yoshioka et al., 1986) and electronmicroscopic studies showed very little digestion of proteins other than α-connectin by the treatment. These results showed that an elastic filament, α-connectin, is selectively digested by the treatment. With progression of the digestion, isometric tension activated by calcium was reduced. The decay rate of isometric tension was less than that of the resting tension. Calcium ion sensitivity of active tension and maximum shortening speed did not change by digestion. These results suggest that the digestion of connectin does not infuluence directly the reaction of acto-myosin and thereby the cause of the reduction of active tension is the disorder of sarcomere.

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STRUCTURAL CHANGES IN THE THIN FILAMENT DURING A TWITCH OF FROG SKELETAL MUSCLES.

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The intensity changes in the 18-nm actin second layer-line during a twitch of bullforg skeletal muscles were measured by using a synchrotron radiation at Photon Factory, Tsukuba. In sartorius muscle with a sarcomere length of 2.3μm, the intensity began to increase shortly after a stimulus and reached its maximum at 30-40ms after it, while the tension attained a peak at about 110ms. The intensity began to decrease before the tension reached its maximum and decayed with a time constant of 0.4s. In semitendinosus muscle with a sarcomere length of above 4.0μm, the intensity increased with a time course similar to that in sartorius muscle, although the developed tension was very small. The time constant of its decay was 0.2s.

These results suggest that (1) the intensity change of this layer-line during a twitch is mainly due to the structural changes induced by binding of calcium to troponin molecules, and (2) the structure of the thin filament returns to its resting state more slowly when myosin heads are bound to actin molecules.

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SARCOMERE LENGTH-TENSION AND FORCE-VELOCITY RELATIONSHIP IN MOUSE SKELETAL MUSCLES EXAMINED BY LASER DIFFRACTION METHODS.

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The sarcomere length (SL) was continuously measured in thin fiber bundle prepared from the EDL and SOL muscles using laser diffraction methods. In muscle isometric condition, the sarcomeres in the central portion shortened by 0.5-1.5 μm, stretching the sarcomeres in the peripheral portions. The isometric tetanus tension was taken after subtraction of creep tension, and it was plotted against the SL during contraction instead of the resting SL. The curve relating SL-tension showed the plateau between 2.2-2.5 μm and linear descending limb between 2.5-4.0 μm. The difference of this result from SL-tension curve in frog muscle is explained by the difference in the I-filament length. In the afterloaded isotonic contraction, sarcomeres shortened at the average velocity of 30 μm/sec in the EDL and 15 μm/sec in the SOL at 28°C. The sarcomere shortening curve was not smooth but showed fluctuations, indicating that the sarcomeres within laser illuminated area shortened not uniformly but asynchronously among each other.

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SARCOMERE LENGTH-DEPENDENCE OF THE STIFFNESS CHANGES DURING ISOMETRIC CONTRACTION IN FROG SKELETAL MUSCLE AS MEASURED BY ULTRASONIC WAVES. SUGI, H., HATTA, I.*AND TAMURA, Y.+ Dept. Physiol., Sch. Med., Teikyo Univ., Tokyo 173, *Dept. Appl. Phys., Fac. Engineer., Nagoya Univ., Nagoya 464 and +Dept. Phys., Suzuka Coll. Tech., Suzuka 510-02

Using ultrasonic waves (3-6 MHz), we have found that, during isometric contraction of frog skeletal muscle, the stiffness increases in the longitudinal direction, while it decreases in the transverse direction. To ascertain whether the above stiffness changes are concerned with the formation of cross-links between the thick and thin myofilaments, we made the stiffness measurements at various sarcomere lengths. When a resting muscle was stretched progressively from its slack length, the resting stiffness was found not to be affected by the development of resting tension, indicating that the ultrasonic stiffness is insensitive to the strain of the parallel elastic component. When the muscle was isometrically tetanized at various stretched lengths, both the change in the stiffness and the isometric tension were observed to decrease linearly with increasing sarcomere length, approaching to zero around the sarcomere length of 4um. This indicates that the change in the ultrasonic stiffness may reflect the number of the cross-bridges attached to the thin filaments.

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LOCAL MOVEMENT OF FROG SINGLE MUSCLE FIBERS DURING RAMP STRETCH AND RAMP RELEASE. TSUCHIYA, T., TAKEI, T. and SUGI, H. Dept. Physiol., Sch. Med., Teikyo Univ. Tokyo 173

Tension in striated muscle is well known to increase or decrease above or below isometric tension during and after ramp stretch or ramp release respectively and the local movement of a fiber in these phenomena were investigated on single intact fibers of frog. A muscle fiber was stretched or released with constant velocity during steady fused tetanic contraction at low temperature (3-4 C). Carbon powders were attached at the four points on the surface of a muscle fiber so that the total muscle length might be divided equally into five regions and the local movement of a fiber was recorded using nigh speed VTR during ramp stretch and ramp release. During ramp stretch, each region was lengthened equally irrespective of the velocity of ramp stretch. During fast ramp release, each region shortened equally, while during slow release, both end regions shortened remarkably but the middle region scarcely shortened. These results may provide the evidence that both phenomena are brought about by the different mechanisms.

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EFFECTS OF SARCOMERE LENGTH ON REPRIMING OF THE LABILE MAINTENANCE HEAT OF BULLFROG SKELETAL MUSCLE. KITANO,T., KOMETANI,K. AND YAMADA,K.
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Heat production during isometric tetanus can be divided into two parts, the stable and the labile maintenance heats. It is known that the amount of the labile heat is affected by the interval between tetani; it is reduced in a 2nd tetanus repeated shortly after the 1st one and is recovered by increasing the interval between the two (repriming of the labile heat). When labile heat in the 2nd tetanus relative to the 1st one was expressed as a function of time between the two tetani, the time course of the repriming can be described by the equation with two exponential terms. At sarcomere length(s.l.) 2.4μm, the equation was $E(t)=1-0.63\exp(-t/7.81)-0.37\exp(-t/390.7)$. We studied whether the time course of repriming of the labile heat is affected by the s.l. The force and heat were measured at s.l. 2.4 and 4.0μm on semitendinosus muscle of bullfrog at 4°C. The amount of labile heat in the 1st tetanus was decreased from 19.8±2.6 to 13.1±2.0mJg^{-1} (66%) by stretching. At s.l. 4.0μm the amount of the rapid phase of repriming was decreased to about a half of that at s.l. 2.4μm, however the amount of the slow phase was not affected. Time constants of both phases were not affected by stretching.

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DIFFERENCES IN THE TEMPERATURE DEPENDENCE AND NONLINEARITY OF THE TENSION RESPONSE TO SINUSOIDAL VIBRATIONS IN THE TWO TYPES OF FIBERS FROM THE FROG SKELETAL MUSCLE.

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Two types of muscle fibers were present in the anterior tibialis muscles of *Rana japonica* with respect to the response to sinusoidal sinusoidal vibrations. In one type the Nyquist plot showed a large loop in the middle frequency range, and the loop increased in size when the temperature was raised from 0°C to 10°C. At the bottom of the loop, the phase of tension with respect to length became negative i.e., the fiber produced work. In the other type, the loop was much less conspicuous at both temperatures and the fiber did not produce work at any frequency. In either type of fibers, nonlinearity in the tension response had a peak at a middle frequency, which was associated with the frequency which gave maximal work production or minimal work absorption. These frequencies had similar temperature coefficients. Therefore it seems that the nonlinearity is related to the work-producing rate process involved in the cycle of actin-myosin interaction. Although the frequency which gave maximal work production or minimal work absorption was 2-4 times higher in the former type, the frequencies which gave peak nonlinearity were almost identical in the two fiber types. These results suggest that the kinetics of actin-myosin interaction is common in the two fiber types in spite of the apparent difference in the characteristic frequencies of the work-producing rate process.

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HEAT PRODUCTION OF RABBIT EXTRAOCULAR MUSCLE.

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Force and heat production were measured during 1 s isometric tetani on inferior oblique (IO) muscles, one of the extraocular muscles, isolated from rabbits. Measurements were made at various muscle lengths at 20°C. Temperature of muscle increased almost linearly during stimulation, and the steady heat rate (h_b) was obtained from its slope. The h_b was linearly decreased with force when muscle was stretched beyond its optimum length (l_o). Mean values of force (P_o) at l_o, h_b, time to 50% relaxation ($t_{1/2}$) and h_b at zero force obtained by extrapolation in rabbit IO were compared with those in mouse EDL obtained in our laboratory at the same temperature.

	P_o(mN/mm^2)	h_b(mJ/g s)	$t_{1/2}$(ms)	h_b at zero force(mJ/g s)
IO	74.6	87.5	57.2	26.6
EDL	203.0	139.0	28.0	69.2

The ratio of h_b to P_o in IO is larger than that in EDL, which suggests that IO utilizes energy for contraction less efficiently than EDL. The result that h_b at zero force in IO is less than that in EDL is consistent with that $t_{1/2}$ in IO is larger than in EDL.

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EFECT OF CARBON DIOXIDE ON FORCE AND HEAT PRODUCTION OF SINGLE FIBERS FROM FROG.

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Force and heat production were measured simultaneously on single fibers from the frog (R. temporaria) during 4S isometric tetani. Measurements were made in the Ringer solution equilibrated with O_2/CO_2 gas mixture at 9.3-11.1°C. The Ringer solution contained 20 mM $NaHCO_3$, which was kept constant throughout the experiment. The percentage of CO_2 in O_2/CO_2 gas mixture was changed from 0.5 to 54%.

The internal pH of the fibers was measured with a recessed tip pH-sensitive microelectrode. As the percentage of CO_2 was raised from 0.5 to 54%, intracellular pH fell from 7.24 to 5.97. The extracellular pH fell from 7.99 to 6.01.

Maximum force did not change significangly in the range between 0.5 and 5% CO_2 but decreased with further increase in CO_2. Maximum force in 54% CO_2 was about 76% of that in 5% CO_2.

The dependence of the stable heat rate on CO_2 was similar to that of maximum force. The stable heat rate in 54% CO_2 was about 66% of that in 5% CO_2.

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^{31}P NMR STUDY OF THE REGULATION OF GLYCOGENOLYSIS IN IAA-POISONED FROG SKELETAL MUSCLE. YAMADA, T. AND SUGI, H. Dept. Physiol., Sch. Med., Teikyo Univ., Itabashi-ku, Tokyo 173

Based on in vitro biochemical experiments, it is generally believed that glycogenolysis is regulated in two different ways; (1) the Ca regulation at the phosphorylase step and (2) the phosphate-product regulation at the phosphofructokinase step. Recently Wilkie and his associates studied glycogenolysis in living skeletal muscles by use of ^{31}P NMR and presented evidence that glycogenolysis in vivo is regulated by the Ca released from SR but not by phosphate-products. To test this we performed similar ^{31}P NMR studies on IAA-poisoned frog skeletal muscles in which the degradation of glycogen was interrupted at the step of glyceraldehyde phosphate dehydrogenase and the intermediate sugar phosphates accumulated. Applying various tetanic contractions to IAA-poisoned muscles and measuring phosphate metabolites with ^{31}P NMR, we obtained results that glycogenolysis is regulated not only by the Ca from SR but also by the phosphate-products produced by contraction, which is in accord with the two regulatory mechanisms predicted by in vitro biochemical studies.

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EFFECT OF CO_2 ACIDOSIS ON CONTRACTION OF FROG SKELETAL MUSCLE STUDIED BY ^{31}P-NMR YAMADA, K. AND KAWANO, Y. Dept. of Physiol. Medical College of Oita, Oita, 879-56 Japan

Effect of CO_2 acidosis on contraction and metabolite concentrations were studied on bullfrog semitendinosus muscles, which were equilibrated with O_2/CO_2 gas mixture, at 4°C. The Ringer solution contained 18 mM $NaHCO_3$. The percentage of CO_2 in the O_2/CO_2 gas mixture ranged from 5 to 40%. After muscles were equilibrated with each gas mixture, tetanic stimulations of 2-s duration were repeated at 30-40 min intervals and isometric force produced was recorded. ^{31}P-NMR signals (FIDs) were recorded at 4-s intervals before, during and after contraction. At higher CO_2 than 5%, isometric force was reduced and relaxation of contraction was slowed. These changes were similar to those caused by fatigue. These changes progressed and reached a steady state with repeated contractions. [PCr], [P_i], [ATP] were determined from ^{31}P-NMR specra and [H^+] from the chemical shift of P_i speak. [$H_2PO_4^-$] and [ADP]were calculated from these concentrations. The results indicated that the decline of force with higher CO_2 was caused by both [H^+] and [$H_2PO_4^-$]and that the decline of the rate of relaxation by [H^+].

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THE LOCALIZATION AND CHARACTERISTICS OF ADENOSINE CONVERTING ENZYEMES IN T-TUBULAR MEMBRAE. NISHIJIMA,H. AND SAKAI,T. Dept. of Physiol., Sch. Med., Jikei Univ., Tokyo. Japan.

In order to know the localization and characteristics of adenosine converting enzymes in T-tubular membrane of skeletal muscle, the intact sartorius muscle(ISM), isolated sarcolemma(ISL) and fragmented sarcoplasmic reticulum(FSR) from leg skeletal muscle of bull frog were prepared.

ATPase activity in those three materials measured in Ca free reaction solution was inhibited by Mn. Ca-ATPase activity in ISL was not inhibited by Mn, whereas in ISM, up to 70 % of this activity was inhibited by Mn, although the residual activity was not affected by Mn. This activity in FSR was complately inhibited by Mn. Adenylate kinade activity in all materials was not affected by Mn and Ca. AMP deaminase activity in ISL was inhibited by Mn. Both of AMP deaminase and 5'-nucleotidase activities in ISM which could be barely detected were activated by Mn as seen in FSR. These results suggested that these adenosine converting enzymes are present in the outer surface of the T-tubular membrane and these have similar characteristics to those in FSR.

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OBSERVATIONS OF STRUCTURAL CHANGE OF MYOFILAMENTS CAUSED BY THE STRETCH AND RELEASE OF RIGOR MUSCLE FIBERS. SUZUKI, S. AND SUGI, H. Dept. Physiol., Sch. Med., Teikyo Univ. Itabashi-ku, Tokyo 173

To examine the effect of external force on the rigor cross-bridge angle and the fine structure of myofilaments, freeze-etch study was carried out using mechanically skinned frog semitendinosus muscle fibers and glycerinated rabbit psoas muscle fibers. In rigor state, the fibers were stretched or released in various amount of length change. They were frozen rapidly with a propane-jet freezing device and the freeze-etch replicas were examined with an electron microscope. The angle between the major axes of cross-bridges and the thin filament axis was about 80° in both muscles. In the frog rigor fibers, significant change of cross-bridge angle could not be caused by the stretch (10% Lo) and the release (1.5% Lo), indicating a very tight binding between the rigor cross-bridge and thin filament. In contrast with this, the cross-bridge angle was decreased to about 72° by the stretch (13% Lo and 25% Lo) in the rabbit rigor fibers. Further analysis of these results continues in our laboratory to explore this discrepancy between these different muscles. The filament length change by the rigor stretch could not be observed in the frog fibers. However, in the rabbit fibers, the length of both thick and thin filaments seemed to be increased by the rigor stretch, indicating a possibility of elastic extension of the myofilaments as described previously (Suzuki and Sugi, 1983).

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MOVEMENTS OF BEADS COATED WITH PARTIALLY PDM INACTIVATED MYOSIN ALONG ACTIN CABLES IN CHARACEAE. CHAEN, S., SHIMMEN, T.*, AND SUGI, H. Dept. Physiol. Sch. Med., Teikyo Univ., Itabashi-ku, Tokyo 173 and *Dept. Botany Fac. Sci., Univ. of Tokyo, Tokyo 113

In order to examine the role of the double-headed structure of the myosin molecule in muscle contraction, movements of beads coated with PDM-inactivated rabbit skeletal myosin along actin-cables in characeae cells were examined. Myosin-coated beads were prepared as described by Shimmen and Yano (Protoplasma 121, 132-137 (1984)). We compared the streaming velocities of two kinds of myosin samples, both of which are inactivated at various concentrations of PDM. One sample is a mixture of myosin molecules with two native heads and those with two inactivated heads, the other is a mixture of myosin molecules with zero, one and two of their heads inactivated. It was found that the streaming velocities of the former samples were higher than the latter samples at any levels of ATPase activities. Both curves were fitted when the velocities were represented as a function of the fraction of the native myosin molecules. This suggests that each myosin molecule participates in its streaming activity only when both heads are not inactivated by PDM.

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CHANGES IN FIRING PATTERNS OF SINGLE HUMAN MOTOR UNITS IN FATIGUE OF MAXIMAL VOLUNTARY CONTRACTION. KURATA, H., Natl. Inst. Fitness & Sports, Kanoya 891-23, OGAWA, Y. AND YONEMOTO, K., Lab. Sports Med., Jikei Univ. Sch. Med., Chofu 182.

Force exerted is gradually decline while sustaining a maximal voluntary contraction (MVC). Changes in firing patterns of single human motor units in fatigue are still remaining unknown. A force threshold (FT) of a single human motor unit (MU) was measured before and after sustained MVC. Firing frequencies of a MU also measured during sustained MVC. Action potentials of single MUs in an abductor digiti minimi muscle were recorded simultaneously with abduction forces of the Vth finger at the proximal interphalangeal joint of a healthy male adult. The FT of the MU was determined during an ascending and descending force ramp (MVC/5s). A sustained MVC for 20 seconds was inserted between the ascending and descending ramp. This set of force development was repeated 10 times without any interval lasting for 5 minutes. Maximal sustained forces (MFs) decreased in about 30% MVC at the final sustained contraction. Firing frequencies of MUs decreased from 30Hz to below 20Hz. Time courses of the FTs of MUs in the ascending and descending ramp were constant in the MUs with the FT of below 10% MVC, and decreased in those with above 30% MVC. Time courses of the ratios of FTs against MFs at each stage in the ascending (descending) ramp were constant (increased) in the MUs with the FTs of below 10% MVC, and decreased (were constant) in those with higher FTs.

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THE EFFECTS OF MUSCLE STRETCHING ON POSTCONTRACTION POTENTIATION. SUZUKI, S., KAIYA, K*. AND WATANABE, S., Dept., Physiol., Sch. Med., Kyorin Univ., Tokyo 181

In order to reveal the mechanism of postcontraction potentiation, activities of single motor units (SMUs) and surface EMGs in the right biceps brachii were investigated during weak contraction before and after a 5 second 50% (sometimes 25%) MVC. Nine healthy human subjects were tested. Of 26 SMUs recorded just following conditioning contraction, mean firing frequency increased in 58%, decreased in 15%, and did not change in 27%. Firing thresholds for weak contraction decreased in 46% of units after conditioning. The postcontraction surface EMG power spectrum broadened, increased in amplitude, and showed a higher peak frequency. Above findings indicate that muscle contraction potentiates stretch reflex pathways. Stretching the right biceps brachii by elbow extension just following the conditioning contraction, reduced the postcontraction EMG activity. Since muscle stretching tends to suppress muscle spindle after discharge, this finding also provides indirect evidence that reduction of postcontraction potentiation is caused by the decrease of muscle spindle afferent input to motoneuronal activites.

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ACTIVITY OF HUMAN SINGLE MOTOR UNITS DURING TREADMILL WALKING (2). OGAWA,Y., KURATA,H. AND YONEMOTO,K. Lab.Sports Med., Jikei Univ.Sch., Med., Chofu, Tokyo 182

We reported that the recruitment orders of single motor units during treadmill walking were different from those at the force development of isometric ramp contraction in human anterior tibial muscle. The activity of single motor units in gastrocnemius muscle which mainly operated in walking were studied at the treadmill walking in various speeds. The experiments were carried out on a healthy subject. The speeds of treadmill ranged from 26m/min to 102m/min. We made a comparison between the recruitment orders during walking and those at isometric ramp contraction. The recruitment orders at the isometric ramp contraction were nearly constant. The recruitment orders during walking were different from those at the isometric ramp contraction. In anterior tibial muscle, the recruitment orders of motor units during treadmill walking were irregular without regard of the speeds of treadmill, but in gastrocnemius muscle high threshold unit recruited faster than low threshold unit at the fast speed. Namely, the rate of activity in high threshold unit got greater only at 102m/min speed. The probability might exist that high threshold units in gastrocnemius were a dominant contributor during fast walking in man.

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MUSCLE-FIBER TYPES AND THEIR RELATION TO MOTOR-UNIT TYPES IN THE RAT MEDIAL GASTROCNEMIUS. KANDA, K., ASAKI, S.*, NOMOTO, E. AND HASHIZUME, K. Dept. of Physiol., Tokyo Metropolitan Institute of Gerontology, Itabashi-ku, Tokyo 173

The medial gastrocnemius was excised from the rat anesthetized with Nembutal, and was frozen in isopentane cooled by the liquid nitrogen. Cross-sections were cut at approximatly 10 um in a cryostat. After air dried, they were stained for ATPase with and without preincubation in the acid or alkaline buffer solution, and for NADH-D. Staining density of individual muscle fibers were measured by using an image analysis system. It was shown that fibers in this muscle fall into one of four groups, type I, IIa, IIb, and IIc fibers. Histochemical profile of each muscle-fiber type and its relation to motor-unit types are shown in Table 1. The NADH-D staining was dark for types I and IIa, light for IIb, varied for IIc. Total number of muscle fibers composing this muscle was estimated as 18,653 (in one case). Distribution of types I, IIa, IIb, and IIc fibers were 6.8%, 7.1%, 40.5%, and 45.6%, respectively.

Table 1. Histochemical profiles and relation to motor unit types.

Muscle fiber type	I	IIa	IIb	IIc
Alk-ATPase staining	+	+++	++	+++
Ac-ATPase staining	+++	+	++	++
MU-type	S	FR	FF	FR,FI,(FF)

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ACTIVITY OF IA-INTERNEURONS CONTRIBUTING TO THE OCCURRENCE OF 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 mechanisms of the silent period in wrist flexor EMGs, activity of Ia inhibitory interneurons during the silent period was examined in 5 healthy subjects. During wrist flexion (10 degrees, horizontal) as rapid as possible, H-reflex of wrist flexors was evoked by stimulation with delays of 10 ms and 70 ms from the onset of agonist EMG. We tested the excitability changes of the flexor motoneuron pools and of the Ia interneurons activated by GIa afferents from the antagonist wrist extensors. For this, intervals of conditioning stimuli to the radial nerve and test stimuli to the median nerve were varied from 0 to 3 ms. The amplitude of H-reflex evoked by conditioned stimuli at rest (Hta) was smaller than its amplitude of H-reflex evoked by test stimuli at rest (Hca). The amplitude of Hta with stimuli to interval of 1 ms was smallest among the other intervals. The amplitude of H-reflex evoked by test only and conditioned stimuli during movements (Hcm, Htm) were larger than Hta, except the amplitude of Htm at 1 ms stimulus interval with delay of 70 ms. These results support the view that the Ia inhibitory pathway is activated in parallel with antagoist MNs by supraspinal descending motor commands and this contributes to the reciprocal inhibition of agonist MN pool during the silent period.

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CHARACTERISTICS OF BALLISTIC CONTRACTION DURING FORCE MATCHING TASK IN CONJUNCTION WITH REACTION TIME TASK. YONEDA,T.,KIMURA,M. & ISHIDA,A. Dept. of Physiol., Sch. of Physical Edu. Juntendo Univ. Narashino, Chiba.

Accuracy and physiological properties of a self-paced ballistic force matching task(SP-BMT) and those under a reaction time task(RT-BMT) were investigated. Eight healthy adult men were employed. Subjects performed thumb adduction to an isometric bar. They were instructed to exert force as fast as possible to the target forces(10, 30% MVC) which were presented on a CRO screen. Reaction times derived from reaction time task with matching task were larger than simple reaction times. Total variabilities(E) of RT-BMT were larger than those of SP-BMT. Contraction times(TPF) and e.m.g. dwell times(EDT) showed significant differences between SP-BMT and RT-BMT in a few subjects, but not in total. However, amounts of errors, EDT and TPF were not related to the increment of reaction time values. It is suggested that the neuronal mechanism performing ballistic contraction would be independent of neuronal mechanism setting reaction time.

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INHIBITION OF FLEXOR MUSCLE CONTRACTION BY ACTIVATION OF THE BRAIN STEM RETICULAR FORMATION THROUGH PERIPHERAL STIMULATION IN RABBITS. HISAMITSU, T., WU, G.C., SATO, M. AND TAKESHIGE, C. Dept. of Physiol., Sch. of Med., Showa Univ., Shinagawa, Tokyo, 142

It is known that pressing some parts of the body or inversion causes the immobilization reflex (animal hypnosis) in some animals. It was found previously that the flexor reflex was inhibited during animal hypnosis and the center of it located in the mesencephalic and pontine reticular formation. In present study, the effect of (1) press stimulation of the body parts and (2) electrical stimulation of the center of animal hypnosis on the flexor muscle contraction caused by electrical stimulation of motor cortex were examined in rabbits. EMG changes of flexor muscle evoked by the stimulation of motor cortex were abolished or inhibited by press of the ear or paravertebral region, but not by extremities or tail. Electrical stimulation (1 Hz of 600 msec train stimulus consisted of 0.1 msec, 80 Hz pulses, 30-200 μA) of the area around locus coeruleus and brachium conjunctivum, or reticular gigantocellular nucleus inhibited the evoked flexor muscle EMG. After destruction of these regions with DC current, the flexor muscle inhibition caused by peripheral stimulation disappeared or reduced. These results suggested that flexor muscle inhibition during animal hypnosis might be produced through the animal hypnosis center activated by peripheral animal hypnosis inducing stimulation.

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MUSCULAR DYSTROPHIC MICE: GROWTH-DEFICIENT MUSCLES AND CENTRONUCLEATED MYOFIBERS. TOTSUKA, T. AND URAMOTO, I. Dept. Physiol., Inst. Develop. Res., Aichi Prefect. Colony, Kasugai, Aichi 480-03

The diameter distribution was compared between centronucleated and non-centronucleated myofibers on a cross-sectional specimen of the rectus femoris muscle from muscular dystrophic (dy/dy) mice aged from 17 to 120 days. At any age examined, it was very similar in centronucleated and non-centronucleated myofibers, and the proportion in number of the former to the latter was as high as 1/3 to 1. In addition, it was found that a considerable number of centronucleated myofibers had also peripheral nuclei and that the central nuclei tended to migrate neither toward the center nor toward the periphery in the myofibers with growth or age. These findings are not consistent with the widely-accepted view that the centronucleated myofibers in dystrophic muscles are the regenerated ones which are abortive. The pathological implication of the central nucleation was discussed with reference to our bone-muscle imbalance hypothesis where a growth imbalance between bones and growth-deficient muscles was assumed responsible for the pathogenesis.

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EFFECTS OF DAMAGED ENDS ON THE TENSION-VELOCITY RELATIONSHIP IN ISOLATED CARDIAC MUSCLE. SAEKI, Y., KATO, C. AND YANAGISAWA, K. Dept. Physiol., Tsurumi Univ. Sch. Dent. Med., Yokohama 230

The analysis of tension-velocity relationship in isolated cardiac muscle is complicated by the time varying nature of contractile state(twitch) and the damaged ends of the preparation. We, therefore, studied the length transients of living and saponin-treated rat right ventricular papillary muscles in response to various amplitudes of step tension reductions under steady contractile states(Ba^{2+}-induced contracture, steady Ca^{2+}-activated state) at 22 C using a newly developed apparatus that allow us to measure and control the muscle length(ML), the segment length(SL) and tension. Both living and saponin-treated preparations showed the oscillatory length transients, which became faster and less damped with decreasing the activation level (either by decreasing the concentration of Ba^{2+} or Ca^{2+}). The velocity of shortening in the initial shortening phase, measured from the length changes between 30 and 50 msec after the onset of the tension reduction was 2-3 times greater in the SL transient than in the ML transient. At identical loads(the reduced tensions relative to maximum tension at a given activation level) and a given initial SL, the velocity of SL shortening was greater at higher activation level. The velocity obtained from the ML transient was more than 2 times less compared with the SL shortening velocity.

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A MECHANISM OF POSITIVE CONTRACTILE REBOUND AFTER REMOVAL OF ACETYLCHOLINE IN MAMMALIAN ATRIAL MUSCLE. INATOMI, K., IMANAGA, I., KISHI, M.* AND PARHATI, A※ Dept. of Physiol., 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 in canine atrial myocardium. In the previous study, we reported this rebound phenomenon (R) was brought about via muscarinic ACh receptor (m-AChR) without any interaction of intrinsic catecholamines. In this study, 10^{-7} M strophanthidin or low $[K^+]_o$ enhanced R but low $[Na^+]_o$ substituted by sucrose, high $[K^+]_o$ or high Rb^+ replacing K^+ inhibited R. Removal of carbamilcholine (CCh) did not induced R but appeared by addition of atropine during CCh. Both ACh and CCh inhibited plasma membrane Na^+-K^+ ATPase activity. These results suggest that activation of m-AChR induces an increase in $[Na^+]_i$ by inhibition of Na^+-K^+ pump, and then an uptake of Ca^{2+} into the intracellular store sites increases by activation of Na^+-Ca^{2+} exchange. Also La^{3+}, quinacrine or ryanodine abolished R. It may be a possible mechanism of the rebound phenomenon that more Ca^{2+} release from the intracellular Ca^{2+} store site by a rapid inactivation of m-AChR.

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OPTICAL ASSESSMENT OF PACEMAKING AREA IN THE EARLY PHASES OF CARDIOGENESIS OF CHICK EMBRYO USING A 100-ELEMENT PHOTODIODE ARRAY. KOMURO, H., HIROTA, A., SAKAI, T. and KAMINO, K. Dept. of Physiol., Tokyo Ika-Shika Dai, Sch. Med. Tokyo 113.

Pacemaking areas in the early embryonic chick hearts were quantitatively assessed by means of simultaneous multiple-site optical recordings of the electrical activity. The measuring system, with a 10x10-element photodiode array, had a spatial resolution in 30-15μm. Spontaneous action potential-related absorption signals were recorded simutaneously from multiple contiguous regions in 7- to 9-somite embryonic chick hearts stained with a voltage-sensitive merocyanine-rhodanine dye. At the 7- and 8-somite stages, the pacemaking area was located in various regions of the heart, and as development proceeds to the 9-somite stage, it was located in the left atrial primordium. The pacemaking area was basically circular shape. The elliptical shape also was often observed at the 7- to early 8-somite stages. The size of the pacemaking area was estimated to be approximately 1200-3000um^2. It was thus suggested that the pacemaking area was composed of about 40-100 cells, and we propose an idea that not a single cell but a population of cells with pacemaking ability serves as a rhythm generator in early embryonic chick hearts. These data represent the first demonstration of a quantitative assessment of the pacemaking area in the heart.

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PACEMAKING AREA IN THE FROG SINUS VENOSUS ASSESSED BY MULTIPLE-SITE OPTICAL RECORDING OF ACTION POTENTIALS. MOMOSE, Y., KOMURO, H., SAKAI, T. and KAMINO, K. Dept. of Physiol., Tokyo Ika-Shika Dai, Sch. Med. Tokyo 113.

The optical monitoring method was used to study location and size of the pacemaker in the sinus venosus-atrium preparation isolated from bullfrogs. The preparation was stained with a voltage-sensitive merocyanine-rhodanine dye, and spontaneous action potential-related absorption signals were simultaneously recorded from 128 loci, using a 12x12-element photodiode array. In bathing solution was with a low Ca^{2+} -concentration (0.05-0.2mM), the pacemaking area was often seen to locate between the right and left precaval veins. The pacemaking area was approximately circular shape, and size of the area was roughly estimated to be 0.4-0.8mm^2. The position of the pacemaking area fluctuated within a small area. The excitation generated in the pacemaking area spread over the sinus venosus and the atrium. Basically, the excitation spread radially, at a uniform rate. Conduction velocity was approximately 0.04-0.06m/sec in the sinus venosus, but the conduction velocity to the atrium along the pulmonary vein was somewhat higher than that to the right and left precaval veins. In addition, we observed that there was a considerable reduction in electrical activity in the sinus venosus and that the pacemaking site shifted to the boundary between the sinus venosus and atrium, when the preparation was placed in Ca^{2+}-free bathing solution.

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CELL-TO-CELL DIFFUSION OF FLUORESCENT DYES IN PAIRED VENTRICULAR CELLS. IMANAGA, I., KAMEYAMA, M.* AND IRISAWA, H.* Dept. of Physiol., Sch. of Med., Fukuoka Univ., Fukuoka 814-01, *Nat. Inst. Physiol. Sci., Okazaki, 444

The intracellular and cell-to-cell diffusion of fluorescent dyes with various molecular weight were studied in enzymatically isolated paired ventricular cells of the guinea pig heart. Fluorescent intensity was detected by photodiode under an inverted fluorescence microscope and it reasonably reflected concentration of the dye in the cell. Diffusion coefficient of the dye in the cytoplasm (D_{cell}) and permeability of the dye to the gap junctional membrane (P_j) were analyzed by a multicompartment model. Fluorescein (MW: 332), 6-carboxyfluorescein (MW: 376), Lucifer Yellow CH (MW: 457), Lissamine Rhodamine-B200 (LRB-200)(MW: 559), all dyes simply diffused into the cell from the patch-clamp pipette and throughout the cell within 2 min. D_{cell} of LRB-200 (8.6×10^{-7}cm^2/sec) was about 7 times smaller than those of other dyes. P_j of LRB-200 (7.4×10^{-5}cm/sec) was about 10 times smaller than those of other dyes. D_{cell} and P_j showed a reversed correlation with molecular weight of the diffusion probe. Tetraglycine conjugated LRB-200 (MW: 859) passed through the gap junction. Thus the critical bore of the ventricular gap junctional channel may be around 13 Å.

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CALCIUM DEPENDENT ACTIVITIES OF THE BULLFROG ATRIAL MUSCLES. HORIUCHI, E. Dept. of Physiol., Saitama Med. Sch., Saitama 350-04

The recentry synthesized calcium sensitive fluorescent probe, Quin-II (2-[2-Amino-5-methylphenoxy)methyl]-6-methoxy-8-aminoquinoline-N,N,N',N'-tetraacetic acid), and its membrane-permeable acetoxymethyl ester derivate(Quin-IIAM) were added to the Ringer's solution perfusing everted sinus-atrium preparations of bullfrogs. Quin-II(300 μM) reduced contractility of the atrial muscles(-30%) and shortened cardiac interval of the sinus rhythms(-10%) immediately after its application. Quin-IIAM (50 μM, 60 min.) gradually reduced not only the contractility(-20%) but also heart rate(+20% prolongation of cardiac interval). Elevation of intracellular free calcium with application of caffeine(1 mM) restored the effects induced by Quin-IIAM. These results indicate that Quin-IIAM permeate intact cardiac cell membrane as in enzymatic isolated cell membranes and are hydrolyzed by intracellular esterase to membrane-immpermeant Quin-II which bind cytoplasmic free calcium ions. The data presented in this report suggest that lowering of intracellular free calcium level increase the cardiac interval.

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INVOLVEMENT OF Na-Ca EXCHANGE CURRENT IN THE TRANSIENT INWARD CURRENT.

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Loading 1 μM Ca into a single guinea pig ventricular cells by perfusion pipette induced oscillatory transient inward current under whole cell voltage clamp, where Ca currents, K currents and Na-K pump current were blocked. This current was inward at positive potentials in the presence of K inside the cell, and was blocked by 1 mM Ni and 0.1 mM La. It was thus concluded that the main component of the transient inward current is electrogenic Na-Ca exchange.

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Contribution of two types of calcium currents to the pacemaker potentials of rabbit sinoatrial node cells.

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Two types of calcium currents have been found in various excitable cells (IcaT and IcaL). We recorded the two types of calcium currents in isolated S-A node cells of the rabbit in the whole cell voltage-clamp and cell-attached patch clamp method. The IcaT was elicited by a step depolarization from a holding potential of -80mV to potentials more positive than -50mV. The activation range of this current overlaps with the pacemaker potentials, suggesting possible contribution of IcaT to the pacemaker potentials. This view was further evaluated by applying Nickel(40μM) as a specific blocker of the IcaT. Spontaneous action potentials of the S-A node cells significantly slowed down after an administration of 40μM Nickel, which is in good agreement to the view that the IcaT is playing a significant role in regulating the pacemaker potentials.

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GUANOSINE TRIPHOSPHATE (GTP) REGULATES THE RELAXATION PROPERTY OF THE ACETYLCHOLINE (ACh)-SENSITIVE K CHANNEL THROUGH GTP-BINDING PROTEINS.

*HORIE, M., *MIURA, Y, IRISAWA, H. Natl. Inst. Physiol. Sci. Okazaki 444

Using patch clamp technique, relaxation properties of ACh-sensitive K channel were studied in single guinea-pig atrial cells. At microscopic current level, GTP or its analogue recovered the channel activity which had disappeared in the cell-free condition. On depolarizing voltage jumps (-80mV to +80mV), both single and ensemble currents relaxed rapidly with time constant of 19 ms when GTP-binding (G-) proteins were activated by non-hydrolyzable GTP analogue, suggesting that the high activation level of the channel may accelerate the time course of relaxation. In whole-cell experiments, the higher GTP was applied internally (where active form of G-proteins was increased), the larger became ACh-induced current and the faster its relaxation. Open channel probability (Np= mean patch current/unit amplitude) increased at more negative membrane potentials, and the GTP concentration-Np curves gave a smaller half maximum GTP dose at -80 mV than at -40 mV. Thus, the interaction of G-protein with the channel protein may be partially responsible for the relaxation property of the channel.

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PROTEIN KINASE C AND INTRACELLULAR CALCIUM REGULATE THE DELAYED RECTIFER POTASSIUM CURRENT IN HEART CELLS.
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Effects of phorbol ester (TPA) and intracellular calcium on the delayed rectifer potassium current (I_K) were studied in isolated guinea-pig ventricular cells, using intracellular perfusion technique. At a concentration of intracellular calcium ($[Ca]_i$) of pCa 10, external TPA 10^{-9} M increased the amplitude of I_K by 60% without changing the voltage dependency. This effect was not observed at $[Ca]_i$ of pCa 11, indicating that calcium ion was required for TPA action. The increase of I_K by TPA was blocked by 10μM H-7, an inhibitor of protein kinase C (PKC). Another activator of PKC, 1-oleoyl 2-acetyl glycerol (50μg/ml) also increasd I_K in a similar manner to TPA. These findings support the view that increasing of I_K by TPA is mediated by PKC.

The dose-response curve between $[Ca]_i$ and I_K in the absence of TPA revealed that $[Ca]_i$ The above pCa 8 increased I_K. The curve was shifted to the direction of lower $[Ca]_i$ by TPA application. It was concluded that intracellular calcium ion not only activates I_K channel directly, but it indirectly enhances I_K via activating PKC.

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INVOLVEMENT OF INTRACELLULAR FACTOR(S) IN "RUN DOWN" OF THE CARDIAC L-TYPE Ca CHANNEL.
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Activity of the L-type Ca channel is known to be reduced ("run down" or "wash out") when the internal side of the membrane is perfused with an artificial solution. To investigate possible mechanisms involved in this phenomenon, we applied following agents to patches in which the Ca channels were led to run down (in mM): Ca chelators (EGTA 20, BAPTA 2), nucleotides (ATP 5, GTP 1), cAMP 0.1 or the catalytic subunit of cAMP-dependent protein kinase (C subunit) 0.002, pyrophosphate 2.5 or phosphate 120, protease inhibitors (leupeptin 10 μg/ml, benzamidine 1, phenylmethylsulphonylfluoride 0.1),and reducing agents (dithiothreitol 1, glutathione 0.5). None of them or combination of them, however, restored the channel activity in the inside-out patch. Only C subunit slightly and transiently facilitated the opening of the channel in a MgATP-dependent manner.

The tissue extract from guinea-pig or bovine heart recovered the channel activity even in the absence of ATP. In the presence of the extract, C subunit or cAMP was able to increase the open probability of the channel further.

It was concluded that the "run down" of the Ca channel involves some unknown intracellular molecule(s) other than cAMP-dependent protein kinase.

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A NEW OIL GAP METHOD FOR INTERNAL PERFUSION AND VOLTAGE CLAMP OF SINGLE CARDIAC CELLS.
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We designed a new technique to achieve fast voltage clamp combined with internal perfusion. The single guinea-pig cardiac cell, dissociated by collagenase treatment was stretched across an oil-gap (30-40 um) from a pool of Tyrode to a pool of internal solution. Part of the cell membrane was disrupted in the internal solution by crushing on the cell a tapered tip of a glass capillary. Through the open end, the cell was equilibrated with test solutions and electrical current was injected for the voltage clamp of the membrane in the Tyrode pool. The capacitive current decayed with a time constant of 10-60 usec depending on the capacitive area. The series resistance was around 600-800 kohm and the seal resistance was 30-100 megaohm. The activation time course of the inward rectifier K channel was clearly observed on hyperpolarization. The sodium current was recorded without interference from the capacitive current.

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CALCIUM-ACTIVATED NON-SELECTIVE CATION CHANNEL IN GUINEA-PIG VENTRICULAR CELLS. ONO,K.,IKEMOTO,Y.,EHARA,T.AND NOMA,A. Dept. Physiol., Fac. Med., Kyushu Univ., Fukuoka 812

The Na^+-free contracture of single ventricular cells was induced by exposing the cell to Na^+-free solutions at room temperature. The cell-attached single channel recording using Na^+ or K^+ pipette solution revealed activation of channels having a conductance of around 10-20pS during the contracture, probably due to an increase of the intracellular Ca^{2+}. The similar kind of channel was found to be activated by more than 0.3μM Ca^{2+}in the inside-out membrane patches. The reversal potential was not markedly changed by replacing Na^+ with K^+ in the internal solution. The open time histogram was single exponential and the closed time histogram was double exponential. The open probability was increased by raising $Ca^{2+}$and became near 1 at 10μM Ca^{2+}. This effect was due to prolongation of the mean open time and shortening of the closed time. The kinetics of the channel was independent of the membrane potential. The channel may be classified as Ca^{2+}-activated non-selective cation channel and in part account for the Ca^{2+}-mediated conductance reported in the whole cell studies.

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EFFECTS OF ACETYLCHOLINE ON INTRACELLULAR CA TRANSIENT AND TENSION IN FERRET VENTRICULAR MUSCLE. KURIHARA, S., KONISHI, M., OKAZAKI, O. AND KOBAYASHI, K., Dept. of Physiol., Jikei Univ. Sch. of Med., Tokyo 105

Aequorin was injected into 50-100 superficial cells of ferret papillary muscle, and light (function of $[Ca^{++}]_i$) and tension were simultaneously recorded. Acetylcholine (ACh)(0.01-1.0 uM) slightly inhibited peaks of light and tension in twitch response without significantly changing their time courses. In the preparation treated with isoproterenol (Iso)(0.2 uM), ACh dose-dependently inhibited light but tension was rather resistant. The effect of ACh on tetanus triggered by repetitive stimulation (40 ms, 10 Hz) in the presence of ryanodine (5 uM) was observed. In normal Tyrode's solution containing beta receptor blocker (1 uM bupranolol), ACh slightly shifted the relation between $[Ca^{++}]_i$ and tension to the left (to lower Ca^{++} range). Iso shifted the relation to the right, and the effect of Iso was antagonized by ACh. ACh probably changes Ca^{++} sensitivity of the contractile element in the intact ventricular muscle treated with Iso but this effect is not remarkable in untreated preparation.

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EFFECTS OF CAFFEINE ON POTASSIUM AND CALCIUM CURRENTS IN GUINEA PIG SINGLE VENTRICULAR CELL. YANO,K.AND TSUDA,Y. 1st.DEPT.MED.FAC.MED.KYUSHU UNIV.,FUKUOKA,812.

Effects of caffeine(Caff) were studied in isolated single ventricular myocyte of guinea pig using whole cell clamp technique.Extracellular solution was as follows: NaCl 150, KCl 5.4,$CaCl_2$ 1.8,Glucose 10.0,HEPES 5.0, pH 7.4 .Patch electrodes were filled with KCl 20,K-Aspartate 110, EGTA 5.0,ATP-K_2 2.0,Glucose 5.5,HEPES 5.0,pH 7.2 .24°C.3mM Caff increased maximum slow inward current(L-type,Ica) and decreased I_{kl} slightly, however showed no remarkable change in I_x.Peak voltage of I_{ca} shifted to hyperpolarizing direction by 7~8mV in 3mM Caff. Substituted Ba for Ca I_{Ba} was enhanced by 3mM Caff,however,depressed by 10mM Caff. In I_{Ba} no shift of I-V relation was observed either 3mM or 10mM Caff.These results suggest (1) low concentration of Caff(3mM) has dual effects to increase intracellular calcium and inhibit phosphodiesterase causing catecholamine-like action. (2) shift of I-V relation and inactivation curve might be due to screening effect of surface charge inside the salcoremmal membrane by increased intracellular calcium by Caff.(3) effects of 3mM Caff on I_{kl} also could be explained by the effects of intracellular calcium on surface charge inside the membrane.

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SINGLE CHANNEL ANALYSIS OF THE LATE SODIUM CURRENT.

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Single Na channel currents were recorded from guinea pig ventricular myocytes in a cell-attached mode. The current-voltage relationship of the single channel current was linear and its conductance was about 14 pS (13.7 ± 2.3 pS) at 12°C. Two types of Na channel activities were observed even after 100 msec from the beginning of the depolarizing pulse. (1) Short isolated openings (mean open time ≃300 μsec) which evolved randomly during a long depolarizing period (500 msec). This opening occurred only once each 100 pulses for each channel. (2) A burst-like Na channel openings lasting for entire period of depolarization (500 msec) which occurred on very rare occasion, once each 4000 pulses for each channel. The latter type of activity accounted for more than 80 % of the late Na current. The size of late Na current per single ventricular cell was estimated as a TTX-sensitive current in whole cell clamp configuration, in that a constant inward TTX (60 μM)-sensitive current of about 20 pA was recognized at -50 mV. At more positive potentials, this current decayed slowly with a time constant of 214 msec at -30 mV, for example. These late Na currents probably account for the TTX-induced shortening of action potential duration (435 ± 150 msec, control vs 373 ± 128 msec, in the presence of 60 μM TTX).

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HOW DOES THE SODIUM CURRENT CONTRIBUTE TO THE MAXIMUM UPSTROKE VELOCITY OF ACTION POTENTIAL ($\dot{V}_{max}$)?

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In cardiac muscle, $\dot{V}_{max}$ as an index of sodium channel availability has been extensively used instead of measuring I_{Na} obtained directly by the voltage clamp method. In order to examine whether the use of $\dot{V}_{max}$ is appropriate or not, dose-response curve for TTX and h-∞ curves were obtained by action potential or by voltage clamp experiment. No significant discrepancy between the curves measured with action potential and those with voltage clamp experiments was observed in this experiment. In reconstructing action potentials by using the H-H type equations for sodium current and leakage current, which had been determined with our own preparations, it was found that this consistency was not due to the kinetic property of the sodium channel but to the contribution of background current to the total membrane current. Caution should therefore be exercised in using $\dot{V}_{max}$ as a representative of I_{Na} for examining the kinetic property of Na channel.

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STUDIES OF MEMBRANE CURRENTS IN VENTRICULAR MYOCYTES DURING DEVELOPMENT OF RAT HEART.

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Ventricular cells were enzymatically isolated from rat hearts at ages of 14 embryonic days(14ed) and 1 postnatal day(1pd). The membrane currents were recorded using the patch pipettes. Cells obtained from 14ed rats were spherical in shape(~20μm diameter), having the resting potential of -37mV, the input resistance at RP of 416MΩ and the membrane capacitance of 1.56μF/cm^2. Depolarizing pulses from a holding potential of -45mV elicited Ca currents(i_{Ca}), which were blocked completely by 0.1mM Cd^{2+}. The amplitude of i_{Ca} peaked at +10mV and its maximal current density was 27.8μA/cm^2. The I-V relation of peak amplitudes of i_{Ca} obtained at 1pd was similar, and its density was 23.6μA/cm^2. In the presence of Cd^{2+} or Co^{2+} in bath solutions, the outward currents during depolarizations from the holding potential of -40mV showed no time-dependence at 14pd. In some cells at 1pd, however, small but distinct humps appeared at the onset of depolarizations positive to +10mV, suggesting that the transient outward current develops at this stage. Using the cell-attached patch recordings, with 100mM Ba^{2+} in pipette and 2μM BAY K 8644 in bath solution, two types of Ca channel with different current amplitudes were evoked in cells at 14pd. The current amplitudes at 0mV were 0.6pA and 1.65pA, and the channel conductance was calculated to be 10pS and 33pS, respectively.

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ACETYLCHOLINE (ACh) STIMULATES ATRIAL NATRIURETIC PAPTIDES (ANP) SECRETION FROM ISOLATED ATRIAL MYOCYTES IN RAT. EBISU, H. and KOIDE, T., Res. Lab., Fukuyu Hosp., Nissin, Aichi 470-01, and NANBA, T. and NAGATA, Y., Dept. Physiol., Sch. Med., Fujita-Gakuen Univ., Toyoake, Aichi 470-11

ANP are known to be secreted from cardiac atrium into blood stream and to cause natriuresis or diuresis in mammals. We have separated and collected viable atrial myocytes from adult rat atrium by gentle filtration and centrifugation techniques after trypsin and collagenase treatments. Addition of ACh (10^{-6} to 10^{-4}) clearly stimulated ANP secretion into the medium in a dose dependent manner during 1 h incubation of separated myocyte suspension. Reversely, ACh decreased the intracellular ANP content. And, total (extracellular plus intracellular) ANP content did not apparently changed by ACh addition. The ACh-induced ANP secretion from atrial cells was completely blocked by further addition of muscarinic antagonist atropine (5×10^{-4}). Thus, it is considered that ACh stimulate ANP secretion from atrial myocytes through activation of muscarinic ACh receptor. Acknowledgment: We are grateful to Drs. J. Hayashi and M. Ohni of Cardiovascular Res. Lab. in this University for their kind cooperation in the experiments.

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EARLY AFTER-DEPOLARIZATIONS IN RABBIT SINOATRIAL NODE CELLS. GOTO, K., MIYAMAE, S., SUDO, S., NAKANO, M., MATSUDA, T. AND OKAMUNE, S. Dept. Physiol., Kanazawa Med. Univ., Uchinada, Ishikawa 920-02

The appearance of early after-depolarizations induced by Ca removal was studied in rabbit sinoatrial node cells superfused with 10^{-5} M ouabain. The early after-depolarizations correspond to humps of variable size occurring on the falling phase of repolarization. When quiescent preparations were superfused with Ca-free or K-free solutions containing ouabain, removal of external Ca (Ca=0, EGTA=2 mM) produced rapidly increasing oscillations but did not induce early after-depolarizations. However, removal of external Ca produced rapidly increasing oscillations and early after-depolarizations in quiescent preparations superfused with K-free, Ca-free solutions containing ouabain as the application of K-free, Ca-free EGTA media was prolonged. The early after-depolarizations reached 16 ± 2.8 mV (n=9) before the end of the plateau, while the membrane potential before initiation of the early after-depolarization reached a value of -12 ± 0.8 mV (n=9). The early after-depolarizations induced by Ca removal (Ca=0, EGTA=6 mM) also developed in K-free solutions containing 10^{-6} g/ml tetrodotoxin. Therefore, it is concluded that prolonged exposure to K-free, Ca-free 2 mM EGTA media or Ca-free, 6 mM EGTA media leads to early after-depolarizations in sinoatrial node preparations treated with ouabain or K-free media.

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EFFECTS OF AN132 , A LIDOCAINE ANALOGUE, ON THE CARDIAC MEMBRANE CURRENTS OF VENTRICULAR MYOCYTES ONO, K., KIYOSUE, T. AND ARITA, M Dept. of Physiol., Med. Coll. of Oita, Oita 879-56

The effects of AN132, an analogue of lidocaine (3-(diisopropylaminoethyl-amino)-2',6'-methylpropionanilide), on action potentials and membrane currents of guinea pig ventricular myocytes were studied as compared to those of lidocaine using the tight-seal whole-cell clamp method. While lidocaine (30 μM) had negligible effect on action potential configurations, AN132 at concentrations of 10 and 100 μM significantly decreased the action potential duration (APD_{95}) by 15 and 31 %, respectively. AN132 had greater inhibitory effect on I_{Na} than lidocaine in the experiments where Na_o was reduced to 60 mM by replacing NaCl with sucrose , i.e., 30 μM AN132 and lidocaine decreased I_{Na} by 71 % and 35 %, respectively. Lidocaine (10, 30 and 100 μM) had minor effects on I_{Ca}, I_k and I_{k1} whereas AN132 significantly decreased all the currents, e.g., I_{Ca} was decreased to 85.3, 73.5 and 59.5 % of the control by 10, 30 and 100 μM AN132, respectively. AN132 also diminished the amplitude of I_k dose-dependently and decreased the membrane conductance of I_{k1} measured around the resting potentials.

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AMANTADINE-INDUCED AFTERPOTENTIALS AND AUTOMATICITY IN GUINEA PIG VENTRICULAR MYOCYTES. HIRAOKA, M., HIRANO, Y., KAWANO, S. and SAWANOBORI, T. Dept. of Cardiovasc. Dis., MRI, Tokyo Med. Dent. Univ., Tokyo 113

The ionic mechanism of amantadine-induced afterpotentials and automaticity was studied using the suction pipette whole-cell clamp method in guinea pig ventricular myocytes. In the presence of 25-100 μM amantadine, RMP negative to -70 mV, an afterdepolarization without preceding after hyperpolarization appeared. This afterdepolarization was blocked by 14 μM tetrodotoxin (TTX). After application of 100-200 μM amantadine and RMP depolarized positive to -60 mV, delayed afterdepolarizations and triggered-automaticity, and spontaneous activity developed. These activities were easily and reversibly blocked by 2 mM Co^{2+}. Under the voltage clamp condition amantadine produced mild depression of calcium current (I_{Ca}) and delayed outward K^+ current (I_k). The drug activated a TTX-sensitive inward current at -20 - -80 mV. The inward rectifier K^+ current (I_{k1}) was suppressed by amantadine with a time-dependent block positive to E_k and unblock negative to E_k. There was no activation of the transient inward current after amantadine application. Therefore, it is concluded that the amantadine-induced afterpotentials and automaticity are caused by I_{Ca}, I_k, the activation of the TTX-sensitive inward current and by the modulation of I_{k1}.

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ACONITINE-INDUCED INWARD CREEP CURRENT UPON REPOLARIZATION FROM THE DEPOLARIZED STATES IN THE ISOLATED GUINEA PIG VENTRICULAR MYOCYTES. SAWANOBORI, T., HIRANO, Y. and HIRAOKA, M. Dept. of Cardiovasc. Dis., MRI, Tokyo Med. Dent. Univ., Bunkyo-ku, Tokyo, 113

Aconitine (AC) poisoned fiber reveals tachyarrhythmias due to triggered activity. We studied the effect of aconitine (1.5×10^{-5} M) on the membrane current upon repolarization from the depolarized states in the isolated guinea pig ventricular myocytes. Voltage clamp experiments after AC application showed a decline of the steady state outward current with time around -60 mV, which revealed a development of the inward creep current. These currents were almost completely abolished by 8 mM Na and 3 μM TTX but not by 2 mM Co. It was also observed in the solution replaced K with Cs. The relation between the voltage of the condition pulses and the inward creep current was sigmoid but not zero even positive to 0 mV. The shorter depolarizing pulses increased the amplitude of the inward creep current and the longer depolarization decreased it, while oscillatory current showed the reverse relation. Quinacrine (10 μM), a blocker of Na-Ca exchange current, suppressed the inward creep current and postponeded the appearance of oscillatory current. These results indicate that aconitine induces the inward current upon repolarization, which is caused, in some part by Na-Ca exchange and my partly be responsible for generation of aconitine-induced tachyarrhythmias.

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EFFECT OF VERAPAMIL ON A-V CONDUCTION OF ATRIAL FIBRILLATION OGINO,T. AND DOHI ,Y., 2nd Dep. Int.Med.,Saitama Medical School. Morohongo 38,Moroyamamachi, Saitama 350-04

The use of verapamil on atrial fibrillation with rapid heart rate response reduces heart rate because of its suppressive effect on A-V conduction. Some investigators reported that verapamil causes not only reduction of heart rate but also regularization of ventricular response. Therefore we tried to examine this point experimentaly. After initiation of atrial fibrillation by several methods(ex.Aconitine,POISSON generator etc.) in open chest anesthesized mongreal dogs, we observed the effect of verapamil on A-V conduction. The results are 1, high dose of verapamil causes complete A-V block and regular junctional escape rhythm occured 2, in case of flutter-fibrillation,low dose of verapamil may fixate A-V conduction and then causes regularization of heart beats.

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THE EFFECT OF DILTIAZEM ON IONIC ENVIRONMENT IN MYOCARDIAL CELLS.
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To clarify the change of ionic environment during open heart surgery, myocardial biopsy was performed at the time of non-ischemia, after 60 minutes' ischemia, and during reperfusion period. The specimens were quickly frozen and measured for various elements by means of X-ray microprobe analysis. In control (C) group without diltiazem pretreatment, potassium level decreased at both ischemia and reperfusion, while calcium level increased at ischemia and significantly increased at reperfusion period. In diltiazem (D) group, calcium accumulation at reperfusion was suppressed, and potassium level recovered to the same level as non-ischemic period. In both groups, natrium and chlorine showed an increase at ischemia and at reperfusion period. At the pre-ischemic condition, calcium is higher in D group than in C group. It is suggested that diltiazem may affect phosphatidylinositol metabolites to induce calcium release from sarcoplasmic reticulum into sarcoplasma.

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EFFECTS OF CA ANTAGONISTS ON ACTIVE AND PASSIVE ELECTRICAL PROPERTIES OF CANINE PURKINJE FIBERS.
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We studied whether Ca antagonists influence on the passive properties of cells, and conduction velocity through changes of Ca ion in the cell. We used conventional microelectrode methods. 10^{-6}M verapamil, diltiazem and nifedipine decreased conduction verocity, whereas nicardipine did not. Maximum diastolic potential, $\dot{V}max$, and amplitude were not changed by these drugs. Space constant, and internal longitudinal resistance were not changed by 10^{-6} and 10^{-5}M verapamil, nicardipine and nifedipine(n=3). Diltiazem seemed to increase space constant and to decrease r_i. But we need further investigation in this point.

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FACILITATION OF RECOVERY FROM ANOXIA IN RAT HEART.
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Isolated rat hearts were perfused with oxygenated Krebs solution with a 10 cmH_2O of preload and a 80 mmHg of afterload. Monitoring coronary perfusion pressure, temperatre of perfusate, and left ventricular pressure, anoxia was induced by a perfusion with N_2-saturated Krebs solution. After a 30 min of anoxic period, the heart was reoxygenated and the effect of cold shock on the recovery of contractile function was examined. With the reoxygenation, pressure development gradually recovered and at 60 min after the reoxygenation, the level reached 29.8% of pressure developed before anoxia (n=7), while, the heart (n=7) which was applied several times of cold shock (4-7 °C for 1 min) recovered to 93.8%. Moreover, 3 out of 7 hearts which did not receive cold shock showed gradual but significant elevation in diastolic pressure (oxygen paradox), but none of the heart which were given cold shocks developed oxygen paradox.

These results indicate that excess intracellular calcium ions are removed by the cold shock. Thus, the cold shock will facilitate the recovery from Ca-overload induced depression in metabolic activity, resulting in accelerated recovery of contractile performance.

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EFFECTS OF CALCIUM LOADING ON THE SPONTANEOUS BEATING IN CULTURED HEART CELLS OF CHICK EMBRYO. TOYOTA, H. and MATSUMURA, M. Dept. Physiol. Kawasaki Med. Sch., Kurashiki 701-01

The membrane potential and contraction were investigated in cultured heart cells of 7-12 days chick embryo. Ca ionophore A23187, when extracellularly applied, increased the spontaneous beating rate but decreased slightly the contraction measured as the edge movement of cell aggregates. Also, it shifted the maximum diastolic potential towards less negative potential and generated the diastolic after-potentials. In these conditions, $[Ca^{2+}]_i$ was expected to be elevated. Injection of Ca ions into a cell with iontophoretic current of 2-4 x 10^{-9} A produced a shift of the diastolic potential to more negative level by 2-5 mV. In a few cells, cyclic changes in the diastolic potential towards the depolarized direction were observed accompanied by an increase in the rate of spontaneous activity. This would reflect the cyclic changes in $[Ca^{2+}]_i$ produced by Ca-induced Ca release mechanism. Injection of Ca ions with strong iontophoretic current of 1-2 x 10^{-8} A for a second showed no effect on the shape of the action potential, suggesting that intracellular Ca ions were well neutralized.

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THE EFFECT OF INTRACELLULAR pH ON THE SINGLE Ca CHANNEL IN GUINEA-PIG VENTRICULAR CELLS. KAIBARA,M., KAMEYAMA,M. AND IRISAWA,H. National Institute for Physiological Sciences Okazaki 444.

The mechanisms of the action of intracellular pH (pH_i) on the Ca channel were studied in the guinea-pig ventricular cells using open cell-attached patch clamp technique with a pipette solution containing 50 mM Ba^{2+} and 3 μM Bay K 8644. Changing pH_i (6.2-8.2) affected neither the single Ca channel condactance nor the number of the channels in the patch. The open probability of the channel was increased by increasing pH_i, and vice versa. The open and closed time histograms showed a significant increase in the slow time constant of the closed time at low pH. The dose response relation between the open probability and pH_i indicated that a proton binds to a site having a pK_a of 6.5. The pH_i effect was abolished by 10 μM Rose Bengal, suggesting that a histidine residue might be related to the binding site.

These results suggest that proton decreases the open probability of the Ca channel through the protonation of a site within or close to the channel.

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EFFECTS OF TWITCH POTENTIATORS ON THE CONTRACTION OF RAT PAPILLARY MUSCLE. SUGAYA, R., IWAMOTO, H. AND SUGI, H. Dept. Physiol., Sch. Med., Teikyo Univ., Tokyo 173

The effects of NO_3^-, Zn^{2+} and SCN^- on the contraction and membrane potentials of the rat papillary muscle were studied. NO_3^- (substituted for Cl) and Zn^{2+} (100μM) enhanced the contractile force and reduced the resting and action potentials, but the changes were only modest. On the contrary, the effects of SCN^- (substituted for Cl) were prominent. During the exposure to SCN^-, the contractile force was markedly enhanced at first and gradually decreased thereafter, while the resting and action potentials continuously reduced. Replacement of solution with normal Tyrode led to a further reduction and following relatively quick recovery in the contractile force. These behaviors of the contractile force and action potential with respect to the resting potential were similar to those in the muscle depolarized to various extents by raising K^+ concentration, but the action potential in SCN^- solution was smaller than that in high-K^+ solution at the same resting potential. These results suggest that the effects of SCN^- on the contraction and action potential are mainly due to its gradual depolarizing action, but SCN^- may also have some additional inhibitory effect on the action potential.

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BALLISTOCARDIOGRAM RECORDED BY A TRI-AXIAL FORCEPLATE : DISPLACEMENT AND VELOCITY OF THE CENTER OF GRAVITY OF THE HEARTBEAT SYSTEM. OHMICHI, H. Biomechanics Lab. The International Budo Univ. Katsuura, Chiba, 299-52

The ballistocardiogram during sitting was reexamined by recording of the floor reaction forces generated by the movements of the heart and the blood flow. The three dimensional floor reaction forces were recorded by a tri-axial force plate (Kistler;40x60cm^2), which showed the acceleration of the center of gravity of total human body (M_{tot};70kg). If the mass of the heartbeat system was 0.35kg consisting of the heart muscle 290g and the stroke volume 60g, the acceleration of the center of gravity of the heart-beat system was 200 times as high as that of M_{tot} (; 70/0.35).

The displacement and velocity of the heartbeat system related to time were mathematically derived by numerical integrations of the acceleration using a digital computer (Newton's second law of motion).

The peak to peak values of the floor reaction forces acting on a resting man sitting on the force plate were approximately 0.1, 0.1, and 0.01 kg in forward, vertical, and laterl directions, respectively. The p-p values of the displacements of the C.G. of heatbeat system were 5-7, 2-3, and 1-1.5 cm in respective directions.

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OXYGEN SAVING EFFECT OF NEGATIVE WORK IN DOG LEFT VENTRICLE. SUGA, H., YASUMURA, Y., NOZAWA, T., AND FUTAKI, S. National Cardiovasc. Ctr. Res. Inst., Suita, Osaka 565

We studied whether ventricular contractions performing negative work (EW<0) consume less O_2 than normal ejecting contractions both developing comparable systolic pressures. We connected the left ventricle of excised cross-circulated dog hearts to a volume servo pump, and made the ventricle to produce negative work by imposing positive work on it from the pump. We measured both left ventricular myocardial O_2 consumption (Vo_2) and systolic pressure-volume area (PVA) (Suga: Am J Physiol 236: H498, 1979). PVA represents the total mechanical energy generated by contraction. PVA is equal to the area circumscribed by the end-systolic pressure-volume (P-V) line, end-diastolic P-V curve, and the systolic segment of P-V trajectory in the P-V diagram. PVA correlates linearly with Vo_2 in dog left ventricles (Suga et al.: Circ Res 53: 306, 1983). For comparable systolic pressures of about 90 mmHg, contractions with negative EW of -613 $\pm$ 243 mmHg ml had 27 $\pm$ 11% smaller Vo_2 and 62 $\pm$ 12% smaller PVA than contractions with EW of 624 $\pm$ 240 mmHg. Vo_2 closely correlated with PVA regardless of the polarity of work. We conclude that contractions with negative work develop systolic pressure more economically than ejecting contractions. The amount of saved Vo_2 by the negative work is predictable from the decrease in PVA. (Partly supported by 60C-3 from MHW and B61480102 from MESC)

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RELATION BETWEEN OXYGEN CONSUMPTION AND PRESSURE-VOLUME AREA OF IN SITU DOG HEART. NOZAWA, T., YASUMURA, Y., FUTAKI, S., SUGA, H. National Cardiovascular Center Research Institute, Osaka 565

We have shown that the systolic pressure-volume area (PVA) linearly correlates O_2 consumption (Vo_2) in the excised cross-circulated left ventricle. In the present study, we studied the relation between Vo_2 and PVA in the left ventricle of open-chest, right-heart-bypassed dogs. PVA and Emax were determined by an abrupt occlusion of the ascending aorta (Am J Physiol 250: H685, 1986). Vo_2 was obtained as the product of total coronary flow and arteriovenous O_2 content difference. Vo_2 linearly correlated with PVA in control contractile state regardless of pharmacological denervation. Enhancement of contractile state by dobutamine increased Emax by 60-80% and shifted the Vo_2-PVA line upward, increasing the Vo_2 axis intercept by 38% with intact reflexes and by 79% with blocked reflexes. The slope of the Vo_2-PVA relation had a tendency to increase with dobutamine, but the increase was statistically insignificant. PVA and Emax obtained by the aortic occlusion method can account for changes in Vo_2 with changes in loading conditions and contractility in an in situ dog heart.

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HEMODYNAMIC CORRELATION BETWEEN STENOTIC AND PERIPHERAL CIRCULATION

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The stenotic segment of arteries, such as coronary arteries, may exhibit a change in geometry and size, reponding to the blood pressure. Such severe stenosis will have an important influence on the regulation of the organ circulation.

We simulated the hemodynamic correlation between a compliant severe stenosis and its peripheral circulation, using a two-compartment approximation of the stenosis and the peripheral vascular system and fluid-dynamic theory of the stenotic flow.

Our simulation showed that when the peripheral vascular resistance was decreased, the blood flow was increased gradually and decreased beyond a critical value. It is suggested that a severe stenosis with compliance of the coronary artery may induce a paradoxical change of flow with a change in the peripheral vascular resistance.

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MEASUREMENT OF TISSUE BLOOD FLOW WITH LASER DOPPLER FLOWMETRY

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A single fiber laser Doppler tissue flowmeter was developed and evaluated. A optical fiber (500 um in diameter) is used for both transmitting and receiving the light. The light emerging from the fiber tip is scattered and the backscattered light is again partially collected by the same fiber tip and transmitted to two photodetectors. The photodetector signals are fed to a differential amplifier and a signal processor. The flowmeter was evaluated using a fluid model. In in-vivo studies, the laser Doppler flowmetry was compared with the hydrogen clearance technique. The results obtained from the fluid model verified earlier results, i.e. that the laser Doppler output is proportional to the product of the velocity of erythrocytes and the hematocrit. The laser Doppler flowmetry and hydrogen clearance output showed a correlation coefficient of R= 0.838. Postocclusive reactive hyperemia could easily be seen in the laser Doppler flowmetry. Although it is difficult to calibrate this system in absolute terms the laser Doppler tissue flowmeter is effective to measure the blood flow especially dynamic response of tissue blood flow. This technique generates a very small trauma in comparison with earlier developed methods.

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NONINVASIVE MEASUREMENT OF REGIONAL MYOCARDIAL BLOOD FLOW WITH SHORT-LIVED RADIONUCLEIDS.

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With deveoping devices of positron emission tomography,we were able to quantify the absolute regional myocardial blood flow .We studied two methods in order to do that.The first,it was first dynamic study with $^{13}NH_3$ bolus intravenous injection ,and the second ,was steady-state technique of $C^{15}O_2$ gas continuous inhalation. So that the values of the regional myocardial blood flow were 40～110ml/min/100g by the two methods in patients with hypertrophic cardiomyopathy ,who had left ventricular wall thickness rather than 20～25mm. The partial volume effect can be excluded by this thicknesses.

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NONINVASIVE MEASUREMENT OF FREQUENCY RESPONSE OF ELASTIC PROPERTIES IN HUMAN FINGER ARTERY. Shimazu,H.*, Kinoshiata, S.**, Hiraiwa, A.**, Ito, H.* and Yamakoshi, K.*** *Dept. of Physiol. Kyorin Univ. Sch. of Med. ** Dept. of Mechanical Engng. Waseda Univ. ***Hokkaido Univ.

A noninvasive method to measure the volume elastic modulus (Ev= $\Delta P/(\Delta V/V)$) in human finger arteries was developed. The volume change ratio ($\Delta V/V$) and pulse pressure (ΔP) in the artery were simultaneously determined by a transmittance type of infrared photoelectric plethysmograph and a new type of volume oscillometric technique. The Ev values were obtained at a desired transmural pressure (Pt) level of the arteries which were controlled with the cuff. A clear difference were revealed among the Ev values obtained in the fingers of subjects with different age and sex. The dynamic mechanical properties of the finger artery was also investigated by this technique. The "transfer function" was calculated as the volume change vs. Pt within 0-30 Hz frequency range. Thus, the frequency characteristics of Ev could be detected, and its changes by physiological stress were examined. This should be a useful noninvasive technique of evaluating the changes in arterial elasticity accompanying aging, physiological stress or arteriosclerosis.

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PULSE WAVE PROPAGATION VELOCITY BASED ON THREE COMPONENT MODEL. Osamu OKAI, Yuzo HIGUCHI and Kazumi MAKINO, Department of Physiology, Kyorin University School of Health Sciences, Miyashita 476, Hachioji, Tokyo.

Thus far, pulse wave propagation velocity is thought to be mainly due to the elasticity of the vessel wall. In our analysis an aortic resistance (r) is newly introduced in addition to the elasticity (reversed compliance c), leading to a component of the three component model that the authers previously reported; that is, the equation of the velocity is expressed $v = (w/(c.r))1/2.L$ --- (1) where L is an effective length of the arterial system and w frequency. The equation (1) is based on the lumped parameter model i.e. the three component model derived from the distributed model which is theoretically similar to the arterial system. The validity of the equation (1) was derived from an animal experiment; when various conditions were induced by infusion with acetylcholine, noradrenaline and isoproterenol, and by insertion of a catheter into the aorta, the aortic resistance was increased. Then the pulse wave propagating velocity was decreased. This may be true because the denominator of the equation (1) is increased under these conditions.

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COHERENCE ANALYSIS BETWEEN ARTERIAL PULSE WAVE AND CARDIAC-RELATED SYMPATHETIC ACTIVITY. KIMURA, N., KATO, F. AND HUKUHARA, T., Jr. Department of Pharmacology II, The Jikei University School of Medicine, Minato-ku, Tokyo 105.

Effects of sino-aortic denervation and passive postural changes on the relationship between arterial pulse wave and cardiac-related sympathetic activity were analyzed by using coherence function in vagotomized rabbits anesthetized with ether, immobilized with gallamine triethiodide, and ventilated artificially. Values of the coherence function between arterial pulse wave and renal sympathetic nerve activity were measured at a cardiac rhythm frequency (4 to 5 Hz) (These values are refered as Coh). Carotid sinus and aortic depressor nerves were sequentially cut. Before the sino-aortic denervation, The Coh was 0.89 ± 0.05 (mean $\pm$ SD, n=4). After cutting one, two, and three out of the four sino-aortic nerves, the Coh became 0.93 ± 0.02 (n=4), 0.92 ± 0.01 (n=4), and 0.87 ± 0.07 (n=8), respectively. When all the reflex loops were opened, the Coh steeply decreased to 0.26 ± 0.12 (n=12). When either side of the depressor nerves was intact, the Coh was 0.91 ± 0.07 (n=4). When either side of the sinus nerves was intact, the Coh was 0.83 ± 0.06 (n=4). The above Coh were measured when the mean arterial pressure recovered close to the level before denervation. In animals with intact sinus and/or aortic nerves, the 30° head-up tilt induced a decrease in the Coh and arterial pressure. The 30° head-down tilt induced an increase in the Coh.

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NEURAL MECHANISM OF THE RENAL-SYMPATHETIC REFLEX IN RABBITS. SAEKI,Y., TERUI,N., AND KUMADA,M. Institute of Basic Medical Sciences, University of Tsukuba, Ibaraki-ken 305, Japan

In urethane-anesthetized and vagotomized rabbits, afferent stimulation of the renal nerve(RN) elicited a reflex response in the efferent renal fibers. The response, attributable virtually entirely to non-myelinated afferent fibers, consisted of an inhibitory component, an excitatory component or combination of the two. It was accompanied by a change in arterial pressure determined by the relative size of inhibitory and excitatory components. A reflex response of a comparable magnitude was observed in efferent cardiac sympathetic fibers, whereas the response in cervical sympathetic fibers was minute. We then examined 45 barosensory ventrolateral medullary(VLM) neurons for their responses to afferent stimulation of the RN. (For definition of barosensory VLM neurons, see Terui et al. Jpn. J. Physiol.36:1141, 1986) They were also tested for antidromic activation by stimulating descending bulbospinal axons. Stimulation of the RN evoked responses in 88% of these barosensory VLM neurons, of which 57% responded additionally to antidromic stimulation. None of the five non-barosensory VLM neurons which responded to stimulation of the RN were antidromically activated. In view of the fact that barosensory VLM neurons subserved the arterial baroreceptor-sympathetic reflex through their descending spinal axons, it was suggested that the renal-sympathetic reflex was also mediated by barosensory VLM neurons.

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EFFECTS OF CAROTID SINUS NERVE STIMULATION ON NEURONES IN THE NUCLEUS TRACTUS SOLITARII PROJECTING TO THE ROSTRAL VENTROLATERAL MEDULLA. TANAKA, Y. AND HIRAI, N. Dept. Physiol., Nihon Univ. Sch. Med., Itabashi, Tokyo 173.

The relation among the rostral ventrolateral medulla (pressor area, RVLM), the nucleus tractus solitarii (NTS) and the carotid sinus nerve (CSN) in the blood pressure regulation was investigated in adult cats anaesthetized with ketamine and α-chloralose. Preparations in which electrical stimulation of the CSN (50Hz, 0.3ms, 10sec) induced pressor response were only used in this study. While monitoring blood pressure, stimulating electrode was placed in the RVLM. Forty-five neurones being responded antidromically to RVLM stimulation were recorded in the NTS (0.5-1.0 mm rostral to the obex). CSN stimulation activated 16 of these neurones with the mean latency of 5.9 msec. Occlusion of the common carotid artery yielded the increase in the activity of some neurones in advance of the pressor response. Microstimulation (<20 μA) of the NTS where the neurones were recorded in clusters, induced the pressor response. These results suggest that the NTS involves the pressor region relaying the volleys in the CSN to the RVLM.

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ROLES OF THE VENTROLATERAL MEDULLA OBLONGATA IN THE CHANGE OF BLOOD PRESSURE INDUCED BY STIMULATION OF THE TRIGEMINAL NERVE. HIROSE, Y., KATAKURA, N., KUBOTA, Y. AND NAKAMURA, Y.* Depts. Dent. Anesthesiol. and Physiol.*, Fac. Dent., Tokyo Med. Dent. Univ., Bunkyo-ku, Tokyo 113

The ventrolateral medulla oblongata is regarded as a major site of blood pressure (BP) regulation. We studied the role of this medullary region in the BP change induced by stimulation of a sensory branch of the trigeminal nerve (the inferior alveolar nerve, IA) in chloralose-anesthetized, paralyzed cats. The results are as follows: 1) Systematic microstimulation studies of the medulla revealed that the most remarkable change in the arterial BP was induced from the region from 2 mm rostral to 1 mm caudal to the obex, about 4 mm lateral to the midline, 2 mm above the ventral surface of medulla. The site corresponded to the dorsal portion of the lateral reticular nucleus and its dorsally adjacent region. 2) IA stimulation evoked a long-lasting negative field potential superimposed by a burst of unitary discharge in this region. 3)IA stimulation induced a BP rise concomitant with an increase of spike firing of the neurons in the ventrolateral medualla, whose stimulation induced a BP elevation. 4) A lesion in the ventrolateral medulla caused a striking reduction of the BP rise induced by stimulation of the ipsilateral IA as well as a slight fall of the resting BP level. The results suggest that the ventrolateral medulla plays an important role in the BP change induced by IA stimulation.

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DESCENDING PATHWAYS MEDIATING FOREBRAIN INHIBITION ON BAROREFLEX VAGAL BRADYCARDIA IN RATS. NOSAKA, S. AND MURATA, K.※ Dept. Physiol., Mie Univ. Sch. Med., Mie 514

Baroreflex vagal bradycardia is suppressed during defence reaction. In chloralose-urethane anesthetized rats, descending pathways responsible for the inhibition was localized. Consistent beta blockade was achieved by continuous infusion of propranolol. Hemivagotomy was conducted to confine the target vagal structure to one side. It was found that vagal bradycardia provoked by electrical stimulation of the aortic depressor nerve (ADN) ipsilateral to the target vagal structure, was suppressed by electrical stimulation of either ipsilateral or contralateral hypothalamic defence area (HDA). Hemitransection of the midbrain contralateral to the ADN stimulated, almost abolished inhibitory action of contralateral HDA. Midline incision along the entire brain stem eliminated inhibitory action of contralateral HDA. Inhibitory action of ipsilateral HDA was abolished by electrolytic destruction of the parabrachial region. In contrast, at caudal pontine level, extensive lesioning of the lateral reticular formation was required to abolish inhibitory action of ipsilateral HDA. In conclusion, descending pathways mediating HDA inhibition were bilateral. Contralateral pathway crosses the midline mostly in the brain stem level. Ipsilateral pathway courses through the parabrachial region at rostral pontine level, and then is dispersed to descend through a wide area in the lateral reticular formation at caudal pontine level.

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CHARACTERISTICS OF THE CULTURED MULTIPOLAR NEURONS WHICH RESPONDED TO NORADRENALINE IN SHR AND WKY RATS. OKADA, J. AND MIURA, M. Dept. Physiol., 1st Div., Gunma Univ. Sch. Med., Maebashi 371

By using cultured neurons of the lower brainstem of rat embryos, we discovered that the mode of response of the multipolar neurons to catecholamines differs significantly between spontaneously hypertensive rats (SHR) and Wistar-Kyoto (WKY) rats. In this study, we compared the mode of response of the multipolar neurons of the other brain structures to noradrenaline between SHR and WKY rats. (1) No significant difference between both strains was observed in the neurons derived from the thalamic brain ($P<0.04$), midbrain ($P<0.02$), and spinal cord ($P<0.4$) (Neurosci. Res., Suppl., in press, 1987), while significant difference between both strains was observed in the neurons of the lower brainstem ($P<0.001$) [Brain Res., 399, 1986]. (2) No significant difference between both strains was observed in the neurons derived from the dorsal half and ventral half of the lower brainstem. (3) When the cultured neurons of the lower brainstem of 15-day-old embryos were stained by antiserums to DBH and PNMT, about 20% of neurons from each strain were positive for DBH, while about 10% of those neurons positive for PNMT. In common with both strains, the multipolar neurons which responded to noradrenaline showed low immunoreactivity to DBH and PNMT.

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POSTNATAL DEVELOPMENT OF AORTIC BAROREFLEX MECHANISM. SHIMIZU, T., YAMASAKI, M., KANNO, T. and NAGAYAMA, T. Dept. of Physiol., Fukushima Med. Coll., Fukushima 960

We measured previously the magnitude of the brain ischemic reflex bradycardia and examined the structure of the aortic nerve under an optical microscope in anesthetized rabbits at different ages. It was found that the magnitude of the reflex bradycardia at the maximal elevation of arterial pressure and the number of myelinated aortic nerve fibers increased as a function of age up to around 8 weeks after birth. In the present study, the structure of aortic nerve was electron microscopically observed. The aortic nerve was bilaterally cut off immediately after perfusing the cervical region with Karnowsky's solution in 4 rabbits per group aged 1 day, 5, 28, 56 and 168 days. An average of the number of myelinated fibers in the left aortic nerve was 218 ± 72.8 in 1 day group and 492 ± 79.5 in 56 days group which was 95.4% of that in 168 days mature group. The number of myelinated fibers significantly correlated with the basal mean arterial pressure. The sensitivity of the aortic baroreflex system, however, seems to be not different between these groups when the previous data were reexamined. The result suggests that the magnitude of basal arterial pressure may affect myelination of aortic nerve afferent fibers and the aortic baroreflex mechanism develops functionally and anatomically into the mature pattern around the age of 8 weeks in rabbits.

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NEUROGENIC CONSTRICTION OF THE ANESTHETIZED RABBIT PORTAL VEIN CAUSED BY CEREBRAL ISCHEMIA. TAKEUCHI, T., HORIUCHI, J. AND TERADA, N. Dept. of Physiol., Yamanashi Med. Col., Tamaho, Yamanashi 409-38

Blood mobilization by the rabbit portal vein during graded cerebral ischemia was studied in normo-, hypo- and hyper-volemia. After the route of blood supply to the brain was surgically restricted to the right internal carotid artery, the artery was compressed with a micrometer so as to regulate the right internal carotid arterial flow (ICF) at six different levels of 0, 1, 2, 3, 4 and 6 ml/min. The rabbits were immobilized with Flaxedil and ventilated with a respirator after the bilateral aortic and sinus nerves were severed. Blood and Dextran solution 0.6% of the body weight were depleted (0.6% hemorrhage) and injected (0.6% volume loading), respectively. The portal venous segment volume (PVV) recorded by plethysmography began to decerase when the ICF reduced lower than 4 ml/min in all volemic states. The maximum decrease of the PVV caused by complete interruption of blood supply to the brain was -83±13 (mean± SE) mm^3 (-26%) of the original volume of 321±13 mm^3 in normovolemia, -58±18 mm^3 (-20%) of 294± 13 mm^3 after 0.6% hemorrhage and -111±22 mm^3 (-31%) of 361±10 mm^3 after 0.6% volume loading. Such the maximum decrease of the PVV in normovolemia was mainly produced by neurogenic factor (95%) and the rest was thought to be humoral.

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FIXED-ACTION PATTERNS FOR CARDIAC OUTPUT REDISTRIBUTION.
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Observations in conscious rats with electromagnetic flow probes chronically implanted at peripheral arteries showed that the increase in carotid flow during spontaneous grooming, accompanying profuse salivation, was stereotypically compensated for by a decrease in hindquarter (terminal aortic) flow induced by excitation of regional vasoconstrictor fibers. On the other hand, the adrenomedullary beta-adrenergic increase in hindquarter flow in the transposition response, induced by transposing the rat from the home cage to a new cage, was compensated for by a mostly neural decrease in superior mesenteric and renal flows. A fixed-action pattern program including excitation of regional sympathetic vasoconstrictor fibers via separate descending pathways, besides motor behavior, accelerator excitation, adrenomedullary secretion, and parasympathetic discharge, is hypothesized for either response.

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PARTICIPATION OF CENTRAL OPIOID RECEPTORS IN CONTROL OF THE PORTAL AND RENAL SYMPATHETIC NERVE ACTIVITIES DURING GRADED CEREBRAL ISCHEMIA. HORIUCHI, J., TERADA, N. AND TAKEUCHI, T. Dept. of Physiol., Yamanashi Med. Col., Tamaho, Yamanashi 409-38

The role of central opioid receptors on the portal (PNA) and renal (RNA) sympathetic nerve activities was studied during graded cerebral ischemia. Sympathetic nerve activation and systemic arterial pressure (SAP) rise were produced by cerebral ischemia in urethan-anesthetized rabbits. Injection of naloxone into the fourth ventricle (0.1mg/kg) increased SAP by 15.3+1.4% (mean+SE), PNA 22.0+1.4% and RNA 23.9+2.0% in bilateral aortic nerves (AN) intact group and SAP by 27.8+3.2%, PNA 34.9+0.4% and RNA 29.8+4.8% in the AN denervated group, respectively. The maximum value of PNA appeared earlier (4.2+0.9 sec) than that of RNA caused by interruption of blood supply to the brain in all groups. The naloxone injection significantly augmented the rate of RNA increase produced during graded cerebral ischemia in the intact group. This augmentation completely disappeared after the AN denervation. These results indicated that the inhibitory effect of the AN on the renal sympathetic nerve activity was mediated by central opioid receptors.

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NEURAL MECHANISMS OF CARDIOVASCULAR REFLEX RESPONSES DURING CHEMORECEPTOR EXCITATIONS. FUKUDA,Y., SATO,A., SUZUKI,A.* and TRZEBSKI,A.*
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Excitation of arterial chemoreceptor has been known to cause changes in blood pressure and heart rate. We are interested in analyzing the neural mechanisms of these reflex responses. For this purpose, we used anesthetized and immobilized animals in order to eliminate secondary effects of responses of respiratory functions. Parasympathetic and sympathetic nerve innervating heart and renal sympathetic nerve innervating blood vessels were recorded. The inhalation of various low concentrations of O_2 produced marked reflex increases in both cardiac vagal and cardiac and renal sympathetic nerve activities. The inhalation of various high concentrations of CO_2 produced a reflex decrease in cardiac vagal nerve activity and a reflex increase in cardiac and renal sympathetic nerve activity. It is summarized that chemoreceptor excitation elicited by either hypoxia or hypercapnia caused definite changes in cardiac parasympathetic and cardiac and renal sympathetic nerve which is partly reflected changes in blood pressure and heart rate.

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RESPONSE IN MUSCLE SYMPATHETIC NERVE ACTIVITY AND VENTILATION TO SYSTEMIC HYPOXIA AND HYPERCAPNIA IN HUMAN SUBJECTS. SAITO, M., OHYABU, Y., IWASE, S. AND MANO, T., Toyota Tech. Inst., Tempaku-ku Nagoya 468, Kogakuin Univ., Nishisinjiku Tokyo 160, Nagoya Univ., Chikusa-ku Nagoya 464.

In animal experiments, the stimulation of arterial chemoreceptors lead to an excitation of muscle vasoconstrictor neurons. We attempted to confirm whether this occurs in conscious human subject. For this object, the activity of sympathetic nerve suppling the skeletal muscle in the leg was recorded by microneurographic technique from the tibial nerve during various steady states of hypoxia (HPX; to 45 mmHg of PETo2), and hypercapnia (HPC; to 60 mmHg of PETco2), which were lasting for 3 min. During the experiments, heart rate, ventilation and end-tidal Po2 and Pco2 were also monitored. Muscle sympathetic activity(MSA) expressed as burst rate was increased significantly by 24% during HPX. During HPC, however, there was no difference in the average value of MSA burst rate from the control value. The increase in tidal volume and respiratory rate were smaller during HPX(61 and 7%) than those during HPC(176 and 67%). The results suggest that the muscle sympathetic nerve is activated by the chemoreflex during hypoxia also in humans. During hypercapnia, however, this activation seems to be masked, in part, by the reflexes from the pulmonary and/or intrathoracic receptors.

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CHANGES OF MUSCLE TEMPERATURE, VENOUS OUTFLOW AND THE HEMATOCRIT IN RABBIT HINDLIMBS DURING HYPOXIA. IFUKU, H., ITO, H., ANDO, S.* AND TAKEMIYA, T. Div. of Physiol. Inst. of Health & Sports Sci., Univ. of Tsukuba, Sakura, Niihari, Ibaraki 305

It has been reported that vasodilation induced by hypoxia produce a slight increase of hematocrit whereas hyperoxia and/or sympathetic vasoconstriction cause the decrease of hematocrit. Experiments were tried to follow again in the vital hindlimb preparation of rabbits anesthetized with urethane. Systemic hypoxia was produced by 5 min inhalation of 5% oxygen mixtures, and muscle core temperature by thermocouple, total blood flow from the muscle by drop counter, hematocrit by capillary tube and total plasma protein concentration by refractometer were measured simultaneously. Hypoxia produced significant increase of muscle temperature in intact preparation, but the blood flow and hematocrit showed no marked increase. In the denervated preparation, increasesof muscle temperature, blood flow and hematocrit were not observed. Pure oxygen inhalation showed no marked change. These data suggest that hypoxia produces vasodilation through the decreasing activity of sympathetic vasoconstrictor, and plasma fluid shifts tend to occur.

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DIFFERENT CHANGES IN CARDIAC AND RENAL SYMPATHETIC NERVE ACTIVITY DURING CORONARY OCCLUSION IN THE AWAKE CAT. NINOMIYA, I., MATSUKAWA, K., HONDA, T., AND NISHIURA, N. Department of Cardiac Physiology, National Cardiovascular Center Research Institute, Suita, Osaka.

This study was undertaken to scrutinize the difference in the response of cardiac sympathetic nerve activity (CSNA) and renal sympathetic nerve activity (RNA) to coronary artery occlusion. The magnitudes and time courses of percent changes in CSNA and RNA, recorded simultaneously in 8 cats, were compared with each other during 100-s occlusion of the left anterior descending coronary artery in awake state. Response patterns in CSNA and RNA differed significantly. CSNA increased more drastically than RNA at the early stage of occlusion (10-40 s) associated with excitement and/or body movement. At 40 s of occlusion, CSNA increased maximally by 27±14% (mean ± SE) whereas RNA unchanged. Arterial pressure and heart rate decreased to 85±6 mmHg and 149±6 bpm from 116±5 mmHg and 172±5 bpm of the preocclusion values, respectively. At 90 s of occlusion, CSNA and RNA decreased by 8±9% and 26±11% while arterial pressure and heart rate decreased to 78±8 mmHg and 135±6 bpm. We concluded that RNA was inhibited significantly more than CSNA by cardiac reflex.

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THE TIME COURSE OF THE ARTERIAL BLOOD PRESSURE CHANGES CAUSED BY HEAD-UP TILT, ESPECIALLY RELATED TO SYMPATHETIC TONE. TAKEO,T.,OZAKI,T.,SUGA, S.,IGARASHI,K*.,YOZA,H.,TANNO,T.,AKITSU,H. and HASEGAWA,N. Dept. of Physiol., Hirosaki Univ.Sch.of Med.Hirosaki Univ.,Hirosaki and National Sanat.Iwaki Hosp.,Namioka

In the present report, the temporal course of the arterial blood pressure changes caused by tilting from supine and horizontal position to 60° head-up position were studied from the standpoint of sympathetic tone. In addition to the blood pressure, pulse, cardiac output(C.O.), total peripheral resistance(T.P.R.) were measured by the pulse wave and Korotkoff sound graph recorder(PARAMA) in healthy adults. The ballistocardiogram, plethysmogram, EEG, ECG were traced simultaneously. Furthermore, the effect of the moderate supine exercises on the blood pressure changes caused by tilting were discussed. The diastolic blood pressure, T.P.R. and pulses were increased by tilting, although the systolic blood pressure and C.O. were scarcely changed. Immediately after exercise, both systolic and diastolic blood pressure were increased slightly by tilting. In some cases, in which T.P.R. were decreased by tilting, pulses and C.O. increased considerably. From the above results, it seems to be likely that the blood pressure changes caused by head-up tilting may be due to mainly sympathetic vasomotor and partially cardioinhibitory reflexes, that were shown in increased T.P.R. and diastolic blood pressure and increased pulses and C.O., respectively.

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SIGNIFICANCE OF CARDIAC INNERVATION FOR SYSTEMIC ARTERIAL PRESSURE OSCILLATION. KANEKO,M. AND MIYAKAWA,K. the 2nd Dept.of Physiol., Sch.Med., Shinshu Univ., Matsumoto 390

Significance of the innervation of the heart for the production of systemic arterial pressure oscillation(SAPO) was studied by intravenous injection of atoropine and β-blocker in rabbits. SAPO was elicited by the "side pressure exertion procedure". By the injection of doses of metoprolol or propranolol the oscillation was subjected to a decrease in wave height and in gradient of the ascending limb of each wave. By the use of larger doses or repetitions of the injections the oscillation became smaller and disappeared. Atropine gave two kinds of effects on the oscillation, namely depressive and facilitatory ones. In former cases it decreases the gradient and diminished the wave height, eliminating the oscillation at last. In a few cases of the latter effects, atropine enlarged the oscillation. In cocnlusion, it can be said that without the innervation of the heart, the SAP oscillation can not be maintained. SAP is the product of the cardiac output and total peripheral resistance. The oscillation can not be elicited solely by the periodic change of the total peripheral resistance, but by the concomitant periodic change of cardiac output which was effected by its autonomic innervation. Once the heart is detached from the central oscillator, the oscillation can not be maintained any more.

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CEREBRO-VASCULAR EFFECTS OF VASOPRESSIN CARRIED IN THE CEREBROSPINAL FLUID AND IN THE BLOOD. NAKAI, M. AND YAMANE, Y. Natl. Cardiovasc. Ctr. Res. Inst., Osaka 565, and 2nd Dept. of Medicine, Kan-sai Med. Univ., Osaka 570.

First, the effects of vasopressin in cerebrospinal fluid on the diameter of brain arteries were examined. Perivascular application of vasopressin with a cranial window technique resulted in a dose-dependent contraction of the brain pial artery in 15 cats. The threshold concentration for contraction was 3×10^{-10} M, the ED_{50} ($1.6 \pm 0.2)\times10^{-9}$ M, and the maximum reduction in artery diameter 37 $\pm$ 2%. The contraction was inhibited by the vasopressin antagonist. Perivascularly-applied-noradrenaline-induced contraction was not modified at all in the presence of vasopressin. In the subsequent series of experiments, the responses of cerebral blood flow to a reflex increase in plasma vasopressin induced by hemorrhagic hypotension were studied. The induced hypotension (74 to 76 mmHg) was above the lower limit of the cerebrovascular autoregulation. The blood flow was determined by the radiolabelled microsphere technique. Hypotension increased the plasma vasopressin level from 58 $\pm$ 10 pg/ml in normotensive state to 197 $\pm$ 29 pg/ml. Although a size of a difference did not reach the statistical significance, the vasopressin antagonist i.v. lowered the cerebral cortical blood flow observed in the hemorrhagic hypotension from 127 ml min^{-1} 100 g^{-1} in the control experiment to 92 ml min^{-1} 100 g^{-1}.

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EFFECTS OF ALPHA-HUMAN ATRIAL NATRIURETIC POLYPEPTIDE ON CORONARY CIRCULATION IN CONSCIOUS DOGS. UEMURA, N., MORITA, H., MOTOCHIGAWA, H., YOSHIDA, H., KAWADA, M., TSUCHIYA, K., NAKAMURA, J., AND HOSOMI, H.
Dept. Physiol., Kagawa Med. Sch., Kagawa 761-07

The present study was designed to evaluate the effects of alpha-human atrial natriuretic polypeptide (α-hANP) on coronary circulation in conscious dogs. Thirteen dogs, 6 dogs with intact cardiac nerves and 7 dogs with intrapericardial cardiac denervation, were chronically catheterized in the descending aorta, left atrium and superior vena cava. A magnetic flow probe was placed at the root of the ascending aorta, and an ultrasonic flow probe on the left circumflex coronary artery. The urinary bladder was catheterized retrogradely with a Foley catheter. Synthetic α-hANP (0.3μg/min/kg body weight) was infused intravenously for 20 minutes. In intact dogs, urine flow and excretion of Na and K were significantly increased. Left atrial pressure, cardiac output, mean arterial pressure and coronary blood flow were significantly decreased. Cardiac denervated dogs also showed similar results. These findings suggest that α-hANP first decreased preload, which resulted in a decrease in mean arterial pressure and cardiac output, leading to the observed decrease in coronary blood flow. Secondly, that during infusion of α-hANP, coronary blood flow was not decreased by the cardiac nerves.

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EFFECTS OF ATRIAL NATRIURETIC POLYPEPTIDE ON ISOLATED VASCULAR SMOOTH MUSCLES. KAWAI, Y. AND OHHASHI, T.
Dept. Physiol., Shinshu Univ. Sch. Med., Matsumoto 390

Effects of atrial natriuretic polypeptide (ANP) on isolated monkey, rabbit and dog arteries and veins were investigated. Addition of ANP caused a concentration-dependent relaxation in these preparations precontracted with norepinephrine, 5-hydroxytryptamine or prostaglandin $F_{2\alpha}$. The relaxant response of internal carotid arteries to ANP was greatest in monkeys, moderate in rabbits and least in dogs. Such species difference was also found in the other arterial preparations. There was a marked regional difference in the response of monkey arterial preparations to ANP. The decreasing order of the response was as follows : renal >> pulmonary ≧ femoral = carotid = mesenteric >> middle cerebral > basilar arteries. The threshold concentration for the ANP-induced relaxation in monkey renal arteries was about 10^{-12} M. The affinity of middle cerebral and basilar arteries for ANP was 100 - 1000 times lower than that of renal arteries. In general, the responses of monkey veins to ANP were smaller than those of their accompanying arteries. The decreasing order of the response in monkey veins was as follows : pulmonary > portal = mesenteric > femoral > renal > inferior caval veins. These results suggest that there are marked species and regional differences in the response of isolated vascular smooth muscles to ANP.

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EFFECTS OF VASOACTIVE SUBSTANCES ON THE FLOW RESISTANCE THROUGH VASA VASORUM

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We previously reported a new preparation to measure the changes of flow resistance through vasa vasorum in the isolated canine thoracic aorta. In this study, effects of vasoactive substances on the flow resistance through vasa vasorum were attempted to evaluate in the preparation.

5-Hydroxytryptamine (5-HT, 10^{-8}-10^{-6}M), norepinephrine (10^{-7}-10^{-5}M), epinephrine (10^{-7}-10^{-5}M) and dopamine (10^{-6}-10^{-4}M) increased dose-dependently the flow resistance. On the other hand, many kinds of vasodilators, isoproterenol (ISP, 10^{-7}-10^{-5}M), adenosine, ADP, ATP (10^{-5}-10^{-4}M), acetylcholine (ACh, 10^{-7}-10^{-5}M), histamine (His, 10^{-6}-10^{-4}M) and sodium nitroprusside (10^{-9}-10^{-5}M), decreased dose-dependently the flow resistance. Pretreatment with methysergide (10^{-9}-10^{-6}M), propranolol (10^{-8}-10^{-6}M), famotidine (10^{-9}-10^{-6}M) and atropine (10^{-9}-10^{-7}M) reduced dose-dependently the 5-HT- and ISP-, His- and ACh-induced increase and the decrease of flow resistance, respectively.

These results suggest that the flow resistance through vasa vasorum is increased by the stimulation of 5-HT receptors and decreased by the stimulation of beta, H2 and muscarinic receptors. Thus, circulating vasoactive substances may play a role in regulation of flow resistance through vasa vasorum.

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HETEROGENEITY IN RESPONSES TO HISTAMINE IN ISOLATED MONKEY PULMONARY VEINS.

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The present study was attempted to elucidate regional differences in responses of isolated monkey intra- (IPV) and extra-pulmonary veins (EPV, mediastinal space portions) to histamine (Hist). Hist caused concentration-dependent contractions in the IPV and EPV. The maximal tension in EPV was significantly smaller than in IPV. Hist (10^{-8} – 10^{-4} M) and 2-pyridilethylamine (H_1– agonist, 2PEA, 10^{-4} –10^{-3} M) produced a concentration-dependent relaxations in EPV precontracted by the perfusion with 4.2×10^{-6} M $PGF_{2\alpha}$. The Hist- and 2PEA-induced relaxations were completely reduced by removal of the endothelial cells. Dimaprit, a H_2– agonist, also induced marked relaxations in IPV and EPV, being more potent in EPV. The dimaprit-induced relaxation, however, was not attenuated by rubbing of the endothelium.

These results suggest that there is a marked regional difference in the histamine receptors in monkey intra- and extra-pulmonary veins, and that the difference may be, in part, related to distribution differences of H_1– and H_2– receptors in the endothelial and venous smooth muscle cells between EPV and IPV.

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EXISTENCE OF HISTAMINE H_1- AND H_2 RECEPTORS IN LYMPHATIC SMOOTH MUSCLES

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The effects of histamine on spontaneous activity in isolated bovine mesenteric lymphatics were investigated to elucidate the possible role of histamine in the regulation of active lymph transport mechanisms. An administration of histamine caused positive and/or negative chronotropic effects in the rhythm of spontaneous contractions. Pretreatment with α- and β-adrenoceptor blockade did not affect the histamine-induced positive and negative chronotropic effects, respectively. H_1-receptor antagonist, diphenhydramine, inhibited the histamine-induced positive chronotropic effects in a dose-dependent manner. On the other hand, H_2-receptor antagonist, cimetidine, suppressed the negative chronotropic effects. In addition, a H_1-receptor agonist, 2-pyridilethylamine and a H_2-receptor agonist, dimaprit, induced the dose-dependent positive and negative chronotropic effects in the lymphatic spontaneous contractions, respectively. These results suggest that the histamine-induced positive and negative chronotropic effects may be not related to an action of excitation in transmural aminergic nerve fibers, and that the rhythm of spontaneous contractions of bovine mesenteric lymphatics may be accelerated by stimulation of H_1-receptors and suppressed by stimulation of H_2-receptors in the smooth muscles.

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EFFECT OF AORTIC NERVE STIMULATION ON RESISTANCE OF SUPERIOR MESENTERIC ARTERY IN THE RABBIT. MINAMIYAMA, M. AND HANAI, S.. Depart. of Vascular Physiology, National Cardiovascular Center Research Institute, Suita 565

The purpose of this study is to clarify the role of the principal artery (> 0.3 mm diameter) in the mesentery as a resistance vessel during the electrical stimulation of the aortic nerve in the rabbit. Rabbits were anesthetized with urethane and nembutal under the spontaneous respiration. We measured abdominal aortic pressure (Pao), intestinal arterial pressure (Pa) and intestinal venous pressure (Pv) with pressure transducers. We measured blood flow rate through the intestinal artery (Qa) with an electromagnetic flow meter, and calculated the resistance of the mesenteric principal arteries (Ra = (Pao - Pa)/ Qa) and that of intestinal vascular bed (Ri = (Pa - Pv)/ Qa) Ra slightly increased at 10 sec after onset of electrical stimulation of the aortic nerve before bilateral cervical vagotomy, while Ri decreased. Thereafter Ra decreased at 30 sec Ra decreased gradually during hypotension induced by the aortic nerve stimulation. The patterns of Ri changes during reflex hypotension before and after vagotomy was essentially same. We concluded that the principal artery in the mesentery was controlled by vasomotor nerves during the baroreceptor reflex and the profile of the resistance change was modulated by the bilateral vagotomy.

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LOCAL CIRCULATORY RESPONSES IN SMALL PULMONARY ARTERIES TO MICROEMBOLIZATION IN CATS. SHIRAI, M., SADA, K. AND NINOMIYA, I. Department of Cardiac Physiology, National Cardiovascular Center Research Institute, Fujishiro-dai, Suita, Osaka 565, Japan

Pulmonary arterial tree was embolized with 180, 300, 500 or 840 μm glass-beads, and the changes in internal diameter (ID), flow velocity and volume flow of embolized and non-embolized branches were measured using an X-ray TV system in anesthetized cats. A vasoconstriction was observed in embolized branches of 200-800 μm ID, but not in those of 800-1200 μm and in non-embolized branches. The ID constricted maximally in just proximal portions of the emboli by 22, 23 and 17% with 180, 300 and 500 μm beads, respectively. The constriction decreased in the more upstream portions. In the bifurcating portion, volume flow to an embolized branch decreased owing to a decrease in ID and flow velocity, but that to a non-embolized branch increased owing to an increase in flow velocity. We concluded that microembolization of small pulmonary arteries induced a local vasoconstriction in the upstream arteries (< 800 μm ID) of the emboli. Such vasoconstriction contributed to the redistribution of blood flow from embolized to intact arteries.

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CHANGES IN RENAL SYMPATHETIC NERVE ACTIVITY, RENAL BLOOD FLOW, AND ARTERIAL PRESSURE ASSOCIATED WITH EATING IN CATS. MATSUKAWA, K. AND NINOMIYA I. Department of Cardiac Physiology, National Cardiovascular Center, Research Institute, Fujishiro-dai, Suita, Osaka 565, Japan

We analyzed the relationship between changes in renal symapthetic nerve activity(RNA), renal blood flow(RF), and arterial pressure(AP) associated with eating in awake cats. An electomagnetic flow probe was implanted at the left renal artery. The right RNA was recorded by silver-wire electrodes. Eating was evoked for about 30s by presenting food. RNA increased simultaneously with the onset of eating, but AP followed it by 5.5s. RNA and AP increased maximally by 61% and 17%, whereas RF unchanged or slightly decreased during eating. Accordingly, renal vascular resistance(RVR) increased by 29%. The increase in RVR was blocked by phentolamine. In denervated kidney, RVR unchanged at the early period of eating and RF increased passively due to the elevation in AP. Thereafter, RVR gradually increased and RF returned to the pre-eating level. We concluded that at the early period of eating RNA increased RVR and maintained RF constantly, and at the later period hormonal or autoregulatory mechanism seemed to increase RVR.

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EFFECT OF DECREASED CORONARY BLOOD FLOW RATE ON RELATION BETWEEN CARDIAC WORK AND MYOCARDIAL OXYGEN CONSUMPTION IN ISOLATED CANINE HEART.
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To investigate the effect of decreased coronary blood flow rate (CBF) on the relation between cardiac work, expressed as the pressure-volume area (PVA), and myocardial oxygen consumption (MVO_2), and its mechanisms, we measured PVA, MVO_2 and uptake of catecholamine (CA) in the heart under the control CBF and decreased CBF. There was a straight-line correlation between PVA and MVO_2 in the control CBF. The decreased CBF attenuated the intercept of the MVO_2 axis (A) despite no significant changes of the slope of this line and decreased the uptake of CA. These results suggested that decreased CBF attenuated the basal metabolism, i.e., A in the left ventricle due to decrease in the uptake of CA.

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ESTIMATION OF CARDIOVASCULAR DYNAMICS IN AGED SUBJECTS DURING HEAT EXPOSURE.
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Gerontological changes in cardiovascular and thermoregulatory responses to passive tilting were investigated using six old (61-73 yr) and 10 young (21-39 yr) men at 26 and 40°C of ambient temperature. After an hour of resting, subject lay supine for 15 min followed by a 70 degree head-up tilt for 15 min at 26°C, and same protocol was repeated successively at 40°C. Continuous measurements of esophageal temperature (Tes) and heart rate (HR) were made during two positions, in addition, blood pressure (BP), forearm blood flow (FBF) and cardiac output (CO) were measured at 4-5 min intervals. At 26°C, sudden redistribution of blood flow by head-up tilt elicited anti-hypotensive responses such as significant increase of HR or remarkable decrease in FBF in young men and thus CO remained unchanged with transient fall of systolic BP, while no cardiovascular responses seemed to be elicited in old men. During heat exposure, increased values of HR, CO and FBF with a drop in BP were observed in supine position in both age groups, but subsequent head-up tilt diminished FBF and systolic BP only in young men. Tes rose in response to tilting in both age groups at each ambient temperature. These findings suggest the sympathetic nerve reflex of aged men might deteriorate as a response to orthostatism, however it was well-driven by thermal stimulation.

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HEMODYNAMIC CHANGES CAUSED BY POSTURING KNEE CHEST POSITION FROM STANDING.
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In hypoxia attack many patients are known to often posture knee chest position. In the present report, the temporal course of the hemodynamic changes caused by posturing from standing to knee chest position were studied from the standpoint of heart rate, stroke volume, cardiac output and total peripheral resistance in 12 subjects without any circulatory disturbance. In addition to the arterial blood pressure, heart rate, stroke volume, cardiac output, total peripheral resistance were noninvasively measured by the pulse wave and Korotkoff sound graph recorder (GP-303S, PARAMA, TOKYO) about 1, 5, 10 and 15 minutes after posturing knee chest position from standing for 5 minutes. The systolic and diastolic blood pressure were unchanged by posturing knee chest position. Cardiac output and stroke volume were slightly increased, whereas heart rate and total peripheral resistance were decreased. From the above results, it was suggested that increased stroke volume and cardiac output were caused by increased venous return and the following strengthening of ventricular contraction, whereas decreased total peripheral resistance might be due to increased cardiac output.

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CHANGES IN PLASMA CATECHOLAMINES UNDER ACUTE AND CHRONIC EXPOSURE TO HYPOBARIC HYPOXIA.
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Studies were made on plasma catecholamines (NE, E, DA, L-DOPA) in five healthy subjects staying for three days at the summit of Mt. Fuji (3,770 m) and five staff members of the weather station there. NE at rest increased by twice on average with ascending to the summit but returned to the pre-climbing level in three days, i.e. before descending. E varied similarly but with a delay to NE. DA and L-DOPA showed large fluctuations during the stay. NE and E in the staff were higher and lower, respectively, in comparsion with the values in the subjects before climbing or just before descending. It appeared, therefore, that the NE once decreased would again increase to around the sustained high level and the E would further decrease if the stay of those subjects became comparably long. The systolic arterial blood pressure in the subjects decreased considerably with the ascending, while their diastolic blood pressure remained unchanged. Its return toward the pre-climbing level was only slight or appeared absent even if stayed longer. Alterations in hemodynamics in the subjects probably associated with the decrease in systolic blood pressure were suggested from continuing decreases in total plasma proteins and very large decreases in WBC count.

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RESPONSES IN THE CARDIAC SYSTEM OF β_1-BLOCKED HAMSTERS EXPOSED TO -Gz ACCELERATION.
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The responses of the cardiac system of the slightly anaesthetized hamsters to -Gz acceleration (tail to head, 4G and 6G) were examined after their β_1-receptors were blocked by Atenolol. Electrocardiogram and impedance plethysmogram were recorded through a telemeter. The procedure of the experiment was the same as reported in the last meeting. The heart rate maintained the control level during the initial stage of -Gz exposure, and thereafter decreased slightly. While the stroke volume decreased remarkably during -Gz exposure, and it returned to the control level immediately after the cessation of the exposure. The cardiac output also decreased to 80% during -4Gz, and to 73% during -6Gz exposure. The decrease of the cardiac output was probably resulted from the shift of body fluid. The changes in the cardiac system of β_1-blocked hamsters were similar to those of the bilateral labyrinthectomized animals than to those of the intact ones, which has already reported elsewhere. It is supposed that the vestibulo-autonomic system contributes to the cardiac responses due to -Gz acceleration.

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THE DEPRESSOR EFFECT OF SECRETIN IN CONSCIOUS RATS.
HASHIMOTO, R. AND KIMURA, F., Dept. Physiol., Yokohama City Univ. Sch. Med., Yokohama 236

We examined the effects of intracerebroventricular (i.c.v.) or intravenous (i.v.) injection of secretin on systemic blood pressure (BP) in conscious rats. Both i.c.v. and i.v. administration of secretin caused significant depressor effects. In i.c.v. groups, 1) The rats injected with 0.5ug secretin demonstrated about 20 mmHg depression in BP 4 min after starting i.c.v., which recovered within 5 min after this effect, and when 2) 1.0ug secretin was injected, the BP began to fall as soon as i.c.v. started, and also reached about a 20 mmHg depression that continued for more than 12 min. In i.v. groups, 2ug secretin was injected in different volumes and routes; i.e. 1) 30ul. intraatrial injection via the jugular vein, 2) 10ul. via the same route, and 3) 25ul. intracaval injection via the femoral vein. 25-30 mmHg BP depression occured in all of the groups 1-5 min after starting i.v.. Control animals, which received the same volume of saline, showed no significant changes as compared to the values before the injections.

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A NEW GENETICALLY HYPERTENSIVE RAT STRAIN WITH ABNORMALITY IN VASOPRESSIN SECRETION. TERANISHI, Y. AND IRIUCHIJIMA, J. Dept. Physiol. Hiroshima Univ. Sch. Med., Hiroshima, 734

A new strain of genetically hypertensive rats was established from Wistar rats by selective inbreeding. At present, the colony of the new strain has reached F15 generation. The tail-pressure was about 150 mmHg in males and 140 mmHg in females on the average.

The strain has two characteristics: (1) Pressor amounts of vasopressin were secreted after ganglion blockade with hexamethonium (C6). (2) The majority of colony was salt-sensitive: loading of 8% salt diet and tap water for 10 weeks elevated arterial pressure markedly in about 70% of male rats picked up randomly from the colony.

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THE RELATIONSHIP BETWEEN CARDIAC ARRHYTHMIAS AND SLEEP STATES IN THE SPONTANEOUSLY HYPERTENSIVE RAT. NOJIMA,K.*OTSUKA,K* *SAITO,N* KABA,H. SAITO,H. SETO,K AND *OZAWA,T* Dept.Physiol. and Dept.Geriat., Kochi Med.Sch., Kochi 781-51

Wehave already reported the arrhythmogenic properties of paradoxical sleep in male Wistar rats. The pupose of this study is as follows ; (1) whether or not, there exists the similar relationship between sleep states and and occurrence of arrhythmias in spontaneously hypertensives (SHR). (2) whether or not , salt loading alters the frequency of arrhythmia occurrence. Two male normotensive rats (WKY) and five male spontaneously hypertensive rats (SHR) were used for this study. Ambulatory ECG - EEG monitoring was continued for 10 days. Two percent NaCl was given to drink for 6 days after the control observation for 4 days of the de-ionized water. Systolic blood pressuer did not change in WKY, but elevated in SHR for 158 to 201mmHg after salt loading. The mean heart rate did not change in WKY, but it decreased during the paradoxical sleep in SHR. Bradyarrhy-hmia episodes were also observed most frequently during PS in SHR. The incidence of BA episodes showed no significant change after salt loading in both rats, but the duration of them was prolonged from 1.7 to 2.3sec only in SHR. These results suggest the development of the restting of arterial baroreseptors and the augumented baroreflex control of bradyarrhythmias in SHR in responce to salt loading.

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CHANGES OF WHEEL RUNNING ACTIVITY IN SPONTANEOUSLY HYPERTENSIVE RATS (SHR) AND WISTAR KYOTO RATS (WKY). MATSUI, H., OKAMURA, K. AND NOMURA, M. Dept. of Physiol. Sch. of Med. Fujita-Gakuen Health Univ. Toyoake, Aichi 470-11.

SHR shows extreme hyperactivity and hyperresponsivility compared to the normotensive WKY in openfield and operant behaviors, locomotor activity and especially aversive conditioning such as electric shock. We have examined the activity of the wheel running test in both SHR and WKY 4 weeks after birth. The young 4 weeks WKY showed the running frequency less than 900 per 24 hrs. At light phase (7 a.m. to 7 p.m.) its frequency was less than 200 per 12 hrs, and at dark phase (7 p.m. to 7 a.m.) it was more than 600. On the contrary, 4 weeks SHR showed running frequency of more than 2,000 per 24 hrs. At light phase the frequency was about 1,200 to 1,800, and at dark phase it was 600 to 800. That is; in young SHR running frequency was rather high in the light and low in the dark, whereas it was reversed in WKY. These hyperactivity in SHR was not considered to be related to hypertension, because blood pressure in young SHR 4 weeks after birth was not yet high compared to the young WKY.

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EFFECTS OF CHRONIC BILE-DUCT LIGATION ON THE BARORECEPTOR REFLEX IN DOGS. HOSOMI, H., MORITA, H., UEMURA, N., MOTOCHIGAWA, H., KAWADA, M., YOSHIDA, H., NAKAMURA, J. AND TSUCHIYA, K. Dept. Physiol., Kagawa Med. Sch., Kagawa 761-07

The purpose of the present experiments was to examine the effects of chronic bile-duct ligation on the baroreceptor reflex system. The open-loop gain of the baroreceptor reflex system and pressor response to noradrenalin were measured in seven dogs with chronic bile-duct ligation for 4 to 6 weeks, and the data were compared with those of seven control dogs. The liver function of the dogs with chronic bile-duct ligation was significantly impaired. The open-loop gain was assessed as $(\Delta AP_I/\Delta AP_S)-1$, where ΔAP_I and ΔAP_S represent the immediate and steady-state decreases in arterial pressure at the aortic arch following a fast step-wise reduction in blood volume. The value of open-loop gain was 8.8 ± 0.9 (mean $\pm$ SE) in the control-group and 5.3 ± 2.1 in the group with chronic bile-duct ligation ($p<0.05$). The maximum increase in arterial pressure in response to a bolus injection of noradrenalin (0.5 μg/kg iv) was 29.3 ± 4.4 mmHg in the control-group and 19.7 ± 1.6 mmHg in the group with chronic bile-duct ligation ($p<0.05$). These findings suggest that chronic bile-duct ligation leads to a decrease in responsiveness of the vascular smooth muscle to noradrenalin which in turn results in a decrease in open-loop gain of the baroreceptor reflex system.

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ROLE OF AUTONOMIC NERVOUS SYSTEM IN THE INCREASE IN CARDIAC OUTPUT DURING TREADMILL EXERCISE. MORITA, H., FURUYA, F., FUJIKI, N., UEMURA, N., MOTOCHIGAWA, H., NAKAMURA, J., TSUCHIYA, K., KAWADA, M., YOSHIDA, Y. AND HOSOMI, H. Dept. Physiol. Kagawa Med. Sch., Kagawa 761-07

The role of neural control in the increase in cardiac output (CO) during treadmill exercise (3, 6, 12 km/hr, 6% incline, for 2 min each) was examined in chronically instrumented conscious dogs with an arterial catheter in the descending aorta and an electromagnetic flow probe around the ascending aorta. In dogs with intact cardiac nerves, exercise (12 km/hr) increased heart rate (HR) and CO by 142±22% and 150±6%, respectively, while stroke volume (SV) did not increase (4±3%). Thus, the contribution of SV to the increase in CO was only 3%. In dogs with denervated hearts, exercise increased CO by 180±15%, while HR increased by 655±4%, which was significantly less than that in intact dogs. Thus, the contribution of SV to the increase in CO during exercise was 52% in dogs with cardiac denervation. These results suggest that in intact dogs the contribution of SV to the increase in CO during exercise is minimal. However, in the absence of normal innervation of the heart, tachycardia during exercise is attenuated and the contribution of SV becomes more important.

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The Relationship between Arterial Catecholamines and Sympathetic Nerve Activities to Adrenal Gland and Heart during Coronary Occlusion in Cats. HONDA, T., and NINOMIYA, I. Department of Cardiac Physiology, National Cardiovascular Center Research Institute, 5-7-1 Fujishiro-dai, Suita, Osaka 565, Japan.

Adrenal preganglionic sympathetic nerve activity (AdSNA), cardiac sympathetic nerve activity (CSNA), and arterial epinephrine (Epi) and norepinephrine (NE) were measured together with arterial pressure and heart rate (HR) before and during coronary occlusion. With coronary occlusion, AdSNA significantly increased to 168 ± 20 % of the control value at 20 sec, whereas mean CSNA, arterial pressure, and HR decreased significantly. Arterial NE and Epi progressively increased from 0.54 ± 0.05 and 0.29 ± 0.03 ng/ml to 1.41 ± 0.16 and 0.59 ± 0.08 ng/ml at 3 min after the onset of occlusion, respectively. The correlation between AdSNA and arterial Epi ($r=0.71$, $p<0.01$), and between AdSNA and arterial NE ($r=0.57$, $p<0.05$) were significant. In adrenalectomized cats, arterial Epi and NE did not increase during coronary occlusion. We concluded that, with coronary occlusion, AdSNA increased reflexly and in turn caused the increases in arterial Epi and NE.

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RAPID INFUSION OF BLOOD INTO AORTA AND CEREBRAL ARTERIAL PRESSURE.
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We indicated previously in the rabbit that the rapid infusion of blood into aorta produced a considerable drop of systemic arterial pressure (SAP) after its temporary rise, and the volume of hindlimb and hypogastrium, which was estimated by electrocapacitography, increased during and after the infusion, while the volume of head under the occlusion of external carotids tended to decrease paralelly with the hypotensive response. It appears that cerebral blood vessels constrict passively with the drop of SAP. The cerebral arterial pressure (CAP) measured through internal carotid artery went abreast with SAP. The relationship between SAP and CAP was investigated by means of regression analysis. Denoting the maximum increments of SAP and CAP at initial phase and the maximum decrement of SAP and CAP during the depressor response respectively x, u, y and v mmHg, we obtained the regression lines: $y = 0.68x - 1.90$; $v = 0.77u - 4.27$. It is clear that CAP, as compared with SAP, was lower in the level during the initial phase as well as during the hypotensive phase of the response, and rather a cerebral vasodilation is suggested.

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EFFECTS OF SPINALIZATION ON INTRACRANIAL PRESSURE RESPONSE OF BRAIN STEM ELECTRICAL STIMULATION.
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Electrical activation of different brain stem sites produced changes in intracranial pressure (ICP) and systemic arterial blood pressure (SABP). The elevated ICP with a rise in SABP by stimulation was explained by an increase in cerebral blood volume (CBV) possibly resulted from neurogenic cerebral vasodilatation or an increase in SABP. This study shows the effects of spinalization on the ICP changes by cat's brain stem stimulation. Stimulation of sites in the pressor area of the cardiovascular center produced rises in ICP and SABP. After spinalization stimulation of the same sites which produced marked rises in ICP and SABP in the control stimulation also induced a rise in ICP and no change in SABP. Though disappearance of the rise in ICP was frequently observed by stimulation of the other sites. If neurogenic cerebral vasodilatation occurs by a change in the brain stem neuronal activities, CBV may change and an influence by the changes may be observed in ICP. The results support the explanation that the change of neuronal activity in the brain stem may produce cerebral vasodilatation.

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AGE-RELATED CHANGES IN PRESSURE PULSE WAVE ALONG THE AORTA IN WHHL RABBITS.
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Pressure pulse waves were analyzed of the aortas in WHHL rabbits with inherited hyperlipidemia and premature atherosclerosis in relation to the rheological properties of aortic walls. Pressure pulse waves were detected by microtip pressure transducers placed to the aortic arch, the thoracic aorta and the abdominal aorta. Longitudinal and circumferential strips 5mm wide were made from the excised thoracic aorta and subjected to the stress-strain test. Pressure pulse waves measured at each aortic portion showed an increase in amplitude of the percussion wave with aging, followed by the gradual disappearance of dicrotic notches and waves. A positive relationship was found between the wall thickness and the month of age with the correlation coefficient of 0.66($p<0.01$). Elastic moduli at the stress of 5×10^5dyn/cm^2 and 10^6dyn/cm^2 calculated from the stress-strain curve increased with advancing age in longitudinal and circumferential strips. Therefore, age-related changes in the pressure pulse wave were intimately related to the increased wall thickness in addition to the increased elastic moduli due to the compositional changes in the wall.

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WALL SHEAR STRESS PATTERN AROUND SOME UNILATERAL STENOSIS MODELS.

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Low wall shear stress was shown to play a very important role in the focal development of atherosclerosis in recent human studies. Precise knowledge about the three dimensional (3D) distribution of wall shear stress is essential to correlate these findings to the fluid dynamic parameters. We report a model experiment to measure 3D shear stress distribution up- and downstream of some arterial stenosis models. Axisymmetric stenoses with some area reduction ratios and unilateral stenoses with various height were examined.

The 3D shear stress distribution pattern measured in unilateral stenoses at low Reynolds number revealed an increase in shear stress far downstream on the bottom wall and a reduction of shear stress on the opposite top wall. Although the distribution pattern generally agreed with the horse-shoe vortex structure obtained by flow visualization technique, it was thought to be necessary to investigate the detailed 3D structure of the flow and the wall shear stress quantitatively, in order to make comparisons with pathological findings.

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THE EFFECT OF THE EXCISION OF BILATERAL GANGLIA CERVICALE SUPERIUS ON THE LINGUAL BLOOD FLOW OF THE RAT.

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The purpose of this study is to investigate the effects of excision of the ganglia cervicale superius in the rat on the lingual blood flow, the value of CR (time constant) for the peripheral blood vessel, and the blood volume in the peripheral blood vessel using electromagnetic flowmetry and photoelectric plethysmography. Ten male Wistar rats were anesthetized with sodium pentobarbital (30 - 40 mg/kg, IP). They were divided into two groups, the excision group and non-excision group. Ringer-Locke's solution at 15°C (20 ml/10 sec) was applied to the surface of the tongue. The data were compared before and after the application. The theoretical formulation, $v_o = f_o \times CR$ was derived, where v_o and f_o are the mean values for blood volume and blood flow, respectively. In the excision group, the formulations exhibited no significant difference for both cases of thermal stimulation. However, in the non-excision group, the value of f_o in the after case increased by approximately 1.6 times over that of the before case.

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LONG-TERM PROFILE OF PHYSIOLOGICAL VARIATIONS IN ARTERIAL PRESSURE AND HEART RATE DURING SLEEP IN CATS OPERATED FOR CHRONIC EXPERIMENTS

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In chronic experiments, the physiological conditions of experimental animals change greatly immediately after operation. Then, when should we get the control data, especially for sleep research? Subjects are 3 male cats. Recordings were started from the 2nd day after operation for chronic monitoring of EEG, EOG, EMG, ECG, and arterial pressure. We took the records from 12:00 to 18:00 as data. These recordings were continued for about 40-80 days in one cat. And then, cats were injected Nembutal again after 24-hours polygraphic recordings. Sleep-waking states were analyzed at 12.5s intervals. Mean arterial pressure (MAP) and heart rate (HR) were scored at the mid points of each interval. After operation, there were long-term variations in MAP and HR in sleep in the cats. MAP and HR in slow wave sleep were higher than in paradoxical sleep for 2-8weeks after operation, but this relationship was inverted later. This change might be not due to anesthesia, but due to another factor. Therefore, the selection of date for taking control data may be important in such sleep study.

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ROLE OF PULMONARY VASCULAR RESISTANCE IN PULMONARY HYPERTENSION CAUSED BY VENTILATION WITH HIGH Pco_2. NAKAMURA, J., TSUCHIYA, K., MORITA, H., UEMURA, N., MOTOCHIGAWA, H., KAWADA, M., YOSHIDA, H., AND HOSOMI, H. Dept. Physiol., Kagawa Med. Sch., Kagawa 761-07

We investigated the role of pulmonary vascular resistance (PVR) in pulmonary hypertension caused by ventilation with high Pco_2. Fifteen dogs were used, each was anesthetized with pentobarbital sodium, then the chest was opened and the lungs were ventilated. Blood (2 ml/kg bw) was quickly withdrawn from the abdominal aorta, leading to a decrease in pulmonary arterial pressure (PAP), pulmonary arterial flow (PAF) and left atrial pressure (LAP). Relationship between pressure difference (PAP-LAP) and PAF was determined. PVR is the slope of this pressure-flow relationship. This experimental procedure was conducted under ventilation with room air and again with high Pco_2 in intact, vagotomized and vagotomy plus carotid sinus denervated dogs. In the intact dog, ventilation with high Pco_2 significantly increased PAP from 17.7±1.4 to 24.1±2.4 mmHg, LAP from 4.8±1.3 to 8.5±1.4 mmHg, and PAF from 93.5±10.2 to 127.4±15.8 ml/kg/min, respectively. However, PVR was not changed by ventilation with high Pco_2, while it was significantly changed by vagotomy or vagotomy plus carotid sinus denervation. These findings suggest that the pulmonary vascular bed can behave as a resistance vessel, but pulmonary hypertension caused by ventilation with high Pco_2 might be induced not by an increase in PVR but by an increase in LAP and PAF.

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NEURAL AND HUMORAL CONTROL OF THE PULMONARY VASCULAR BED VIA α_1-RECEPTOR TSUCHIYA,K., NAKAMURA,J., MORITA,H., UEMURA,N., MOTOCHIGAWA,H., KAWADA,M., YOSHIDA,H., HOSOMI,H. Dept. Physiol., Kagawa Med. Sch., Kagawa 761-07

We examined neural and humoral control of the pulmonary vascular bed via the α_1-receptor in dogs. The lower lobe of the left lung of the dog was vascularly isolated from the pulmonary circulation and perfused with autologous blood using a pulsatile pump. The mean pulmonary arterial perfusion pressure (MPAPP) was monitored before and after quick mild hemorrhage (2 ml/kg body weight) from the abdominal aorta and also during electric sympathetic nerve stimulation (SNS) (2 msec, 20 V, 10 cps and 30 cps, for one minute) of the thoracic chain. The pulmonary vascular resistance (PVR) was estimated from the pressure-flow relationship before and after α_1-blockade (prazosin: 500 μg/kg b.w.) of the isolated lung. SNS increased MPAPP. The increase was significantly lessened by α_1-blockade from 0.35±0.07 mmHg (mean±SE) to 0.18±0.04 mmHg at 10 cps and from 0.70±0.16 mmHg to 0.30±0.08 mmHg at 30 cps. α_1-blockade also decreased PVR from 1.40±0.30 mmHg·kg·min/ml to 1.12±0.30 mmHg·kg·min/ml, significantly. These findings suggested that there was neural control of the pulmonary vascular bed via the α_1-receptor, but it did not play an important role in the physiological state, and there was also tonic humoral control of the pulmonary vascular bed via α_1-receptor.

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CENTRAL AND PERIPHERAL EFFECTS OF ALPHA-2 AGONIST (CLONIDINE) ON BAROREFLEX CONTROL OF HINDLIMB VASCULAR BED. KAWADA, M., YOSHIDA, H., MORITA, H., UEMURA,N., MOTOCHIGAWA, H., TSUCHIYA, K., NAKAMURA,J. AND HOSOMI,H. Dept. Physiol., Kagawa Med. Sch., Kagawa 761-07

This experiment evaluated the central and peripheral effects of an alpha-2 agonist (clonidine) on baroreflex control of the hindlimb vascular bed in dogs, where the isolated hindlimb was perfused with blood from a donor dog. In the first protocol, we studied the effects of clonidine (3, 10, 30 or 100 μg/kg i.v., to a recipient dog) on the reflexogenic increase in perfusion pressure (ΔHPP) of vascularly isolated, neuraxis intact hindlimb vascular beds that follows quick mild hemorrhage. After clonidine administration to a recipient dog, open-loop gain of the baroreflex system estimated by quick mild hemorrhage method significantly decreased from the control value. Clonidine administration at 3, 10 or 30 μg/kg did not affect ΔHPP significantly, while clonidine administration at 100 μg/kg decreased ΔHPP significantly. In the second protocol, we studied the peripheral effects of clonidine on baroreflex control of hindlimb vascular beds. After clonidine (3 or 30 μg/kg i.v.) administration to the donor dog, hindlimb perfusion pressure and ΔHPP increased significantly. These findings suggest that clonidine interferes with the overall responsiveness of the baroreflex system, but augments responsiveness of the peripheral vascular bed to endogeneous catecholamine.

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ALPHA-ADRENERGIC RECEPTOR MEDIATED CORONARY VASOCONSTRICTION IN DOGS DURING TREADMILL EXERCISE. FURUYA, F., MORITA, H., UEMURA, N., MOTOCHIGAWA, H., NAKAMURA, J., TSUCHIYA, K., KAWADA, M., YOSHIDA, H., FUJIKI, N. AND HOSOMI, H. Dept. Physiol., Kagawa Med. Sch., Kagawa 761-07

Alpha-adrenergic receptor mediated coronary vasoconstriction was examined in chronically instrumented concious dogs. Left circumflex coronary flow velocity (CFV) was measured during treadmill exercise (12 km/h and 6 % inclines, for 2 min) with beta-adrenergic blockade, or combined alpha- and beta-adrenergic blockades. Exercise increased double product (DP). CFV/DP was used as an index for evaluating the coronary vasoconstriction. During exercise with beta-blockade, CFV/DP decreased by -36±5 (mean± SE, n=6) %. This decrease in CFV/DP was completely blocked by pre-treatment of alpha-blockade (n=5). These results suggest that treadmill exercise causes alpha-adrenergic coronary vasoconstriction. To examine the role of the cardiac nerve in alpha-adrenergic coronary vasoconstriction during exercise, the same exercise was performed in dogs with cardiac denervation (CD). During exercise with beta-blockade in CD dogs, CFV/DP did not change significantly (-6±7 %, n=6). These results suggest that during treadmill exercise alpha-adrenergic coronary vasoconstriction occurs, which is predominantly due to the cardiac nerve rather than circulating catecholamines.

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EFFECTS OF LOW CEREBRAL PERFUSION PRESSURE ON THE BARORECEPTOR REFLEX SYSTEM. FUJIKI, N., MORITA, H., UEMURA, N., MOTOCHIGAWA, H., NAKAMURA, J., TSUCHIYA, K., KAWADA, M., YOSHIDA, H., FURUYA, F. AND HOSOMI, H. Dept. Physiol., Kagawa Med. Sch., 761-07

We examined the effects of low cerebral purfusion pressure on the open-loop gain (G) of the baroreflex system in nine pentobarbital-anesthetized dogs. To isolate the brain vascularly from the systemic arterial circulation, the common carotid and vertebral arteries were perfused at different levels of perfusion pressure by a pulsatile pump. G was estimated with a quick mild hemorrhage (2 ml/kg in 1-2 sec) through a catheter inserted into the abdominal aorta. Auditory brain stem response (ABSR) was also monitored, and brain stem function was indexed by the interpeak latencies between waves I and III (I-III IPL). We measured G and I-III IPL at different levels of cerebral perfusion pressure. Compared to the control values of G (1.14±0.23) obtained when the difference between systemic arterial pressure and cerebral perfusion pressure (AP-PP) was less than 50 mmHg, G increased to 2.68±0.42 when AP-PP was more than 50 mmHg. This increase in G was significant only when I-III IPL was between 2.1 and 2.5 msec. These results suggest that G is increased by brain stem ischemia when ABSR shows a slight lengthening of I-III IPL.

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ROLES OF NEURAL, HUMORAL AND INTRINSIC CONTROL OF HEART RATE IN DOGS DURING EXERCISE. MOTOCHIGAWA, H., FURUYA,F., FUJIKI,N., MORITA,H., UEMURA,N., NAKAMURA,J., TSUCHIYA, K., KAWADA, M., YOSHIDA, H. AND HOSOMI, H. Dept. Physiol., Kagawa Med. Sch., Kagawa 761-07

The purpose of this experiment was to define the roles of neural, humoral and intrinsic mechanisms of heart rate (HR) control during exercise. Steady-state HR response (ΔHR), to a work load of 12 km/hr at 6% treadmill elevation, was measured in 5 cardiac nerve intact dogs (INT) and 6 cardiac denervated dogs (CD). In each group, the experiment was repeated with (β) and without (ND) administration of a β-blocker (propranolol 1 mg/kg body weight). ΔHR in the INT-ND dog was 120±15 (mean±SE)% of preexercise value (100±5 beats/min). ΔHR in the CD-ND dog was 62±4%. Difference in ΔHR between INT-ND and CD-ND dogs was 58 (=120-62)%, which probably represents nervous control of HR. ΔHR in the CD-β dogs was 34±3%, which probably represents the extent of intrinsic HR regulation. Therefore, the remaining 28 (= 62-34)% difference between CD-ND and CD-β dogs seems to be due to the humoral mechanism. ΔHR due to humoral mechanism in INT dogs was estimated as 17 (=120-103)%, since ΔHR in the INT-β dogs was 103±15%. These findings suggest that lack of neural control in CD dogs was not compensated for during exercise by humoral or intrinsic mechanism of HR control, although the extent of humoral control was slightly augmented to compensate for the loss of the neural mechanism.

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EFFECTS OF CALCIUM ANTAGONISTS (DILTIAZEM AND NIFEDIPINE) ON BAROREFLEX CONTROL OF ARTERIAL PRESSURE. YOSHIDA, H., KAWADA, M., MORITA, H., UEMURA, N., MOTOCHIGAWA, H., NAKAMURA, J., TSUCHIYA,K. AND HOSOMI,H. Dept. Physiol., Kagawa Med. Sch., Kagawa 761-07

Diltiazem (D) and nifedipine (N) are selective calcium entry blockers acting at the plasma membrane. D attenuates the sensitivity of the carotid sinus baroreceptor, while N augments it. N also augments baroreflex control of renal nerve activity. The aim of this experiment was to evaluate the effects of D and N on baroreflex control of arterial pressure. Experiments were performed before and after administration of D and N to 14 anesthetized dogs, using a quick mild hemorrhage (2 ml/kg body weight in 1-2 sec) to estimate the overall open-loop gain of the baroreflex system, defined as the ratio of posthemorrhage hypotension without the reflex to that with the reflex, and the baroreflex change in heart rate. Mean arterial pressure slightly decreased after administration of D and N. The heart rate responses were not significantly affected by administration of D or N. Open-loop gain was significantly decreased in a dose dependent manner by administration of D (5, 10, 15, 20, 25 or 45 μg/kg bw, iv) or N (10, 20, 30, 40, 50 or 100 μg/kg bw, iv). These findings suggest that calcium antagonists (diltiazem and nifedipine) attenuate the overall open-loop gain of baroreflex control of arterial pressure.

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EFFECTS OF AGING ON MEAN LEVEL AND STABILITY OF ARTERIAL PRESSURE IN CONSCIOUS WHHL RABBITS. KATSUDA, S., WATANABE, Y.* AND HOSOMI, H.** Dept. Physiol. and *Exp. Anim. Lab., Kobe. Univ. Sch. Med., Kobe 650 and **Dept. Physiol., Kagawa Med. Sch., Kagawa 761-07.

Effects of aging on mean level and stability of arterial pressure (AP) were studied in 12 Watanabe-heritable hyperlipidemic (WHHL) rabbits aged 12 to 35 months and 25 normal Japanese white rabbits aged 6 to 30 months. A pressure catheter was indwelt in the aortic arch via the left subclavian artery under pentobarbital anesthesia. A few days after the operation, they were in a good state of health and appetite. Mean arterial pressure (MAP) was sampled by A/D converter every second for 6 hrs and fed into a computer. Mean (M), variance (V) and standard deviation (SD) were calculated from each MAP record. There was no significant correlation between M and SD in the WHHL rabbit. The values of M and V in the WHHL rabbit were significantly larger than those in the normal rabbit. M did not significantly change with aging, while SD increased significantly with aging in the WHHL rabbit. We can conclude that development of atherosclerosis with aging in the WHHL rabbit causes malfunction of the baroreceptors, which contribute to hypertension and lability of AP.

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SERIAL OBSERVATIONS OF ERYTHROID BURSTS FORMATION FROM HUMAN PERIPHERAL BLOOD MONONUCLEAR CELLS. TERASAWA, T., ITO, T AND MATSUDA, M. Tohoku Dent. Univ., Koriyama, 963.

To elucidate the morphological changes of erythroid progenitors accompained with their differentiation and maturation, we try to observe the cells at the early stages of erythroid bursts formation. Peripheral blood mononuclear cells from healthy volunteers were separated by using Ficoll-Isopaque technique. Erythropoietic cell culture was carried out for 14 days using the methylcellulose assay. Colonies formed in the culture were collected individually. Cells were stained with May-Grunwald Giemsa solution and ultrastructual observations were also carried out. On day 14 of incubation, although well-hemoglobinized burst consisted of various maturational stages of erythoid cells, from proerythrobalsts to mature erythrocyte, polychromatophil and orthochromatophil eryhtroblasts were predominantly. In addition, small lymphocyte like cells were also observed. On day 9, white burst containing basophilic erythroblasts and proerythroblasts was recognized. On day 6-7, colony consisting of several doublet cells was observed. Morphological features of these cells were ovoid and large nucleus. Cells exhibited poor organelles which contained mitochondria and ER. Nuclear chromatins were homogeniously distributed.

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FIBRINOGEN-INDUCED ERYTHROCYTE AGGREGATION. MAEDA, N., SEIKE, M. AND SHIGA, T. Dept. Physiol., Sch. Med., Ehime Univ., Ehime 791-02

To clarify the mechanism of fibrinogen-erythrocyte binding in inducing erythrocyte aggregation, the effect of various enzymatic degradation products of fibrinogen and the related compounds on the erythrocyte aggregation was examined. The velocity of erythrocyte aggregation was measured by the automated rheoscope combined with a TV-image analyzer and a computer (Shiga, T. et al.: Am. J. Physiol., 245, H252, 1983). (1) Low molecular weight fibrinogen (305 kDa), which was produced by the partial cleavage of C-terminal region of Aα chain of fibrinogen, showed the same velocity as native fibrinogen (340 kDa). (2) The removal of sialic acid from Bβ and γ chains of fibrinogen did not affect the velocity. (3) Among fibrinogen degradation products by plasmin, fragments X (250 kDa) and Y (150 kDa) could aggregate the erythrocytes, while fragments D (90 kDa) and E (50 kDa) could not. From the view point of the velocity, one mole of fibrinogen, two moles of fragment X and five moles of fragment Y were equivalent. (4) Fibrinopeptides (A and B) and artificial tetrapeptides (Gly-Pro-Arg-Pro and Gly-His-Arg-Pro, bound to γ and Bβ chains at D domain of fibrinogen, respectively) did not affect the fibrinogen-induced erythrocyte aggregation. Conclusively, the erythrocyte-binding site in fibrinogen could be focused in Aα chain near D domain of trinodular structure.

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ANALYSIS OF ERYTHROCYTE DEFORMATION UNDER OSCILLATORY SHEAR STRESS (II). KON,K. MURAKAMI,J., OKAZAKI,M. AND SHIGA,T. Dept. Pysiol., Sch. Med., Ehime Univ.,Ehime 791-02

Circulating erythrocytes are repeatedly exposed to oscillating shear stress, thus it is important to reveal the frequency response of the cellular deformation. The oscillation of cellular deformation, cells were suspended in 14% dextran solution (280 mOsm, 9.8cP), was observed by a cone-plate rheoscope with a stepping motor which regulated the velocity of cone rotation. The rotation velocity of 0.8° cone was sinusoidally modulated in a range of 9-32 dyn/cm^2 in shear stress, and the range of modulation frequency was 0.59-2.72 Hz. The extent of cellular deformation was quantified by the deformation index (DI).

DI changed alternatively with applied oscillatory shear stress. At modulation frequencies less than 1.8 Hz, DI's of intact cell agreed with those measured at corresponding stationary shear stress. However, above 2 Hz, the cellular deformation could not follow the changes in shear stress. The retardation was not detected when cells were suspended in hypotonic dextran solution (183mOsm). This is due to a decrease in intracellular viscosity, which causes an increase in the deformability. When cell membrane was modified with diamide (0.2mM), the distinct impediment in frequency response was observed.

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GHOST DEFORMABILITY MEASURED BY LASER DIFFRACTOMETRY. NAGASAWA, T. AND KINOSHITA, Y. Dept. of Physiology, Osaka City Univ. Med. Sch. Osaka 545

Ghost deformability has been measured to study membrane deformability in the absence of internal viscosity effects. Human blood was washed in 5 mM Tris, 140 mM NaCl (pH 7.4) and removed the white cells. Ghosts were prepared by lysing red cells in 40 vol. of ice-cold 5 mM Tris, 7 mM NaCl, 1 mM MgATP, pH 7.4) and washing 3 times to yield white ghosts. 1/10 volume of hypertonic Tris-NaCl (5 mM Tris, 1.4 M NaCl, 1 mM MgATP, pH 7.4) was added to the ghost suspension and then incubated at 37°C for one hour to promote resealing. Ghost deformability was measured by laser diffractometry using high refractive arabinogalactan medium. Suspending medium osmolarity had no effect on the maximum value for the deformability. There was no change in maximum deformability index of ghosts over the range pH 5.0 to 9.0. Ghost showed a progressive loss of deformability with increasing incubation temperature (45-50°C for 10 min). Diamide (1-20 μM) decreased the ghost deformability and dithiothreitol (1 mM) recovered the reduced deformability to normal level. These results suggest that the membrane deformability can be measured using ghosts by laser diffractometry.

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IMPROVED ERYTHROPOIETIN ASSAY BASED ON FETAL MOUSE LIVER CELL CULTURE. SAKATA, S., ENOKI, Y., SHIMIZU, S. AND KOHZUKI, H.
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Clonal origin of erythroid colonies was examined in semisolid culture to develop a reliable erythropoietin (EPO) assay based on the erythroid colony formation of fetal mouse liver cells. Time course of colony formation implied a cell-aggregation when more than 10^4 cells were plated. Linear relationship between the number of colonies and the number of cells plated suggested that colonies originated from single progenitor cells when less than 7500 cells were plated. This conclusion was further confirmed by examining the ratio of the number of colonies formed in the presence to that in the absence of EPO. A two-fold enrichment in CFU-E concentration could be achieved by Ficoll-Paque centrifugation. Plasma treated with acid-boiling (AB) stimulated colony formation most and contained no colony inhibitor. Dose-response curve for the plasma was parallel to that for the standard EPO. EPO titers of AB-treated plasmas, from mice under erythropoietic stimulation, normal and anemic human subjects and patients with chronic renal failure, were determined by the present improved procedure.

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STRUCTURAL AND FUNCTIONAL CHARACTERIZATION OF A β-VARIANT HEMOGLOBIN IN A JAPANESE DIABETIC. ENOKI, Y., OHGA, Y., KOHZUKI, H., SAKATA, S. AND SHIMIZU, S., Second Dept. Physiol., Nara Med. Univ., Kashihara, Nara 634

In a 68-year-old female with hyperglycemia, her glyco Hb level was initially mistaken to be enormously elevated, but afterwards, by reverse-phase HPLC and gel electrophoresis, the seeming elevation was found to be due to the presence of a β-variant Hb. The primary structure of the variant Hb, isolated by Bio-Rex 70 chromatography and chromatofocusing, was determined as $\alpha_2\beta_2^{136Gly\rightarrow Asp}$ (Hb Hope) by peptide mapping of the tryptic digests and the amino acid analyses of the peptides. The oxygen affinity was four-fold depressed as compared with Hb A_0. Responses to such allosteric effectors as Cl^-, 2,3-DPG and CO_2 were definitely decreased and the Bohr effect was also reduced. The native abnormal subunit, when isolated by the Bucci-Fronticelli method, exhibited four fold lower oxygen affinity than the normal subunit. All these facts can be rationally explained by assuming a salt bridge formed between Asp replaced at β136 sites and the βN-termini. Lower stability of the Hb to heat and isopropanol was also observed. This is the first report of Hb Hope in non-Afroamerican population.

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PRESSURE-FLOW RATE RELATION OF ERYTHROCYTE SUSPENSION IN PERFUSION OF NUCLEPORE MEMBRANE. Kikuchi,H., Uyesaka,N. and Shinagawa,Y. 1st Department of Physiology, Nippon Medical School, Sendagi, Bunkyo-ku, Tokyo 113

This study was designed to evaluate the characteristics of blood flow through nuclepore membrane by measuring the pressure (P)-flow rate (Q) relationships. The perfusion of nuclepore was made according mainly to vertical tube method (Nichol et al 1951) and partly to conventional perfusion method by a variable speed pump.

The P-Q curve was consisted of a smooth curve convex to the pressure axis, tending to a straight line at a high rate of flow. This asymptotic line was found to have a negative intercepts of the flow axis, which was dependent not only on the radius of the pore of membrane but also the hematocrit values of erythrocyte suspension. The echinocytic shape change induced by taurocholic acid caused decrease in rate of flow, but did little change in the slope of the asymptotic line (flow resistance at a high rate of flow) resulting in increase in the negative intercept values of the flow axis. The flow rate was influenced not by micro-dust in solution but by total volume of erythrocyte suspension. These phenomena mentioned above except for basic shape of the P-Q curve was not found out when the perfusion was carried out using bullfrog's hind limbs or rigid glass tube. A possible mechanism of the filtration characteristics of erythrocyte suspension was discussed.

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THE EFFECT OF OSMOLALITY AND VISCOSITY ON A BLOOD FLOW THROUGH VASCULAR NETWORK. Uyesaka,N., Furuhama,K. and Shinagawa,Y. 1st Department of Physiology, Nippon Medical School, Sendagi, Bunkyo-ku, Tokyo 113

The perfusion of bullfrog's hind limbs was made according to vertical tube method with slight modification. Glutaraldehyde-fixed hind limbs were utilized for the investigation of red cell deformability and of some hydrodynamic factors in a flow. The solution of various osmolality (100-749 mOsm/kgH_2O) and of various viscosity (1.5-2.5 cp, at 22 ℃) were prepared by NaCl and by dextran (M.W. 50,000), respectively.

The perfusion of erythrocyte suspension under various osmotic conditions in fixed hind limbs showed that the flow rate decreased as the red cell deformability decreased. Decrease in flow rate was caused, however, not only by erythrocyte deformability but by the effect of osmotic pressure on vascular bed when perfusion was carried out using intact hind limbs. The flow rate decreased as the viscosity of solution increased and the increase in flow resistance was larger than the expectative value as a lenear function of viscosity, and these phenomena were more distinguishable when the perfusion was made using fixed hind limbs. This suggested that the flow rate depended not only on the interaction of erythrocytes and viscous solution but on some smoothing effect of normal vascular wall on a flow. These results showed some important roles of vascular bed as well as deformability of erthrocytes in a maintenance of microcirculation.

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THE EFFECT OF RADIOGRAPHIC CONTRAST MEDIA ON THE PRESSURE-FLOW RATE RELATION IN THE PERFUSION STUDY OF BULLFROG'S HIND LIMBS S.Okada[1], N.Uyesaka[2], T.Kato[1], Y.Shinagawa[2] [1]Department of Radiology, [2]1st Department of Physiology, Nippon Medical School, Sendagi, Bunkyo-ku, Tokyo, Japan

The effect of radiographic contrast media (RCM) on blood flow though vascular network was investigated by measuring the pressure-flow rate relation of contrast solution and of erythrocyte suspension. The perfusion of the bullflog's hind limbs was made by means of vertical tube method (Nichol et al Am.J.Physiol. 1951) with a slight modification. Intact hind limbs and fixed find limbs were used.

When the fixed hind limbs were used, the pressure-flow rate relation was influenced by the viscosity of RCM and by the effect of RCM on red cell deformability. The echinocytic shape change induced by metrizamide solution, which have strong effect on red cell membrane, and by hypertonic iothalamate solution caused distinguished increase in flow resistance. When the intact hind limbs were used, the effect of RCM on vascular bed had strong effect on the pressure-flow rate relation. Ioxaglate had less rheological effect on pressure-flow rate relation than metrizamide and iothalamate in each experiment. It could be concluded that RCM should be isotonic, low viscous and less chemotoxic.

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RHEOLOGICAL STUDY OF ERYTHROCYTES IN A PATIENT WITH MYELODYSPLASTIC SYNDROME (MDS)

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Rheological behavior of erythrocytes in a patient with myelodysplastic syndrome (MDS) was investigated by the measurement of membrane fragility, red cell shape, blood viscosity and pressure-flow rate relation of erythrocyte suspension. The erythrocytes of MDS patient showed several stages of abnormal shape changes. Remarkable decrease in osmotic fragility, however, was observed in MDS patient. On the contrary the patient's erythrocytes showed marked increase in mechanical fragility studied by impact-force method which was quantitative and simple method developed in our laboratory and was able to investigate membrane fragility under physiological condition. Measurement of viscosity revealed increase in blood viscosity of MDS patient due not to plasma component but to erythrocytes. The pressure-flow rate relation of erythrocyte suspension in the bullfrog's hind limb was studied by perfusion method. The erythrocyte suspension of MDS patient caused distinguished increase in resistance of flow. It was made clear that decreased deformability of patent s erythrocyte caused. increase in blood viscosity and in resistance of blood flow, and it appeared that low hematocrit value of MDS patient might compensate the undesirable effect of decreased deformability to maintain rheological homeostasis in vivo.

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KINETIC ANALYSIS OF THE ACTIVATION OF PLASMINOGEN BY t-PA.

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In order to elucidate the role of fibrin in the activation of plasminogen(Glu-plg) by tissue plasminogen activator(t-PA), the kinetics of the activation was studied in the presence of fibrin(fn), fibrinogen(fg), fragment D and fragment E.

In the absence of fn and its related substances, t-PA activated Glu-plg with K_m of 1.1 μM, k_{cat} of 0.005 sec^{-1} and kcat/Km of 0.0045 $\mu M^{-1} sec^{-1}$. The presence of increasing amounts of fn resulted in drastic increase in k_{cat} and decrease in K_m with K_m^{inf} of 0.048, k_{cat}^{inf} of 0.038 and Km/kcat of 0.79. Increasing amounts of fragment D caused increase in k_{cat} and decrease in K_m, while that of fg or fragment E gave rise to increase in k_{cat}. The magnitude of the enhancement of activation were 175 fold for fn, 24 for D, 20 for E and 9 for fg in terms of Km/kcat. The results suggest that roles of D and E domeins of fibrin may be different in the enhanced activation of plg by t-PA.

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ACTIVATION PATHWAY OF GLU-PLASMINOGEN BY UROKINASE AND TISSUE PLASMINOGEN ACTIVATOR.

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When purified Glu-plasminogen (Glu-plg) was activated by urokinase (UK) or tissue plasminogen activator (t-PA), the activation of Glu-plg proceeded rapidly in the presence of fibrin. Formation of modified plasminogen (Lys-plg) was observed in the presence of fibrin clot. The addition of α_2-antiplasmin(α_2AP) to the mixture of Glu-plg, UK or t-PA, and fibrin resulted in significant formation of Lys-plg, which shows that α_2AP did not prevent the formation of Lys-plg from Glu-plg by plasmin in the presence of fibrin. In contrast to purified system, the activation of Glu-plg by UK or t-PA in the presence of plasma clot resulted in little formation of Lys-plg. These results suggest that Glu-plg was mainly directly activated by UK or t-PA to Glu-plasmin (then Lys-plasmin) in the plasma or plasma clot.

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STUDIES ON THE FIBRINOLYTIC ENZYME SYSTEM IN THE HEPATOBILIARY SYSTEM (XVI)--ENZYMATIC CHARACTERISTICS OF THE PLASMINOGEN ACTIVATOR SECRETED BY CULTURED HEPATOCYTE-- OSHIBA, S., *ARIGA, T.,*WATANABE, K., *SEKI, T., YOSHIDA, M. AND IMAI, H. Dept. of Physiol., Nihon Univ. Sch. of Med., Tokyo, *Dept. of Nutr. and Physiol., Nihon Univ. Coll. of Agric. and Veter. Med., Tokyo

We have established the primary-culture conditions of rat hepatocytes necessary for the secretion of plasminogen activator (Hepatic plasminogen activator, HPA). The present report is described on the purification of the activator and its enzymatic characteristics which were studied comparatively with urokinase (UK) and a biliary plasminogen activator, bilokinase (BK). HPA was purified by Sp-Sepharose and fibrin affinity chromatography, and was purified 1800-fold. Molecular weight of HPA was estimated to be about 60000. HPA has high affinity to fibrin, demonstrating that HPA is an enzyme similar or identical with BK, but not with UK.

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ACID STABLE TRYPSIN INHIBITOR IN HUMAN AND EXPERIMENTAL ANIMALS. YOSHIDA, E., SUMI, H., MARUYAMA, M., TSUSHIMA, H., IKEDA, R., SUGIKI, M., MATSUOKA, Y., MORIMOTO, N., HAMASUNA, S. AND MIHARA, H. MIYAZAKI MEDICAL COLLEGE, MIYAZAKI 889-16

Acid stable trypsin inhibitor (ASTI) occured in urine, plasma and other biological fluids and its activity increased in various physiological and pathological states. However, it is still unknown about physiological significance, origin and metabolism of ASTI. To clarify these problems, experimental animal models must be very useful. A sensitive enzyme-linked immunosorbent assay (ELISA) for ASTI was developed using antibody raised against purified human ASTI in urine. We demonstrated the developement of ELISA, measurement of ASTI in human biological fluids and tissue extracts, and investigation of ASTI in several experimental animals.

ASTI activity was observed in all animals; higher in a guinea pig and a rat, lower in a dog. Cross reactivity with antibody to human ASTI determined by single radial immunodiffusion was positive in a Japanese monkey and rhesus, negative in other animals. ASTI in a monkey was not able to be quantified by our ELISA. Existence of ASTI in human and all animals suggested the signigicance of ASTI in body. Developement of quantitative measurement of ASTI in animals is expected and may be performed by purified animal ASTI.

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TRYPSIN-PLASMIN INHIBITORS (TPIs) ENZYMATICALLY PRODUCED FROM PLASMA PRECURSOR PROTEIN. H. Sumi, S. Takasugi, E. Yoshida, R. Ikeda, M. Maruyama, Y. Matsuoka, M. Sugiki, N. Morimoto, S. Hamasuna and H. Mihara Dept. of Physiol., Miyazaki Med. College, Japan.

Several TPIs having the same antigenicity to urinary trypsin inhibitor have been found in plasma, ascites and malignant tumors. We now show the enzymatic formation of TPIs from plasma precursor protein, and describe some of their properties. Five ml of human plasma was incubated with various amounts of proteases (0-10 mg/ml PB, ± Cys) for 30 min at 37 C. After stopping the reaction with 5% PCA, a marked increase in TPI activity was found in the sup. fraction when SH-proteases such as bromelain, papain and ficin were used as the treated protease. However, lesser activity was observed with the same amounts of several serine-protease. The maximal TPI activity produced by bromelain treatment was about 40 U/ml plasma, which represented a 10-fold increase compared to that of the control plasma (5 U/ml). Gel filtration revealed two TPI activity peaks with mol. wts. of about 14,000 (main form) and 8,000 (minor form) . Highly purified main TPI was non-His protein with single chain molecule (N-terminal Ala) and had strong activities on trypsin and chymotrypsin, but weakly on plasmin. These results and previous our findings (Thromb. Haemostas. 47: 14, 1982) suggest that such enzymatic formation of TPI from precursor protein (pro-inhibitor) may be a very important mechanism in the regulation of plasma and tissue fibrinolysis.

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A POTENT AND SELECTIVE INHIBITOR OF PSEUDOCHOLINESTERASE. HIJIKATA-OKUNOMIYA, A.,*OKAMOTO, S.,*WANAKA, K. AND *BOUGAKI, M. School of Allied Med. Sci., Kobe Univ., Kobe and *Research Proj., Saiseikai Hosp., Kobe

Structure-activity relationship of C-terminal side of synthetic arginine derivatives was described concerning the inhibitory activity for pseudocholinesterase (PseudoChE) (horse serum, SIGMA): 1) Substitution of 2-position of 4-methylpiperidine amide portion in N_{α}-quinolinesulfonyl-L-arginine derivatives with (a) H, (b) (2R)-COOH and (c) (2R)-$COOCH_3$ resulted in their I_{50} values as (a) 0.83, (b)$>$150 and (c) 1.7 μM respectively, and 2) introduction of 4-phenyl group (into piperidine amide in N_{α}-dansyl-L-arginine derivatives) caused the increase of inhibitory activity. These results indicated large difference in the stereogeometry of the active site of PseudoChE from that of thrombin, and thus, we obtained a new selective inhibitor for PseudoChE, N_{α}-dansyl-L-arginine-4-phenylpiperidine amide, whose Ki values for PseudoChE and thrombin were 0.016 and 5.0 μM respectively. When it was mixed with PseudoChE, marked increase of fluorescence intensity and blue shift (570→500 nm) in the emission maximum were observed. Titration curve suggested the stoichiometrical binding of the inhibitor with the enzyme.

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SPECIES DIFFERENCE OF INTRACELLULAR CALCIUM ION EFFLUX IN PLATELETS. TANIMOTO, Y., HATTORI, Y.* AND SUZUKI, S.* Dept. Hematochem., Cent. Inst. Exp. Anim., Kawasaki 213

The species differences of intracellular calcium ion efflux in activated platelets of animals were investigated. The Ca^{2+}-sensitive photo-protein aequorin was introduced into human, monkey, dog, rabbit, and rat washed platelets by incubation with EGTA and ATP. Intracellular calcium ion concentrations in mediating thrombin-induced platelet activation differed in value among animals but the phases of efflux were almost the same.

In the platelets stimulated with collagen, the phases of Ca^{2+} mobilization of each animal differed. Two phases of Ca ion efflux in collagen-induced platelet activation of human, monkey, and rat became one phase upon addition of indomethacin.

These studies indicated the difference of the values and the phases of intracellular calcium ion efflux with each stimulation in animals.

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A PATCH-CLAMP STUDY OF MAMMALIAN PLATELETS AND THEIR IONIC CHANNELS. MARUYAMA, Y., Dept. of Physiol., Faculty of Med., Univ. of Tokyo, Hongo 7-3-1, Bunkyo-ku, Tokyo 113.

The whole-cell and cell-attached voltage-clamp variations of the patch-clamp technique were employed to study the passive electrical properties and ionic channels of mammalian platelets. Platelets were freshly isolated from blood of human, rabbit, and rat. Input resistance of a platelet was about 60 GΩ and input capacitance measured by phase-sensitive detection method was about 128 fF. The predominant ion channel of an unstimulated platelet was a voltage-gated K^+ channel resembling the delayed rectifier K^+ channel of nerve and muscle. The activation of the channel could be fitted by n^4-kinetics, and was half-maximal at about -35 mV. The time constant of inactivation was virtually independent of voltage and varied from cell to cell. Recovery from inactivation was slow and dependent on the size and duration of the preceding conditional voltage-step. Steady-state inactivation was half-maximal at about -50 mV and this value was very close to the zero-current potential directly measured by the current-clamp mode. The predominant single-channel conductance of the K^+ channel was 9 pS and estimated density of the channel was about 25/μm^2 apparent membrane area. The naturally occurring platelet activator, ADP, could induce Na^+-influx through activation of Na^+-permeable channel regulated by cytosolic Ca^{2+} concentration.

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KINETICS OF PLATELET ADHESION ONTO MATERIAL SURFACE.

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A novel apparatus was constructed, to study of the platelet adhesion onto material surface. A rheoscope (consisted of inverted microscope and transparent cone-plate viscometer) was combined with TV camera, image processor, particle analyzer and computer.

1. The static image of the adhered platelets was obtained by averaging consecutive 8 Video frames. Then , by subtracting the static image from the next Video frame, the image of flowing platelets were obtained. The number and total area of platelet spots (both adhered and flowing) were decoded and fed into the computer, which calculated the time courses of total area, number, or area/number of the observed spots.

2. The basic features of the platelet adhesion on polymethylmethacryate plate were studied: e.g., the time courses of platelet adhesion and the influence of platelet concentration.

3. The kinetic parameters of the adhesion were estimated, by comparing the experimental data with the simulated time course on the basis of a simplified kinetic model. It is shown that the addition of platelets to the adhered spots is faster than the adhesion to the free surface.

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A BASIC STUDY ON He-Ne LASER-INDUCED THROMBUS FORMATION IN THE MICROCIRCULATION OF A RABBIT.

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Many factors are involved in thrombus formation. Chemical properties and interaction of these factors are well studied in vitro and hypotheses on thrombus formation in vivo are proposed. The present study was performed to study the mechanism of thrombus formation in vivo and to examine thrombotic indexes.

For the purpose, a vessel in a rabbit ear chamber was irradiated by He-Ne laser according to Kovács et al (1975) and the process of thrombus formation was recorded by VTR. Dose of Evans blue and irradiation time to induce thrombus formation at about 5 min were examined. Evans blue had a slight effect on platelet aggregation, but no effect on blood coagulation. Thrombus formation and occlusion occured faster in arterioles than in venules. Larger constriction was observed in arterioles of younger rabbits (5 months old), but not in those of older ones (9 months old) and venules (5 and 9 months old), suggesting that vessels grown in a chamber reflect age of animals.

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REGULATION OF BODY FLUID WITH DRINKING BEHAVIOR AND CHANGES IN BLOOD VOLUME AND PLASMA SODIUM CONCENTRATION. SUGIMOTO, E., YAWATA, T., OKUNO, T. AND MORIMOTO, T. Department of Physiology, Kyoto Prefectural University of Medicine, Kyoto 602

Thermally dehydrated rats consume dilute NaCl solution(ca. 50 meq/l) for about 2 h, and then slightly hypotonic NaCl solution(ca. 120 meq/l), when they are provided with both 1.8% NaCl solution and tap water simultaneously. To analyze the mechanism of the shift, changes in blood volume(BV) and Na concentration([Na]) of plasma were measured continuously for 4 h. With the rehydration of 4 h, BV recovered by 1.0 ml/100 g body wt and plasma [Na] by 5.4 meq/l(means of 6 experiments). The shift of [Na] of drinking water was observed when plasma [Na] was recovered by 65%, while blood volume recovered only by 43%. Urinary output was observed when plasma [Na] recovered by 88% and BV by 72%. Namely, rats lower plasma [Na] at the initial stage choosing dilute NaCl solution, and then expand blood volume with the consumption of isotonic NaCl solution. Urinary output was observed after recovery of blood volume. The result, together with the result of balance study, suggest that blood osmolality is regulated in precedence of blood volume.

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THE HYDRATION OF CREATININE OBSERVED BY H-NMR SPECTROSCOPY
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The behavior of water in the creatinine solutions at different pH of 1 to 12 was examined by the NMR relaxation times T_1 and T_2 of the water protons.

The samples prepared within the limit of its solubility were of 0 to 0.7 M at pH = 5 - 8 in the 0.2 M phosphate buffer, of 0 to 0.9 M at pH = 10 - 12 in 1 M NaOH, and 0 to 4 M at pH = 1 - 2 in 1 M HCl solutions.

Corresponded with the changes in pH, the creatinine solutions in all concentrations showed a peak of 3.0 $\pm$ 0.1 sec in T_1 near at pH = 7, but a trough of 0.6 $\pm$ 0.2 sec in T_2 at about pH 5 to 8.

In the increased concentrations at each different pH, their T_1 and T_2 decreased exponentially. Therefore, according to Zimmerman's formula, $1/T = h/T_b + (1 - h)/T_f$, the h numbers of hydration for a unit mole of creatinine (mol H_2O/mol) were calculated as the $T_f = T$ of pure water, and $T_b = T$ either at asymptotic point of T_2 or at the saturation point of T_1, and were obtained as 30 at pH = 5 - 8, 5 at pH = 1 - 2, 1 at pH = 10, and 0.1 at pH = 12 from T_2, and also as about 40 at all values of pH for T_1.

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THE PRESENCE OF ATRIAL NATRIURETIC PEPTIDE IN CANINE CEREBROSPINAL FLUID AND THE BRAIN AS ITS POSSIBLE ORIGIN. MASUDA,T.,*MASAKI,Y. AND **MARUMO,F. Dept. of Emerg. and Clit. Care Med.,**Dept. of Med. and *Technical Assistant,Kitasato Univ. Sch. Med.,Sagamihara,Kanagawa 228

The presence of the atrial natriuretic peptide (ANP) in canine cerebrospinal fluid (CSF) was clearly demonstrated and an attempt was made to determine its origin as either the brain or atrium. The concentration of ANP in canine CSF was 1.6±0.55 pg/ml (n=16), and showed no evident correlation with that in the plasma (r=0.38). Physiolosical and pharmacological doses of human α-ANP (α-hANP) were continuously infused intravenously in 5 dogs, but the ANP level in CSF was not influenced by the systemic administration of α-hANP. Only α-ANP could be obtained from the CSF samples, while both low and high molecular weight peaks were observed for plasma ANP, the atrium and hypothalamus tissue extracts by gel permeation chromatography. These results prove the presence of ANP in canine CSF and that it does not come from blood that has seeped across the blood-CSF barriers, but may originate from the brain.

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ROLE OF SECRETION MECHANISM OF ATRIAL NATRIURETIC PEPTIDE FROM THE ATRIUM UNDER PHYSIOLOGICAL CONDITIONS. F.MARUMO, and H.SAKAMOTO, Dept. Med. Kitasato Univ. Sch. Med., Sagamihara, Kanagawa 228

The secretion of human atrial natriuretic peptide (ANP) in response to isotonic saline-induced volume expansion and furosemide-induced contraction in 12 healthy men, was studied. ANP concentrations were measured by radioimmunoassay. The total ANP contents were calculated by multiplying the circulating plasma volume (CPV) times the plasma ANP concentration, assuming that most of the ANP remained in the blood vessels. CPV and extracellular fluid volume (ECFV) were also measured. After overnight dehydration, plasma ANP concentrations significantly increased after isotonic saline was infused, but the urine ANP concentrations did not essentially change. After furosemide-induced volume contraction, plasma ANP concentrations significantly decreased, but urine ANP concentrations did not essentially change. As the CPV and ECFV changed, the total plasma ANP also changed. This statistic coOrelation was highly significant. These results indicate that amount and type of ANP secretion may change depending on circulating plasma volume.

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ATRIAL NATRIURETIC FACTOR DURING HEAD-OUT WATER IMMERSION AT NIGHT.
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The present investigation was undertaken to test the hypothesis that a circadian variation in the atrial natriuretic factor (ANF) response is responsible for the nocturnal inhibition of renal responses to head-out water immersion (HOI). Plasma ANF responses to 3-h HOI (water temperature = 34.5 $\pm$0.5 ^{o}C) were studied during day (0900 - 1400 h) and night (2300 - 0400 h) in six hydropenic male human subjects. Diuresis and natriuresis induced by HOI were significantly attenuated at night as compared to the day. Plasma renin activity was nearly twofold greater during the day compared with night during time control period (TC) but it decreased to the same low level during HOI at both day and night. In contrast, plasma ANF level during TC was 30 - 40 pg/ml without showing any circadian variation. Moreover, plasma ANF showed a similar twofold increase in 1 h of HOI and was maintained at this elevated level throughout the 3-h HOI period in both the daytime and the nighttime series. Upon termination of HOI, plasma ANF decreased linearly to the pre-HOI level within 1 h. It is concluded that nocturnal inhibition of renal responses to HOI can not be attributed to circadian differences in the plasma ANF level.

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INHIBITION OF INSPIRATORY NEURONS BY DECREMENTING EXPIRATORY NEURONS AROUND THE BÖTZINGER COMPLEX. MANABE,M. AND EZURE,K. Tokyo Metropolitan Inst. for Neurosci.,2-6 Musashidai, Fuchu-shi,Tokyo 183

In Nembutal anesthetized, immobilized and artificially respired cats, we identified a group of inhibitory expiratory neurons in and around the Bötzinger complex. Their firing was increased by phasic or steady lung inflation. However they never fired during the inspiratory phase due to central inspiratory inhibition. Their firing pattern was of decrementing or non-augmenting type even during a brief ceasing of the respirator, being clearly different from nearby expiratory neurons of augmenting type. The antidromic mapping test showed that they projected their axons into the contralateral VRG and the Bötzinger complex, though no ipsilateral tests were done. Then intracellular membrane potentials of the inspiratory VRG neurons were averaged using extracellular spikes of the expiratory neurons as triggers. Hyperpolarizing potentials locked to the triggering spikes were obtained. They were IPSPs since their polarity was reversed when averaged during passage of hyperpolarizing current. Furthermore the coincidence of the latency of the IPSP with that of the antidromic activation showed that the connection is monosynaptic.

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PROJECTIONS OF BRAINSTEM NEURONS TO THE UPPER CERVICAL RESPIRATORY NEURONS AND THE PHRENIC MOTONEURONS IN THE CAT. A RETROGRADE DOUBLE LABELING STUDY USING FLUORESCENT DYES.
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Projections of the cells in the region of dorsal (DRG) and the ventral respiratory neuron groups (VRG) as well as in raphe nuclei in the brainstem to the upper cervical (C1-C2) respiratory neuron groups and to the phrenic motoneuron pools were examined in cats by using two kinds of fluorescent dyes; propidium iodide (PI)/4'-6-diamidino-2-phenylindol (DAPI) and diamidino yellow (DY)/Fast blue (FB). One dye was injected into the C1-C2 segments and the other into the C4-C6 segments by means of a Hamilton syringe. After 4 to 5 days survival, the serial sections of 60 or 100 μm were prepared from the brainstem and upper cervical segments. Both in the region of DRG and VRG, the cells labeled by each dye injected into two segments were found more numerous in contralateral side than in ipsilateral one. On the other hand, in raphe nuclei, the cells labeled by each dye were more numerous in ipsilateral side. Doubly labeled cells were also found in DRG and VRG as well as in raphe nuclei, ranging from 1.3 to 3.6% of all the labeled cells in each cell groups.

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LOCATION OF MEDULLARY NON-PHASIC UNITS EXCITED BY STIMULATION OF CENTRAL AND/OR PERIPHERAL CHEMORECEPTORS. KOGO, N., ICHIKAWA, K.*& ARITA, H. Inst. of Basic Med. Sci., Univ. of Tsukuba, Niihari, Ibaraki 305

Non-phasic units (146) were recorded extracellularly from the medulla in decerebrated, spontaneously breathing cats. The firing rate changes were studied during 100% CO_2-saline injections into the vertebral artery and the carotid artery. 53/146 units were excited by the vertebral artery injections in the same time course as ventilatory augmentation. 18/53 units did not reacted to peripheral chemoreceptor stimulation, i.e., they responded exclusively to central chemoreceptor stimulation. Their distributions were found in the "C" chemoceptive area, in the vicinity of ventral respiratory group (VRG) neurons and in the dorsal area ventral to the solitary tract,possibly corresponding to the common areas supplied by penetrating vessels of the basilar artery. 35/53 units were excited by peripheral chemoreceptor stimulation, i.e., the neurons with convergence of chemo-afferents, and were found to be packed densely in the nucleus paragigantocellularis lateralis, though also found in the vicinity of the VRG neurons. The remaining 93 units were the neurons with somatic properties (51) and non-responsive neurons (42).

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PROJECTIONS OF SUPRASPINAL STRUCTURES TO THE PHRENIC MOTOR NUCLEUS IN RATS STUDIED BY A HRP MICROINJECTION METHOD: COMPARISON WITH THOSE IN CATS. ONAI, T., SAJI, M. AND MIURA, M. Dept. Physiol., 1st Div., Gunma Univ. Sch. Med., Maebashi 371

We studied, with the horseradish peroxidase (HRP) method, supraspinal structures projecting to the phrenic motor nucleus of the rat cervical spinal cord. A double-barrel coaxial electrode was employed. To determine the site of the phrenic motor nucleus, the inner barrel electrode was used for recording antidromic potentials evoked by stimulation of the phrenic nerve and the outer barrel electrode was used for injecting HRP iontophoretically. In common with 5 experiments, significant number of labeled cells were distributed in only 2 regions of the medulla oblongata, the nucleus para-ambigualis (paraAMB) and the area ventral to the nucleus ambiguus of the rostral medulla oblongata (v-AMB), probably corresponding to the nucleus retrofacialis of the cat. The same as in the cat, negligible number of labeled cells were found in the nucleus raphe and the nucleus parabrachialis and Koelliker-Fuse nucleus of the rostral pons. The distribution is as follows; (1) the ipsilateral paraAMB (33.8%); (2) the contralateral paraAMB (22.2%); (3) the ipsilateral v-AMB (8.4%); (4) the contralateral v-AMB (1.9%). Different from cats, rats showed a negligible number of labeled cells in the nucleus tractus solitarii and the ipsilateral dominance of labeled cells in the paraAMB and v-AMB.

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ACTIVITY OF RESPIRATION-RELATED NEURONS IN RVL OF RAT MEDULLA (IN VIVO). ONIMARU, H., ARATA, A.* and HOMMA, I. Department of Physiology, Showa University, School of Medicine, Shinagawa-ku, Tokyo 142

We recorded respiration-related (R-R) neuronal unit activities in rostral ventrolateral medulla (RVL; containing C1 adrenergic neurons) of adult rats (anesthetized, vagotomized and artificially ventilated) and examined effects of hyperventilation and cooling of ventral surface of medulla. R-R (inspiration-related, I-R and expiration-related, E-R) neurons were commonly encountered in RVL. Decrease in respiratory rate induced by hyperventilation or bilateral cooling of chemosensitive areas of ventral surface was mainly due to prolongation of expiratory times which closely correlated to reduction in firing rate of E-R neurons in RVL. When the whole ventral surface was continuously cooled (15-20° C) by perfusion of Krebs solution, respiratory rate was reduced to about 10 min^{-1}. Then, neuronal activities (late E-R type) which always preceded but were not frequently accompanied with phrenic activity could be recorded from RVL. Present results suggested that these E-R neurons were important in inducing inspiration and in generating respiratory rhythm as observed in preparations (in vitro) of newborn rats.

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EFFECT OF CENTRAL CHEMOSENSITIVITY ON THE COHERENT RELATIONSHIP BETWEEN HIGH FREQUENCY OSCILLATIONS IN INSPIRATORY DISCHARGES OF THE PHRENIC AND CRANIAL NERVES. KATO, F., KIMURA, N., TAKANO, K. AND HUKUHARA, T., Jr. Dept. Pharmacol. II, Jikei Univ. Sch. of Med., Tokyo 105.

We have previously shown that common frequency components ranging 80-130 Hz synchronized with the high frequency oscillations (HFO) in the phrenic nerve activity (Ph) exist in the discharges of the vagus, facial (VII) and hypoglossal nerves (XII). To study the effects of the central chemosensitivity on the coherent relationship between HFOs in Ph and cranial nerve activities, the coherence functions (0-200 Hz, 0.25 Hz/bin) were calculated between Ph and VII (Ph-VII) and between Ph and XII (Ph-XII) of rabbits under artificial ventilation after bilateral section of vagus, aortic depressor and carotid sinus nerves. The non-linear least-squares method was used to evaluate the peak-frequency of HFO. Under normocapnia, Coherence at the peak-frequency of HFO (Coh) was 0.83±13 (mean± SD, n=13-15) and 0.84±0.12 for Ph-VII and Ph-XII, respectively. Hypoventilation significantly elevated Coh between Ph and XII (0.87±0.05), but not Ph-VII (0.83±0.10). Coh between Ph and VII was not significantly changed (0.82±0.11) during hyperventilation in contrast to Coh between Ph and XII which was significantly decreased to 0.79±0.11. Neuronal networks responsible for the synchronization of the HFOs in Ph and cranial nerve activities might receive quantitatively-different influences from central chemosensitive mechanisms.

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INHIBITION OF PHRENIC HIGH FREQUENCY OSCILLATIONS INDUCED BY VAGAL AFFERENT STIMULATION. Takano, K., Kato, F., Kimura, N. and Hukuhara, T., Jr. Department of Pharmacology II, Jikei University School of Medicine, Minato-ku, Tokyo 105

There have been no report concerning with the effect of vagal afferent stimulation on the high frequency oscillation (HFO) in the phrenic nerve activity. Experiments were performed in vagotomized, paralyzed and artificially ventilated rabbits. Aα-δ afferent fiber groups of the vagus nerve were selectively stimulated (0.5 V, 0.1 msec, 2.5-160 Hz). The peak-area (PA) and peak-frequency (PF) of the phrenic HFO were quantitatively estimated by using of the non-linear least-squares method before and during the vagal afferent stimulation. In response to the afferent stimulation, the period of the respiratory burst of the phrenic nerve discharge was reduced at low frequency and prolonged at high frequency stimulation. PA was significantly decreased (mean±SE: 46.3±7.9-9.9±5.6 % of the control, N=4-11) by the stimulation (2.5-160 Hz) even when the respiratory period of phrenic discharge was facilitated. Moreover, in six cases out of ten the phrenic HFO was not observed under the afferent vagal stimulation (160 Hz) in spite of the existence of the respiratory periodic discharges of the phrenic nerve. PF was slightly shifted to lower frequency side by low frequency stimulation (2.5-40 Hz). These results suggest that the oscillating and/or propagating processes of the HFO are more modifiable to the vagal afferents as compared with the respiratory rhythm generating mechanism.

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ACTIVITIES OF MEDULLARY RESPIRATORY NEURONS DURING SWALLOWING. UMEZAKI, T., HORI, T. AND KIYOHARA,T., Dept. Physiol., Saga Medical College, Saga 840-01

Unit activities of 148 medullary respiratory neurons in the nucleus retroambigualis and the ventrolateral nucleus of solitary tract were observed in the anesthetized cat during swallowing induced by pouring water droplet into the pharynx. Although about two-thirds of inspiratory neurons stopped the activity continuously during the whole period of swallowing, the remaining 38% of inspiratory neurons exhibited a transient (40-80 msec) activation of activity which started about 50 msec before the beginning of electrical activity of the thyrohyoid muscle. During this period the activity of all the expiratory neurons was arrested, and subsequently 91% of them showed a strong activation of activity which started approximately at the end of the transient activation of inspiratory neurons. The transient activation of inspiratory neurons resulted in a transient contraction of inspiratory muscles, thereby causing a sharp fall in intrathoracic pressure which was shown by falls in subglottic and intraesophageal pressures. The results suggest that the transient activation of medullary inspiratory neurons during the pharyngeal phase of swallowing creates the pressure gradient between the hypopharynx and the cervical esophagus which contributes to the generation of propelling force for the passage of a bolus and thus this neuronal activity constitutes a part of central programming of swallowing.

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RESPIRATORY REFLEXES ELICITED BY TACTILE STIMULATION OF THE PHARYNGEAL REGIONS IN THE RABBIT. MIYAOKA, Y. AND SHIMADA, K. Dept. Oral Physiol., Niigata Univ. Sch. Dent., Niigata 951.

Previous studies have shown that both inspiratory and expiratory muscle activities can be increased by mechanical stimulation of the nose and pharynx with airflow. The present study examined the influence of tactile stimulation of the nasopharynx and oropharynx on both muscle activities in lightly anesthetized rabbits by recording EMGs from the diaphragm (inspiratory) and pharyngeal constrictor (expiratory). Results indicated that the inspiratory activity was increased by the stimulation of the pharyngeal regions and indicated that the increase elicited from the nasopharyngeal surface of the soft palate was more prominent than those from the posterior walls of the nasopharynx and oropharynx. And the expiratory activity was also increased by the stimulation of the pharyngeal regions. The results suggested that afferent signals from tactile receptors of the pharyngeal regions might be responsible for the increases in both muscle activities of airflow origin.

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EFFECTS OF PEPTIDASE INHIBITORS ON REFLEX RESPIRATORY SUPPRESSION INDUCED BY THIN-FIBER MUSCULAR AFFERENTS. Kozaki Y., Simbulan, D., Tadaki, E., and Kumazawa, T. Dept. Nervous & Sensory Functions, Res. Inst. of Environ. Med., Nagoya Univ., Nagoya 464

In anesthetized, vagotomized, glomectomized, paralyzed and artificially ventilated cats, electrical stimulation of thin-fiber muscular afferents causes respiratory suppression a few minutes after cessation of stimulation. This "after suppression" was reversed when naloxone, an opiate antagonist, was injected into the 4th ventricle (by bolus or continuous infusion). Exogenous Met-enkephalin depressed respiratory outputs. Anti Met-enkephalin IgG tended to attenuate "after suppression". Combination of thiorphan and bestatin, both peptidase inhibitors, infused continuously into the 4th ventricle significantly potensiated "after suppression". Neither agent alone showed this effect. These results further support that endogenous enkephalin driven by stimulation of thin-fiber muscular afferents may be involved in reflex respiratory suppression.

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BARO- AND CHEMORECEPTOR AREAS IN TORTOISE. ISHII,K., ISHII,K. AND *KUSAKABE,T. Dept. of Physiol., Fukushima Med. Coll., Fukushima 960, and *Dept. of Anat., Med. Sch., Yokohama City Univ., Yokohama 236

In tortoise (Testudo hermanni) the dorsal carotid artery was demonstrated to be a reflexogenic area, in addition to the aortic arch, pulmonary artery and the truncal region which were previously reported in the turtle. A fine branch of glosso-pharyngeal nerve terminated in the dorsal (common) carotid artery. Chemo- and baroreceptor impulses were recorded from the peripheral cut end of this nerve. By electronmicroscopic study, a couple of cell clusters composed of granule-containing cells and supporter cells were observed in the media of the vascular wall of these receptive regions. Two types were differentiated in granule-containing cells. The one (G-cell) contained vesicles in size of 1000-1600 Å. Aspects of its inclusions, junctional connection between G-cells, and nerve endings making synaptic contact with the cell were similar to those observed in chemoreceptor regions of many animal species. An intimate contact between the G-cell and the smooth muscle was also observed. The other type cells (LG-cell) contained large dense-cored vesicles in various size (2000-7000 Å), and formed a cluster themselves, or mingled with G-cells. The nerve ending containing clear vesicles was in synaptic contact with LG-cell.

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THE RELATIONSHIP BETWEEN TIDAL EXPIRATORY ACTIVITY AND ITS DURATION. SIBUYA, M., ISOBE, A., IWASE, M. and HOMMA, I. Dept. of Physiol. Showa Univ. Sch. Med. Tokyo 142

The relationship between tidal expiratory activity and its duration was investigated in rabbits before and after bilateral vagotomy and in humans. Involuntary expiratory activity seen in M. biceps brachii reinnervated by internal intercostal nerves in patients with brachial plexus injury of the root avulsion type, as well as abdominal expiratory activity in anesthetized rabbits were studied. The phasic rising segment on the integration curve of the expiratory activities was used to determine the tidal expiratory activity (vertical deviation) and the active expiratory duration (T_{Ea}) (horizontal deviation). CO_2-rebreathing was performed with a plastic bag. An increase in tidal expiratory activity was seen in all situations. T_{Ea} was shortened in rabbits with intact vagal nerves and was prolonged in humans and vagotomized rabbits. Thus the relationship between tidal expiratory activity and the activity duration during CO_2-rebreathing was negative in rabbits before vagotomy and positive in humans and vagotomized rabbits. This indicates that vagal afferent impulses do not significantly influence the expiratory activity in humans. The same conclusion has been made regarding the inspiratory activity by Clark and Euler (1972).

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EFFECT OF INJECTION OF HYPERCAPNIC BLOOD INTO THE ANTERIOR INFERIOR CEREBELLAR ARTERIES ON THE PHRENIC NERVE ACTIVITY IN CATS.
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In the previous studies, it was supposed that the blood supply of the central chemoreceptor in the respiratory control system was almost through the anterior inferior cerebellar arteries (AICA). We examined the respiratory response to bilateral injection of hypercapnic blood into the AICA in anesthetized cats. After vagi and sinus nerve neurectomy, cats were paralyzed and artificially ventilated. Phrenic nerve activity, as the indicator of the respiratory center output, increased with an increase in pCO_2 (or $[H^+]$) of the injected blood. During the injection of the constant pCO_2 blood, inhalation of the hypercapnic gas mixture (8% CO_2 in O_2, 1 min) did not induce the change in the phrenic nerve activity and in the pH of ventral surface of the rostral medulla despite of a decrease in the pH of both caudal and intermediate area. Histological studies of the medulla injecting India ink into the AICA showed that vessels containing ink were exclusively observed in the rostral medulla. Thus, it was suggested that the activity of the central chemoreceptor in the rostral medulla was dependent on the blood pCO_2 level of the AICA.

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APNEA TEST ESSENTIAL FOR THE DIAGNOSIS OF BRAIN DEATH.
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We experienced 6 cases of brain death in whom we performed the apnea test to confirm the cessation of the medullary respiratory functions. Blood gases were analysed before (control) and after pre-oxygenation, after having adjusted PaCO2 around 40mmHg and every three minutes after disconnection from the respirator. Blood pressure and other vital signs were monitored. The mean PaCO2 level before disconnection was 46.2±6.0mmHg.

No one regained the respiration during 10 minutes of the apnea test. The pH and PaCO2 did not change significantly after pre-oxygenation and after adjusting of PaCO2. PaCO2 increased with the rate of 3.04±1.12mmHg/min up to 73.4±15.6mmHg and pH decreased with the rate of 0.016±0.007 down to 7.1±0.03 after disconnection from the respirator.

Apnea test guarantees to increase PaCO2 up to 73.4+15.6mmHg, which is enough to stimulate the medullary respiratory centers, without disturbing the blood or brain circulations.

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THE ROLE OF NEUROGENIC FACTORS INFLUENCING ON THE EARLY PHASE RESPONSES OF EXERCISE HYPERPNEA.
MIYAMOTO.Y.,KAWAHARA,K.,NAKAZONO,Y. AND GRUCZA,R.* Dept. Information Eng. Fac. Eng. Yamagata Univ., Yonezawa 992, *Dept. Appl. Physiol. Med.Res.Cent., Polish Acad. Sci., Warsaw 00-730.

The origin of the abrupt rise of ventilation in response to a step exercise (phase 1) has still remained unsettled. It has been suggested that the response may be caused by some neurogenic factors either mediated centrally or peripherally. Another explanation is that it may be activated through afferents from the right heart baroreceptors which can be stimulated by an increase in cardiac output. We measured cardiac output and ventilation of human subjects simultaneously and continuously during the transition from rest to light exercises. Exercise protocol included a "0"load pedalling passive pedalling, a short-lasting rhythmic isometric exercise by electrical stimuli to the tibial nerve, and a voluntary exercise simulating the previous electrically-induced exercise. We found that a significant decrease in the inspiratory duration and a significant increase in the inspiratory flow immediately after the onset of "0"load and passive pedallings. On the contrary, the initial peak of cardiac output delayed by about 10 sec. No meaningful responses were observed in the electrically-induced and voluntary isometric exercises. Thus, it may be concluded that the respiration and circulation during the early phase of exercise are independently controlled by neurogenic pathways, and an increase in cardiac output is not the cause of phase 1.

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MODULATION OF RESPIRATORY RHYTHM BY STIMULATION OF PERIPHERAL NERVES IN CAT.
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To elucidate the neural mechanisms responsible for the entrainment of the respiratory rhythm to the locomotor rhythm, we investigated the influences of afferent signals from the moving hindlimb on the respiratory movements. The tibial nerve was electrically stimulated at various phases in the respiratory cycle and the induced changes in tidal volume,end -tidal PCO_2 and respiratory interval were recorded and analyzed.

The tibial nerve stimulation elicited the phase-dependent effects on the respiratory movements. Stimulation given in late expiration produced the phase-delay of the onset of the next inspiration. Stimulation in early inspiration decreased the tidal volume in the cycle in which the stimulus was given. These effects were originated in the neural signals emanating from the moving hindlimb. However,the effects were abolished during electrically induced rhythmic exercise. Even when the stimuli were given repeatedly at the same phase as that of the first stimulation,the effects were only observed in the first few respiratory cycles. These results suggested that the phase-dependent neural effects described here were masked by the other prevailing regulation mechanisms of respiration during rhythmic exercise.

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THE NUMERICAL MODEL OF HIGH FREQUENCY VENTILATION. UYEDA, M., TANIFUJI, S+ AND INOUYE, A.++ Dept. of Physiol., Sch. of Med., Gifu Univ., Gifu, +Dept of Appl. Phys., Fac. of Eng., Osaka City Univ., Osaka and ++Dept. of Physiol., Hyogo Coll. of Med.,Nishinomiya

The gas exchange can be maintained during ventilation with such low tidal volume as less than dead space and high frequency. This method is termed high frequency ventilation (HFV). The mechanism of gas transport during HFV have not been investigated in detail. The augmented diffusion or the kinds of convective exchange were postulated for the mechanism. In an attempt to clarify this point we first calculated oscillatory convective diffusion in a straight tube of uniform cross-section. The Navier-Stokes equation for the oscillatory laminar flow in a straight tube had been solved by Womersley (1955). We solved numerically, using finite element method, the oscillatory and non-oscillatory convective diffusion equation whose flow velocity of convection term was exact solution of Navier-Stokes equation. The boundary conditions for convective diffusion equation were that the concentration was unity for the inlet and zero for the outlet and the tube surface. These conditions correspond to the gas exchange region. The concentration gradient was always higher for the oscillatory convective diffusion case than that of stationary Poiseuille flow case.

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REGIONAL INHOMOGENEITY CAUSED BY CONVECTION-DIFFUSION GAS MIXING IN TERMINAL AIRWAY.
TANIFUJI, S., UYEDA, M.+AND INOUYE, A.++ Dept. of Technol., Osaka City Univ., Osaka, +Dept. of Physiol., Gifu Univ. Sch. of Med., Gifu and ++Dept. of Physiol., Hyogo Coll. of Med., Nishinomiya

The gas transport by ventilation is a coupled process of molecular diffusion and convection. The molecular diffusion is homologous to any direction but the convective flow is dependent on flow direction. For the analysis of gas transport in the terminal bronchial tree, Navier-Stokes equation and convective diffusion equation of two dimension were coupled and solved numerically by finite element method. The time dependent solution of flow, pressure and concentration distribution were obtained by the method based on explicit numerical integration scheme in time. We had applied this method to the antisymmetrically branched last six generations of terminal airway and shown possible existence of the branching angle dependent anisotropic flow and flux of gas and uneven distribution of concentration in one breath cycle. For further realistic estimation of uneven distribution of gas concentration caused by the convective diffusion coupled to antisymmetric branching of airway, we calculated the branching angle dependence of both diffusion and convection flux from 18th to 22th generation, distal from dead space region. The calculation was done in three dimentsion and calculation scheme was same as two dimension cases described above using Stokes equation for flow. We concluded from the result that there had to be meaningful uneven distribution.

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ONE-SAMPLING REBREATHING METHOD TO MEASURE DIFFUSING CAPACITY FOR CO. NIIZEKI, K. AND DOI, K. Dept. of Physiol. Yamagata Univ. Sch. of Med., Yamagata 990-23.

To simplify the rebreathing method for obtaining the pulmonary diffusing capacity for CO ($D_L$co), a one-sampling method combined with a simulation technique was developed. The change in CO fraction in rebreathing air depends on the rebreathing volume (V_{RB}), the dead space volume (V_D), the gas volume in the lung-bag-system (V_S) and the $D_L$co. Using the measured V_{RB}, V_D and V_S, the changes in CO fraction in bag and alveolar air were simulated by varying the $D_L$co. The DLco was determined by checking the similarity between the simulated and measured CO fractions at the 7th expiratory period. To confirm the validity of the simulation method, two-sampling rebreathing and single breath methods were additionally carried out in 6 normal subjects in the sitting position. The DLco measured by the simulation agreed well with that measured simultaneously by the two-sampling method and also compatible with that obtained by the single breath method in normal subjects. In patients with emphysema, the $D_L$co determined by the simulation method was lower than that of two-sampling method, probably due to an incomplete mixing. In fibrosis, however, this method gave the good coincidence with the two-sampling method.

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MICROSTEPS ON THE DIFFUSION PATHWAY OF OXYGEN IN THE OX LUNG

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Inhaled oxygen molecules diffuse through alveolar membrane, endothelial membrane, blood plasma and erythrocyte membrane. Five phospholipid bilayers, therefore, exist on the diffusion pathway for oxygen in the lung. Measurements of the dynamic structure of phospholipid bilayers are required for understanding oxygen diffusion barriers in the lung. Viscosity and range of oscillation of phospholipid molecules in the lipid bilayers were measured in enzymatically isolated pneumocytes (47 cp, 47 degr.), endothelial cells (54 cp, 44 degr.) and erythrocyte ghost membranes (162 cp, 38 degr.) at 37°C with the nanosecond fluorescence depolarization technique. The viscosity of the blood plasma (1.7 cp) and of the sonicated erythrocytes (9 cp) were measured with a cone plate viscometer. The conductance of each step was assumed to be proportional to the value of viscosity times thickness. Using the obtained value for viscosity of each step and the known data of its thickness (each phospholipid bilayer 5nm, boundary layer of the blood plasma 0.5 μm and half thickness of erythrocyte 1 μm), the relative contribution of each step to the whole diffusion pathway was estimated to be 8, 8, 4 and 80 % for the phospholipid bilayers of pneumocytes+endothelial cells, boundary layer of blood plasma, erythrocyte membrane and hemoglobin solution, respectively.

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INFLUENCE OF HIGH O_2 AFFINITY OF BLOOD ON THE O_2 TRANSFER IN RESTING DOG GRACILIS MUSCLE. KOHZUKI, H., OHGA, Y., SAKATA, S. AND ENOKI, Y. SECOND DEPT. OF PHYSIOL., Nara Med. Univ., Kashihara, Nara 634

To evaluate the physiological consequences of high O_2 affinity blood *in vivo*, we used resting dog gracilis muscle preparation, perfused alternately with normal and high O_2 affinity dog blood of constant arterial O_2 content (Ca_{O_2}) at varying flow rates (37°C). The high O_2 affinity blood was prepared either by short-term incubation at 37°C (n=9: P_{50}=24.8±1.0 Torr) or by overnight standing at 4°C (n=3: P_{50}=19.0±1.4 Torr) of the blood with 30 mM cyanate in buffered saline. O_2 consumption ($\dot{V}o_2$) of the muscle was O_2 delivery-dependent below a critical level of the O_2 delivery (= Ca_{O_2} x Blood flow), above which it turned out to be the delivery--independent. This relationship was little dependent, both qualitatively and quantitatively, of the O_2 affinity of blood, although the Pv_{O_2} was significantly lower in perfusions with the high affinity blood than in those with the normal blood. The maximal $\dot{V}o_2$, the critical O_2 delivery and the maximal O_2 extraction ratio was 0.30 and 0.45 ml/min·100g muscle and 0.67, the values not different from each other in the normal and high affinity perfusions.

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ESTIMATION OF THE TRANSFER COEFFICIENTS OF OXYGEN AND CARBON MONOXIDE IN THE BOUNDARY OF HUMAN RED BLOOD CELL BY MICROPHOTOMETRIC METHOD. SHIBUYA, I. AND MOCHIZUKI, M. Dept. Physiol., Yamagata Univ. Sch. Med., Yamagata 990-23.

The reaction rates of O_2 and CO with human red blood cells (RBC) were measured by using a microphotometric apparatus (Mochizuki et al., 1973). A small amount of RBC was put in an air-tight reaction cuvette. Gas mixtures containing 5.6%-CO_2 and various concentrations of O_2 and CO were sequentially injected into the cuvette and the change in O_2 and CO saturation of hemoglobin was measured from the change in transmission of RBC at 402 and 416.5 nm. The reaction rate of CO with RBC was significantly influenced by photodissociation of carboxyhemoglobin (COHb). The affinity of CO was reduced to about 1/100 of that reported in a dark condition. To eliminate the photodissociation of COHb, a short-pass filter (400 to 435 nm) and a sector were used. Then, the maximal saturation of COHb was about 85 % at Pco = 3.0 Torr and Po_2 = 100 Torr, indicating photodissociation was almost completely excluded. By comparing the measured reaction rates of O_2 and CO with the theoretical rates obtained from the numerical solutions of the partial differential equations of the diffusions of O_2 and CO, the transfer coefficients of O_2 and CO in the RBC boudary, including RBC membrane and water layer around the RBC, were estimated. Both the values showed good agreement, ranging from 0.1 to 2.5 x 10^{-6} cm$\cdot$sec$^{-1}\cdot$Torr^{-1}.

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METABOLIC RESPONSE OF DEVELOPING CHICK EMBRYOS TO GRADUAL COOLING. OKUDA, A.*, NAKAZAWA, S.*, SUZUKI, Y. AND TAZAWA, H. Dept. of Electronic Engng., Muroran Institute of Technology, Muroran 050

There is no doubt that chickens are dominantly poikilothermic during embryonic stages and develop a marked capacity to maintain body temperature after the time corresponding to hatching. When it comes to an emergence of metabolic response to cooling during embryonic development, however, experimental results are ambiguous. A magnitude of cold relative to a metabolic heat production of embryos may be substantial to examine the metabolic response of developing embryos to cold. The present study was therefore designed at first to estimate the magnitude of heat conductance of eggs. The heat conductance of about 70 mW/^{o}C estimated for incubating eggs indicates that heat loss upon step function exposure to even mild cold (1-2 ^{o}C difference) exceeds metabolic heat production of developing embryos (e.g., 130-140 mW at the last stages of prenatal period). Based on this result, the gradual cooling procedure was designed to make the difference between heat loss upon cooling and heat production very small and examine whether or not a metabolic response to cooling emerges before hatching. Determination of O_2 consumption during gradual cooling of the egg suggests an emergence of metabolic response to lowered temperature before hatching. The thiourea which antagonizes the metabolic effects of thyroid hormones impaired this metabolic response.

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EFFECTS OF ALTERED SHELL DIFFUSIVE CONDUCTANCE ON BLOOD GAS PROPERTIES AND ERYTHROCYTES OF CHICK EMBRYOS. NAKAZAWA, S.*, OKUDA, A.*, SUZUKI, Y. AND TAZAWA, H. Dept. of Electronic Engng., Muroran Institute of Technology, Muroran 050

Effects of widely altered shell diffusive conductance on blood gas properties and hematological variables were investigated in 16-day chick embryos. The alteration of conductance was made by coating partially the shell with epoxy or removing it over the air cell before beginning of incubation. Beyond the control range of water vapor conductance (gH_2O), the arterialized blood Po_2 (Pa_{O2}) did not significantly increase with increasing conductance. Changes in Pa_{O2} and also Pa_{CO2} with widely altered gH_2O were expressed by quadratic regression equation of inverse gH_2O. Hematocrit value (Hct) and mean corpuscular indices also changed with quadratic function of inverse gH_2O. While erythrocyte number and blood hemoglobin concentration were insignificantly changed with conductance, these variables along with Hct were linearly correlated to changes in Pa_{O2}. In connection with lowered gH_2O, the reduced Pa_{O2} might contribute to increases in both cell number and macrocytes and concurrent hypercapnia increased cell volume (MCV), increasing Hct. The small decrease in mean corpuscular hemoglobin as compared with increase in MCV which might be attributed to both hypoxia and hypercapnia accounted for the decrease in mean corpuscular hemoglobin concentration at lowered gH_2O. The whole blood Hb concentration was however maintained high by increased cell number in hypoxia.

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CHANGE IN PH OF EXTRACELLULAR FLUID IN MEDULLA DURING INJECTION OF HIGH CO2-SALINE INTO THE VERTEBRAL ARTERY. ICHIKAWA, K.*, KOGO, N. & ARITA, H. Inst. of Basic Med. Sci., Univ. of Tsukuba, Niihari, Ibaraki 305

Neutral-carrier pH-sensitive microelectrodes were used to measure extracellular fluid (ECF) pH deep in medulla in anesthetized, spontaneously breathing cats. Under steady conditions no systematic pH gradient could be found in the rostral medulla except for the dorsal regions in solitary tract nucleus and vestibular nucleus, where ECF pH was significantly lower (7.10-7.23) than that in the ventral half of medulla (7.25-7.38). When 0.5 ml of 100% CO2-saline was injected into the vertebral artery, we found those points at which ECF pH decreased in the similar time course to ventilatory augmentation; ECF pH started to decrease just before the onset of ventilatory augmentation; the peak change (by up to 0.25 units) corresponded to the maximal facilitation of ventilation; its recovery was analogous to the ventilatory recovery. These points were found to be scattered variously in the regions extending from the vicinity of nucleus ambiguus to the ventral surface. It was confirmed by arterial dye injection that those regions were densely supplied by penetrating vessels of the basilar artery.

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AN ASSESSMENT OF OVERALL OPEN-LOOP GAIN OF CO_2-VENTILATION FEEDBACK CONTROL SYSTEM IN THE AGED. MASUYAMA,H.*,** AND HONDA,Y.** Pulmonary Division, Tokyo Metropolitan Geriatric Hosp., Tokyo 173* and Dept. of Physiol., Sch. of Med., Chiba Univ., Chiba 280**

Overall open-loop gain of the CO_2-ventilation feedback control system (Gco_2) and airway occlusion pressure ($P_{0.2}$) were determined on 8 healthy female aged subjects (75.3±6.1 years old; M±S.D.). After measuring the metabolism, they were subjected to the CO_2 rebreathing test and $P_{0.2}$ measurement, simultaneously. Gco_2 was calculated by dividing the slope of the CO_2 response curve (S) by that of the metabolic hyperbola (S_L). $P_{0.2}$ was evaluated by the slope of the $P_{0.2}$ curve against Pco_2 ($\Delta P_{0.2}/\Delta Pco_2$). No significant differences in the magnitudes of Gco_2 and $\Delta P_{0.2}/\Delta Pco_2$ were observed between the young previously reported and the aged. This suggests that the regulation of hypercapnia plays a most important role in the respiratory control regardless of the aging.

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POST HYPOXIC VENTILATORY DEPRESSION IN ANESTHETIZED RAT. MARUYAMA,R.,TOZIMA,H.,YOSHIDA,A AND FUKUDA,Y. Dept.Physiol.,Chiba Univ. Sch.Med.,Chiba 280

Change in breathing pattern following exposure to acute isocapnic hypoxia(progressive hypoxia)were studied in halothane anesthetized spontaneously breathing rat. After termination of hypoxic exposure the ventilation was significantly depressed for a long period time.(post hypoxic depression)
The magnitude of post hypoxic depression and recovery time depended on the severity of hypoxia; which was accompanied with reduction in respiratory frequency due to prolongation of expiratory time.
The post hypoxic ventilatory depression did not occour when the carotid sinus nerve bilaterally sectioned.
The results suggest a possibility post hypoxic depression of ventilation may be due to reduction afferent dischages from carotid chemoreceptor.

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STIMULATION AND INHIBITION OF RESPIRATORY RHYTHMICITY DURING ACUTE HYPOXIA IN ANESTHETIZED RAT. FUKUDA, Y. AND KIMURA, H. Dept. Physiol. II, Sch. Med., Chiba Univ., Chiba 280

Effects of acute hypoxia on discharge patterns of various efferent respiratory nerves were investigated in the halothane anesthetized, vagotomized and artificially ventilation rat. Acute hypoxia caused the increase in respiratory frequency, and augmented the phrenic and superior laryngeal inspiratory activities with extremely increased vagal pharyngeal expiratory activity. This respiratory stimulation was followed by the reduction in respiratory frequency with well maintained inspiratory expiratory discharges. Changes in respiratory frequency were largely due to alteration of expiratory time. Furthermore, observations of the slow but early onset of laryngeal inspiratory activity showed that the timing of the start of inspiratory activity determined the expiratory time. The inspiratory time was not significantly altered during hypoxia. After carotid sinus nerve section, hypoxia initiated the reduction in respiratory frequency with reduced expiratory discharges, weil inspiratory discharges and their times were fairly well reserved. The respiratory depression, especially reduction in frequency, during hypoxia is likely due to the direct effect of hypoxia on medullary respiratory mechanism.

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EFFECTS OF TEMPERATURE AND DAY LENGTH ON THE OXYGEN CONSUMPTION AND MOVEMENT RATE IN THE BULLFROG. SAKAKIBARA, Y., Dept. of Physiol., Sch. of Med., Chiba Univ., Chiba 280

11 bullfrogs were maintained their averaged body weight(about 220 g) by feeding cat foods during the experimental period of 14 months. By using this single population, effects of temperature(5, 15, 25°C) and day length(8 hours daily; 8L and 14L) on VO2 and movement rate(MR) were examined. Animals were acclimated to either variable at least 7 days and then placed in the metabolism chamber for 4 days(SAKAKIBARA 1986, J. Physiol. Soc. Japan 48 : 386). Slow and rapid pressure signals coming from the test chamber were separated with filters and subserved for VO2 and MR measuring, respectively. In every run, the maximum VO2, appeared within the first 24 hours, were 2(at 5°C) or 4 times (15 and 25°C) each minimum value. VO2 correlated highly with MR. After acclimation to the chamber frogs showed diurnal rhythms under any condition examined. Amplitude of these rhythms were largely affected neither by temperature, nor by day length. But 5°C retarded the beggining of the phase of increasing activity by several hours. Day length did not change the averaged VO2 values. Then my conclusions are as follows. The rhythms of VO2 and MR have a characteristic to manifest in a wide range of temperature. The phase of rhythm may relatively easily be affected by temperature. The metabolic thythm is largely determined by the rhythm of movement activity.

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VENTILATORY AND CIRCULATORY RESPONSE AT THE BEGINNING OF EXERCISE (PHASE 1) MORIKAWA, T., INOUE, S.*, ONO, Y.*, SASAKI, K.*, SAKAKIBARA, Y., TANAKA, Y., MARUYAMA, R., NISHIBAYASHI, Y. AND HONDA, Y. Dept. Orthopedic Surg., Dept. Physiol. Sch.. Med., Chiba Univ., Chiba 280

The ventilatory and cardiac responses to electrically induced, voluntary and passive leg exercises were studied in 16 normal men. In 12 patients with traumatic spinal cord transection at the level of Th5-Th12, these responses to electrically induced exercise, passive exercise and intentional effort to move their legs were studied. In normal subjects, $\dot{V}_E$ increased from t..e first breath after onset of voluntary and electrically induced exercises. Cardiac output was gradually increased after onset of voluntary and electrically induced exercises, and at the fifth breath in the voluntary exercise cardiac output was significantly higher than that in passive exercise. On the other hand in the patients, $\dot{V}_E$ increased from the first breath after they intended to move their legs. But at that stage, cardiac output was not changed. Electrically induced exercise also increased $\dot{V}_E$ at the second and third breath after stimulation. Cardiac output and heart rate were not affected by all three types of exercise. We concluded that afferent neural input from the exercising limbs as well as central command may have played some role of phase 1 hyperpnea. Neural afferents also affected the cardiac response to exercise.

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AN ASSESSMENT OF NASAL FUNCTIONS IN CONTROL OF BREATHING. TANAKA, Y., MORIKAWA, T. AND HONDA, Y. Dept. Surg. Instit. Pulmonary Cancer Research and Dept. Physiol., Sch. Med., Chiba Univ., Chiba 280

Breathing pattern and steady state CO_2 response of 9 healthy adults were compared between mouth and nose breathing. In addition, the effect of warming and humidification of the inspired air was observed during mouth-piece breathing. 1) Dead-space and airway breathing. 2) No significant difference in P_{CO_2}-ventilation response slope was seen between the two types of breathing, but the P_{CO_2}-occlusion pressure response slope was significantly enhanced with nose breathing. This probably indicate the presence of load compensation due to augmented R_R as well as flow-sensitive nasal receptors which elicit hypoventilation. 3) Inhalation of warm and humid air significantly depressed P_{CO_2}-ventilation and -occlusion pressure responses. These results indicated that nose breathing may effectively prevent falling P_{aCO_2}. It was suggested that loss of nasal functions, such as during nasal obstruction, may result in hypocapnia and easily induces apnea during sleep.

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VENTILATORY RESPONSES TO HYPOXIA AND HYPERCAPNIA IN FEMALE ATHLETES. OHYABU,Y., HONDA,Y., SAKAI,J. AND OHYABU,I. Sch. Med.,Chiba Univ.,Chiba 280 Sch. Physical Education, Tokai Univ., Kanagawa 259-11

Sixteen aerobic dancers, 14 volleyball players and 12 non-athletes were examined by an isocapnic progressive hypoxia and Read's CO_2 rebreathing tests.

The results were as follows:

1) Aerobic dancers showed significantly less hypoxic ventilatory response ($\dot{V}_{50}$) than the non-athletes.

2) The significant relationships between hypoxic ventilatory response (A, $\dot{V}_{50}$) and body weight in volleyball players were found. Such correlations in volleyball players became insignificant when the A or $\dot{V}_{50}$ values were recalculated by normalization of ventilation for 70 kg body mass.

3) Hypercapnic ventilatory sensitivity, S, in aerobic dancers and volleyball players was not significantly less than that of non-athletes.

These results suggested that characteristics features of hypoxic response are different among female athletes.

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Daily and seasonal variations in the hypercapnic ventilatory response at rest. MIYAMURA,M. and HIRUTA,S. Lab. Work Physiol., Res. Cent. Hlth. Phys. Fit. Sports, Nagoya Univ., Chikusa-ku, Nagoya 464

The ventilatory response to carbon dioxide at rest was determined repeatedly by the rebreathing method; seven slopes (S) of hypercapnic ventilatory response lines, with 4 hour intervals, were examined in 10 healthy male subjects. Although there are no significant daily variation in the mean value of S, the S value of each subject tends to peak at four in the morning. Furthermore, the hypercapnic ventilatory response lines at rest were measured in the 11 male students with 2 month intervals. It was found in this experiments that pulmonary ventilation (VE(60)) at 60 torr of PACO2, which was calculated from equation (VE = S (PACO2 - B) for each subject, was significantly higher in the summer than that in the winter, whereas a clear seasonal cycle was not apparent in the S values.

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PROPERTIES OF SLN AFFERENT ACTIVITY IN THE RABBIT. TSUBONE, H., MATHEW, O. P.* AND SANT'AMBROGIO, G.* Nat.Inst. Environ. Stud., Ibaraki 305, and Univ. Texas, TX 77550

Respiratory modulation of the superior laryngeal nerve (SLN) afferents and their response to transmural pressure were studied in 24 anesthetized, spontaneously breathing rabbits. The whole nerve activity has a predominant inspiratory augmentation during tracheal breathing and occlusion that can be accounted for by the respiratory drive transmitted to the larynx. During upper airway breathing and occlusion SLN afferent activity increasès in expiration and decreases in inspiration. This respiratory modulation is due to changes in upper airway pressure (Pua): Positive pressure stimulates SLN afferent activity, while negative pressure inhibits it. Mechanical restriction of epiglottal movement reduced the response to Pua changes during upper airway occlusion and application of maintained positive (mean 0.25 kPa) and negative (mean -0.3 kPa) pressures . Surgical removal of epiglottis decreased the baseline activity of SLN to 16.5% of control. These experiments suggest that in the rabbit the epiglottis is the main source of SLN afferent activity and that its displacement, due to changes in Pua, is the most important factor for modulating SLN activity. Recordings of single unit activities from 70 receptors showed that most of them revealed an inspiratory augmentation with tracheal breathing and occlusion, were stimulated by positive pressure and inhibited by negative pressure, reflecting the behavior observed in the whole nerve.

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ON THE pH OF THE HUMAN SALIVA. NANBA RYOZI Faculty of Education, Okayama Univ., Okayama 700

It is known that the properties of saliva are very different according to not only the types of salivary glands but also the environment and the conditions of measurement. Especially, the pH of saliva varies with the various conditions. So it desirable that the pH of saliva should be measured in the oral cavity. This time, the author measured the pH of mixed saliva(submandibular and sublingual saliva) in the oral cavity by means of a glass pH-microelectrode. The results of the experiment are summarized as follows : 1. The pH of saliva in the oral cavity is 5.8 - 7.3 on the average. It is early in the morning, at the time of awakening, that the pH is the lowest in a day. It is at the time immediately after a meal (breakfast, lunch or supper) that the pH is highest and alkaline. 2. The pH of saliva between meals is about 6.3 - 6.6 . 3. It is found that the pH of saliva after bathing is slightly more acidic than the pH between meals.

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INTESTINAL ABSORPTION OF COLOSTRUM PROTEINS IN NEONATAL PIGS.
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The absorptive mechanism of the colostral proteins through the small intestine was investigated in the neonatal pigs without sucking. Cannulae were inserted into the left external jugular vein, thoracic duct and duodenum. Peripheral blood and lymph were collected at 0, 1, 2, 4, 6 hr after infusion of cow's colostrum (40 ml/kg body wt.). Total protein conentrations in serum and lymph increased to 123% and 264%, respectively, at 4 hr after colostrum infusion. Most of the colostral proteins were detected in serum and lymph by electrophoresis and immunodiffusion test. The absorption profile of colostral proteins in serum resembled to that in lymph. The composition of the absorbed proteins, however, was different from that of the colostrum. These results suggest that the intestine of the neonatal pig absorbs selectively exogenous macromolecules.

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Studies on Phenomena through Intestinal Membrane and its Disturbances(III). Nakano,S., Terao,T., Nagami,K. and Yoshioka,T.(Dept. of Physiol.,Tokai Univ. Sch. of Med., 259-11, Isehara, Kanagawa.

In previous studies by use of our devised circulation apparatus, we have investigated a series of experiments on penetration of L-Phenylalanine, L-Tryptophane and Insulin as activepolypeptides through everted intestine of a rat. In the present study, also using the above apparatus, intestinal penetration phenomena of Phenylalanine were investigated under each following conditions by use of we devised a method which can automatically analyze computer program. The obtained experimental result were as follows : 1) When di-, tri-peptides contained with Phenylalanine peptides was applied under in-vitro condition to the mucosal side of this apparatus, it was found that Phenylalanine penetration was decreased clearly in order of Asparatame(Asp+Phe), Tripeptides-1(Phe+Phe+His), Tripeptides-2(Gly+Ala+Phe), Tripeptides-3(Glu+Val+Phe) and Low phenylalanine peptides. 2) In addition to Chymotrypsin and Carboxypeptidase on Asparatame and Tripe-tides-1, Phenylalanine penetration were enhanced. On the contrary, in such a case of Tripeptides-3 and Low phenylalanine peptides, Phenylalanine penetration had no defined change. 3) These observations suggest that the addition proteolytic enzyme. The enzyme could produce there own different Phenylalanine penetration features of intestinal membrane.

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EFFECTS OF HYPOTHALAMIC STIMULATION ON THE CANINE PANCREATIC EXOCRINE SECRETION.
FURUKAWA, N. AND OKADA, H. Dept. Physiol., Kawasaki Med. Sch., Kurashiki 701-01

Effects of hypothalamic electrical (ES) and chemical stimulation (CS) on pancreatic exocrine secretion were studied in chloralose anesthetized and hemispherectomized 21 dogs whose spinal cord was cut at cervical level and pyloric sphincter was occluded. ES (30 Hz, 0.15-0.2 mA, 3 msec) and CS (microinjection of 0.1 M dl-homocysteic acid, 0.6-2.0 µl) were applied to the same point using a double barrel glass electrode. The increased responses on the pancreatic flow by ES were obtained from ventromedial area of the anterior hypothalamus (AH) closed to the optic chiasma, dorsal area of AH (paraventricular nucleus and perifornical area), ventrolateral area of the middle hypothalamus, caudal portion of the ventromedial nucleus (VMH), a part of dorsomedial nucleus (DMH) and the mamillary body. The inhibitory responses by ES were obtained from the defence area of AH, dorsal parts of the hypothalamus, VMH, a part of DMH, and the posterior hypothalamus. CS applied to the same regions generally caused smaller response (80-90%) of the same direction. In some points, ES was only effective, but they were scattered. Most marked increased response by ES and CS was obtained from the ventromedial area of AH. These excitatory and inhibitory responses were induced via the vagus nerves.

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EFFECTS OF THE MID-BRAIN STIMULATION ON THE CANINE PANCREATIC EXOCRINE SECRETION.
OKADA, H. AND FURUKAWA, N. Dept. Physiol., Kawasaki Med. Sch., Kurashiki 701-01

The influence of electrical (ES) and chemical stimulation (CS) of the mid-brain on pancreatic exocrine secretion was studied on 22 decerebrated dogs whose cervical cord was transected and the pyloric sphincter was occluded. CS was performed by microinjection of 0.1 M dl-homocysteic acid (0.6-2.0 µl) through a glass electrode. Increase of the pancreatic outflow was obtained by ES of the dorsolateral and ventrolateral reticular tegmentum, a part of the superior colliculus, the central grey substance, the parabrachial nucleus, the interpeduncular nucleus, the dorsal tegmental nucleus of Gudden, the dorsolateral tegmental nucleus and the superior central nucleus. Decrease in the outflow was obtained by ES of the medial reticular tegmentum, the ventrolateral portion of the central grey substance, the dorsal raphe nucleus, the medial aspect of the lateral lemniscus and its nucleus. CS applied to similar regions described above produced excitatory or inhibitory effects on the pancreatic outflow, but the effective regions were narrower than those in ES. The mean values of the maximal increased pancreatic outflow by ES and CS in each animal reached to 48% and 43% of the maximal outflow (936±108 µl/5 min. n=6) by secretin (4 U/kg i.v.), respectively. Both excitatory and inhibitory effects were induced via the vagus nerves.

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INHIBITORY FACTORS ON PANCREATIC EXOCRINE SECRETION IN THE CONSCIOUS RAT.
KYOKO MIYASAKA AND KENICHI KITANI. Tokyo Metropolitan Institute of Gerontology, Tokyo-173

The factors that turn off the pancreas after a meal were examined in the consious rat. Rats were prepared with cannulae draining pure pancreatic juice and bile separately and with a duodenal and a jugular vein cannula. Experiments were conducted after 5 h fasting between the 3rd and sixth postoperative days. Bile and pancreatic juice(BPJ) was diverted from the intestine for 3 h and was replaced with 0.05 M $NaHCO_3$, then 1 µg/kg/h of rat pancreatic polypeptide(PP), somatostatin-14 and porcine peptide YY, 100 µg/kg/h of atropine(iv), or 2 % sodium oleate (intraileal) were infused. Rat PP, somatostatin-14 and atropine significantly inhibited pancreatic secretion but the inhibition was transient. The effective doses, (1 µg/kg/h) of PP which increased plasma PP concentration as much as the postprandial level and somatostatin, were less than one twentieth those required in the anesthesized animal. PYY and intraileally infused oleate did not significantly affect pancreatic secretion. However, the endogenously released PP by BPJ diversion parallelled the change of protein output. The inhibition of PP release by previous treatment with atropine did not produce any increase in protein output. Therefore, it is suggested that not only inhibitory agents but also the ceasing of stimulation is required to return the pancreatic secretion after a meal to the basal level.

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THE SPHINCTER OF ODDI AND EVACUATION OF BILE. NARUSE, S.
National Institute for Physiological Sciences, Okazaki 444

The evacuation of bile in relation to the activity of the sphincter of Oddi and gallbladder was studied. Four beagle dogs were provided with gastric, duodenal and gallbladder fistulae under ether anesthesia. After one month recovery period the animal was fasted for 18 h. The sphincter of Oddi was canulated with a 3F micro-pressure transducer and bile fistula was connected to another pressure transducer. Gastric and duodenal motilities were also recorded. Basal pressure of the sphincter was higher than that of the common bile duct by 4-5 mmHg. Phasic contractions with amplitudes of 40-60 mmHg were superimposed on the basal pressure during quiescent phase of the stomach and duodenum. During this phase gallbladder pressure was 0-2 mmHg. Basal sphincter pressure was reduced to 3-4 mmHg at each periodic contraction of the gallbladder (about 10 mmHg). The amplitudes of phasic contractions were also reduced and the bile was evacuated into the duodenum. During the peak of duodenal motility gallbladder pressure was reduced to 0-2 mmHg. Basal pressure and amplitudes of phasic contractions of the sphincter were increased to 5-20 mmHg and above 100 mmHg, respectively. It is concluded that the bile was allowed to evacuate into the duodenum for only a brief period of periodic gallbladder contraction, when the pressure of the sphincter of Oddi was lower than that of the gallbladder in fasting dogs.

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METABOLISM AND CHOLERETIC PROPERTIES OF 7-KETO LITHOCHOLIC ACID. KITANI, K., AND KANAI, S. Metropolitan Inst. of Gerontol., 35-2, Sakaecho, Itabashi-ku, Tokyo 173

Metabolism and choleretic properties of 7-keto lithocholic acid (7-keto) was examined in anesthelized male rats under a continuous iv infusion of 7-keto (1.2 μmol/min/100g). Analysis of bile collected from the 7-keto infused rats showed that appreciable amounts of 7-keto are metabolized to both cheno- and ursodeoxycholate, but the major fraction was tauro 7-keto. The bile flow rate began to increase immediately after the start of 7-keto infusion, and increased further in the second hr after a transient decline (or plateau) between 30-60 min. The bile bicarbonate concentration increased in parallel with the bile flow change. On the other hand, the bile salt excretion leveled off or tended to decline in the second hr, resulting in a dissociation of the bile flow and bile salt excretion rate. The results are similar to what we observed with ursodeoxycholate (1), which are difficult to explain on the basis of the conventional theory for bile-salt dependent bile formation. Results suggest that at least two different mechanisms need be considered to explain bile-salt induced choleresis in general.

(1) Kitani K. & Kanai S. Life Sci. 31:1973-1985, 1982

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COMPLIANCE CHANGES OF GASTROINTESTINAL TRACT IN STREPTOZOTOCIN DIABETIC RATS. KARAKIDA,T. and HOMMA,S. Dept.Physiol.Niigata Univ.Sch.Med., Niigata 951

In experimental diabetic rats, motile disorder and enlargement are known in gastrointestinal tract. We recorded intraluminal pressure of isolated alimentary tract of diabetic rats and suggested the disturbance of pacemaker activity. To characterize further the physical properties of diabetic alimentary tract, we measured wet weight, radius, length, volume and intraluminal pressure in response to saline injection into isolated stomach, duodenum, jejunum, ileum and colon, of 3 cm. Small intestine as a whole was longer in diabetic rats than in normal ones, but wet weight/unit length(cm) was similar in jejunum, ileum and colon(except duodenum). Diabetic and normal stomach were similar in wet weight but maximal volume(Vm) injected was 1.5 times larger in diabetic rats. Radius-length plotting of intestine in response to saline injection showed that diabetic preparations tended to be distended more circumferentially than normal, as well as longitudinally.Slope of tension increase of every intestinal segment of diabetic rats was much smaller than that of normal ones in tension-radius relations within certain region. Over that, it steeply increased similarly. Significant increase in cord compliance was found in stomach, jejunum, ileum and colon of diabetic rats when compared with normal. However, significant increase in specific compliance was found just in stomach and jejunum. These results suggest the larger distensibility of diabetic stomach and jejunum than that of normal on food intake.

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STUDIES ON THE SELF-DEFENCE MECHANISM IN GASTRIC MUCOSA (1) THE ROLE OF ENDOCRINE SYSTEM IN THE STRESS ULCER. OSHIBA, S., IMAI, S., SAWAI, H. AND OKADA, M.* Dept. Physiol., Nihon Univ. Sch. Med., Tokyo 173 and *2nd Dept. Int. Med., Natl. Def. Med. Coll., Saitama 359

This study involving hypophysectomized (Hypox) and adrenalectomized (Adrex) rats was attempted to evaluate the role of the pituitary-adrenal axis in the pathogenesis of stress ulcer induced by the application of restraint and water immersion stress, and revealed that 1) the ulcer index of the non-operated (Intact) rats was 12mm^2 at 2hrs and then to 25mm^2 in the next 2. The Hypox and Adrex rats exhibited a significantly lower rise. 2) the gastric mucosal blood flow in the Intact rats was 68ml/min/100g. It fell to 33ml/min/100g at 2hrs and 29ml/min/100g at 4hrs after the stress. In contrast, the value was unaffected by the stress in the Hypox and Adrex rats. 3) the norepinephrine concentration in the gastric mucosa in the Intact rats rose from 0.81nM/g to 1.37 nM/g at 2 and 4hrs after the stress. In the Hypox and Adrex rats, the slight increase was significantly observed. 4) the pepsin activity in the gastric juice in the Intact rats rose from 131U to 151U at 2 and 4hrs after the stress. In the Hypox and Adrex rats, the values were significantly low after the stress, if compared with those of the Intact rats. 5) the gastric juice and mucosa histamine concentration rose in the Intact rats after the stress but dropped in the Hypox and Adrex rats.

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EFFECT OF OCCLUSAL FORCE ON PAROTID SALIVARY SECRETION IN HUMAN. HOSHI,M., KURAHASHI,M., YOSHIDA, M., TAKAKUWA, M. AND INOMATA, K. Dept. of Oral Physiol., Higashi-Nippon-Gakuen Univ., School of Dent., Ishikari-Tobetsu, Hokkaido 061-02

In order to know the physiological roles of occlusal force in human parotid salivary secretion, we studied the effects of strength and frequency of unilateral occlusion on the salivary secretion from both sides of human parotid glands. Parotid saliva was collected bilaterally via modified Lashley cups, and the flow rate of parotid saliva was measured with a device using a pressure transducer. Occlusal force was monitored with a jaw force meter. In first experiment, subjects constantly occluded for one minute at 80 strokes per minute on the different strength of 5, 10 and 20 Kg. In second experiment, subjects occluded for one minute on the constant force of 10 Kg at different frequencies of 20, 40, 80 and 120 strokes per minute. The flow rate of parotid saliva was gradually increased with the increase in occlusal strength, while it was gradually decreased with the increase in occlusal frequency. However, at any strength and frequency of unilateral occlusion, the salivary flow rate of ipsilateral parotid gland was greater than that of contralateral parotid gland. These results suggested that occlusal force is one of effective stimuli in human parotid secretion.

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TIME COURSE CHANGES IN THE FLOW RATE,ION AND PROTEIN CONCENTRATIONS OF PAROTID SALIVA BY TONGUE STIMULATION. YOSHIDA, M., TAKAKUWA, M., INOMATA, K., HOSHI, M. AND KURAHASHI, M. Dept. of Oral Physiol., Higashi-Nippon-Gakuen Univ., School of Dent., Ishikari-Tobetsu, Hokkaido 061-02

The flow rate, ion (Na^+, K^+, Cl^-) and total protein concentrations, and amylase activity of parotid saliva were measured after tongue stimulation with 3 % tartaric acid at various intervals in human. Time course changes in the flow rate, Na^+, K^+ and Cl^- concentrations did not show any inter individual variations. The flow rate, Na^+ and Cl^- concentrations of parotid saliva increased, while K^+ concentration decreased after single stimulation. Maximum changes in the flow rate, Cl^- and Na^+ concentrations of parotid saliva were observed at 7,15 and 22 seconds after stimulation respectively. From maximum changes, the flow rate, Cl^- and Na^+ concentrations of parotid saliva returned to the initial levels at 2-3,2-4 and 10-12 minutes after stimulation respectively. Required time from stimulation to maximum changes in these factors of parotid saliva did not depend on the interval between stimulations (1-20 minutes). When tongue was stimulated every 15 seconds, the flow rate , Na^+ and Cl^- concentrations continued to increase during stimulation. On the other hand, when tongue was stimulated every 5 minutes, K^+ concentration continued to decrease during stimulation. There were large inter individual variations in time course of total protein concentration and amylase activity of parotid saliva.

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PAROTID AND PANCREAS AMYLASE SECRETION INTO GASTROINTESTINAL TRACT IN DIABETIC RATS AFTER FEEDING. KURAHASHI, M. AND INOMATA, K. Dept. of Oral Physiol., School of Dent., Higashi-Nippon-Gakuen Univ., Ishikari-Tobetsu, Hokkaido 061-02

Parotid and pancreas amylase secretion into gastrointestinal tract after feeding was investigated in nomal and streptozotocin-induced diabetic rats. In normal rats, both parotid and pancreas amylase activities were decreased after feeding, while the amylase activities in gastric and small intestinal contents were increased. In diabetic rats, parotid amylase activity was decreased after feeding, and it appeared in gastric content. However, at fasted state, the amylase activities in pancreas and small intestinal content were markedly reduced in diabetic rats compared with normal rats, and they did not show any appreciable changes after feeding in diabetic rats. In normal rats, the electophoretic patterns showed that most part of amylase in small intestine and its content was the amylase of pancreas type, and a little part of amylase was that of parotid type. Although total amylase activities in small intestine and its content were markedly reduced in diabetic rats, ratio of parotid type amylase to pancreas type amylase in small intestine and its content was markedly increased in diabetic rats. These results suggested that the amylase secreted from parotid glands of diabetic rats during feeding acts not only in mouth and stomach but also in small intestine.

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ELECTROMYOGRAPHIC AND MOTILE ACTIVITIES OF ISOLATED GASTROINTESTINAL TRACT OF STREPTOZOTOCIN DIABETIC RATS. HOMMA,S. and KARAKIDA,T.Dept.Physiol.Niigata Univ.Sch.Med. Niigata 951.

We reported previously that in isolated gastrointestinal tract of streptozotocin diabetic rats, frequency of spontaneous intraluminal pressure waves were characteristically lower especially in duodenum when compared with normal ones. To elucidate the mechanisms of this diabetic disorder, electromyographic activities were recorded, as well as intraluminal pressure, of isolated gastrointestinal tract of normal and diabetic rats with the aid of suction electrode from serosal side. Diabetic rats, 1-3 months after single i.v. injection of streptozotocin 60 mg/kg were characterized by body weight loss of 30-50% to the controls, plasma glucose level of 500-600 mg/dl and diarrhea. Increments of intraluminal pressure waves(P) were generally larger in normal than in diabetic preparations except colon. However, significant differences were not found except jejunum. Electromyographic activities, recorded from stomach, duodenum, jejunum, ileum and colon were consisted of just slow waves or spikes on slow ones and corresponded to intraluminal pressure waves. Therefore, they were considered so called basic electric rhythm(BER). Frequency of BER was lower in diabetic preparations especially in duodenum, as well as intraluminal pressure waves. Therefore, it was suggested again that pacemaker activity of diabetic intestine is disturbed, probably due secondarily to diabetic metabolic disorders.

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ROLE OF CONTENTS IN STOMACH TO THE CIRCADIAN VARIATION OF PLASMA ETHANOL CONCENTRATION IN THE RAT. Tachiyashiki, K., Imaizumi, K., Takamata, A., Uesugi, K., Kamada, N. and Ogita, Z-I.#* Dept. Living & Health Sci., Joetsu Univ. of Educ., Joetsu, Niigata 943 and #Dept. Biochem., Res. Inst. for Oriental Med., Toyama Med. & Pharmaceu. Univ., Toyama 930-01.

To study the mechanism responsible for the circadian change of elimination processes of ethanol(EtOH), EtOH(1g/Kg B.W.) was orally administered to female SD rats at 8:00 and 20:00 under non-fasting conditions. The intakes of chow and water at 20:00-8:00 were 3.3 times, 2.2 times larger than those at 8:00-20:00, respectively. The maximum plasma[EtOH] (Max. p[EtOH])(A), time to reach A(B), disappearance time of pEtOH(C) and integration value of EtOH(D) obtained at 20:00, were 1.8, 1.5, 1.7 and 3.2 times larger than those at 8:00, respectively. This means that there is the diurnal rhythm for the time course of p[EtOH]. Liver alcohol dehydrogenase(ADH) activity(pH9.0, 37°C) showed no significant change at both experiments. The remaining rate of EtOH in the stomach for 8:00 experiment was 86 times higher than that for 20:00 experiment. A, B, C and D showed the diurnal variation. Apparent decay rate constant(k) of EtOH showed no diurnal variation in both groups. There was high negative correlation ($\gamma \simeq -0.8$) between each parameter(A, B, C & D) except k value and the remaining rate of EtOH in the stomach. These results suggest that the diurnal rhythm of p[EtOH] under this condition is controlled by the remaining rate of EtOH in the stomach, and independent of the change of liver ADH activity.

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DECREASED EFFECTS OF ORGANIC ACIDS ON THE DISAPPEARANCE OF ORALLY ADMINISTERED ETHANOL FROM THE BLOOD IN RATS. Imaizumi, K. and Tachiyashiki, K. Dept. Living & Health Sci., Joetsu Univ. of Educ., 1 Yamayashiki, Joetsu, Niigata 943.

The authors had already found that when ethanol(EtOH) and organic acids such as acetic acid and citric acid were administered simultaneously to rats, blood(B)[EtOH] decreased significantly than that of EtOH alone. The present study is to elucidate the possible mechanism of the lowering action of B[EtOH] induced by organic acids. Aqueous solutions of organic acid of various concentrations were administered orally to the male SD rats(~300g) before, simultaneous and after administration of EtOH(3g/Kg B.W.). B[EtOH], [EtOH] and contents in the stomach, and the activity of liver alcohol dehydrogenase(ADH) were measured at hourly intervals. In three conditions, maximum(Max.)B[EtOH](I) decreased according to the dose-response with increase of [acid]. The magnitude of the decrease of I and the time to reach to I(II) varied distinctly with the timing of administration of organic acid. The order of the magnitude was before > simultaneous ≈ after. Liver ADH activity was not induced with organic acids. The remaining rate of EtOH in stomach in the presence of organic acid was higher significantly than that of organic acid-free. We found a high negative correlation between the remaining rate of EtOH in the stomach and Max. B[EtOH]. These results indicate that the decrease of B[EtOH] induced by organic acids is derived mainly from decreased rate of gastric emptying of EtOH.

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DEVELOPMENTAL CHANGE AND SEX- AND PORTION-DIFFERENCES TO ACTIVITY OF ALCOHOL DEHYDROGENASE IN THE LIVER OF RAT. Tachiyashiki, K., Imaizumi, K., Takamata, A., Kamada, N., Uesugi, K. and Ogita, Z-I.#* Dept. Living & Health Sci., Joetsu Univ. of educ., Niigata 943 and #Res. Inst. for Oriental Med., Toyama Med. & Pharmaceu. Univ., Toyama 930-01.

Alcohol dehydrogenase(ADH) activity(pH9.0, 37°C) and protein content in the liver of SD rats were determined to clarify differences in each liver portion, sex and age. 1) The specific activities of ADH were not identical with each liver portion. The specific activity of ADH and protein content showed the maximum value in the *lobus hepatis sinistra lateralis*. Both values in the *processus caudatus* and *processus papillaris* were smaller significantly than those of other liver portions. 2) The specific activity of ADH and total ADH activity in the female rats were 2 times, 1.5 times larger than those of male rats, respectively. Therefore, the specific activity of ADH showed significant difference between male and female. 3) The specific activity of ADH showed linear increase until about 12 days after birth. The specific activity of ADH reached to the adult level at about 2 weeks. However, total ADH activity increased sigmoidally against postnatal days. The Michaelis constants(K_m) for ethanol and NAD in 3 to 215 postnatal rats were 0.7-0.9mM and 0.08-0.1mM, respectively. These results indicate that the developmental change of specific activity of liver ADH may be attributed to the increase of ADH activity without changing the affinity of the enzyme for ethanol and NAD.

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OPPOSITE ACTION OF ENANTIOMERS OF PN 202-791 ON CA CHANNEL OF THE B CELL MEMBRANE. SAKAMOTO, Y. AND IMANAGA, I. Dept. of Physiol., Sch. of Med., Fukuoka Univ., Fukuoka 814-01

We examined the effect of PN 202-791, affecting on Ca channel, on the burst-type activities induced by 11.2 mM glucose or 0.1 mM tolbutamide in the pancreatic B cells of mouse. The S enantiomer prolonged the plateau duration of the slow wave induced by both stimulants, but it has no effect on an amplitude, a rate of rise and fall, of spike in concentration ranges from 5 x 10^{-8} to 10^{-6} M. The B cell membrane was slightly hyperpolarized by the S enantiomer (10^{-6} M), and was inversely depolarized by the R enantiomer (10^{-6} M). In the most cells, the electrical activities with small amplitude less than that of spike were distinctly observed on the plateau in the presence of the S enantiomer. In some cells, frequency of spikes was increased by the S enantiomer. The R enantiomer reduced the plateau duration and then blocked the electrical activities induced by both stimulants. Thus, the S and R enantiomers of PN 202-791 show an opposite action on the plateau duration and membrane potential, but the S enantiomer has no an enhancing action on the spike amplitude.

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STIMULATORY EFFECT OF PLATELET ACTIVATING FACTOR ON GLUCOCORTICOID SECRETION BY THE PERFUSED GUINEA PIG ADRENAL. SHIMADA,T., TANAKA,Y., MATSUMOTO,I. AND AIKAWA,T. Dep. Physiol., Nagasaki Univ., Sch. Med., Nagasaki 852

Platelet-activating factor(PAF) is a chemical mediator of anaphylaxis and inflammation. We previously reported that PAF increases the secretion of cortisol and aldosterone from the perfused canine adrenal gland. In the present study, the secretory rates of cortisol(F) and corticosterone (B) from the perfused guinea pig adrenal before and after the infusion of various concentration of PAF over 5 min were examined. The secretion of F and B in response to 1-o-hexadecyl PAF significantly increased at 0.1-10 nM and 1-10 nM respectively. The secretory response of F to 10 nM 1-o-hexadecyl PAF was about three-fold the response to 10 nM 1-o-octadecyl PAF and was almost equal to the maximum response to 1-24 ACTH. The repeated secretory responses of both steroids to 100pg/ml 1-24 ACTH were fairly reproducible, but the second responses to 10 nM 1-o-hexadecyl PAF remarkably decreased in comparison with first responses. These results indicate that PAF may play a role in stimulating the adrenocortical secretion under inflammation or allergic condition in guinea pigs.

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EFFECT OF ANGIOTENSIN II ON ISOMETRIC TENSION OF FOWL AORTA IN VITRO. YAMAGUCHI, K. AND *NISHIMURA, H. Dept. of Physiol., Niigata Univ. Sch. Med., Niigata City 951 and *Dept. of Physiol., Coll. Med., Univ. Tennessee, Memphis, TN 38163, U.S.A.

Angiotensin II (AII) produces a depressor effect in the fowl. To characterize the vasodilating action of AII and its underlying mechanism, we investigated the effect of AII on isometric tension of the fowl abdominal aortic ring precontracted with phenylephrine ($5x10^{-7}$ or 10^{-6} M) in Krebs-Ringer's solution at 37°C. AII (10^{-8}-10^{-5} M) elicited a dose-dependent and reversible relaxation of the ring, without causing any contractile effect. The effect of AII was not inhibited by propranolol, atropine, methysergide, pyrilamine or cimetidine, but was blocked by Sar^1-Ile^8-AII. Removal of the endothelium abolished AII-induced relaxation. However, differing from the endothelium-dependent vasodilation reported in mammals, the AII-induced relaxation was not inhibited by blockers for arachidonic acid metabolism such as indomethacin, quinacrine, SKF-525A, metyrapone and eicosatetraynoic acid. Arachidonic acid caused endothelium-independent relaxation which was completely blocked by indomethacin. AII transiently increased cyclic GMP level in the aortic ring. Eight-bromo cyclic GMP showed potency to relax the ring. Based on these results, we concluded that AII induces endothelium-dependent relaxation of the fowl aorta which may not be associated with arachidonic acid metabolism, and that cyclic GMP may play an important role in the AII-induced relaxation.

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MECHANISMS REGULATING PLASMA ANGIOTENSIN II LEVELS: A COMPARATIVE STUDY. TAKEI, Y. AND YAMAGUCHI, K. Dept. Physiol., Kitasato Univ. Sch. Med., Sagamihara 228 and 2nd Dep. Physiol., Niigata Univ. Sch. Med., Niigata 951

Plasma angiotensin II concentration increased in the quail and eel after hemorrhage or injection of 65% sucrose. However, plasma angiotensin II decreased in the quail after injection of 7% NaCl (isosmotic to 65% sucrose), while it increased after the injection in the eel. Since changes in plasma angiotensin II may parallel changes in renin release as suggested in mammals, renin release might have been inhibited after injection of 7% NaCl in the quail. In mammals, an injection of hypertonic NaCl has been shown to inhibit renin release. The major site responsible for the inhibition seems to be the macula densa, a part of the renal tubule which attaches to the juxtaglomerular cells. It has been shown that this structure senses an increased Na or Cl ions in the tubular urine, and transmits inhibitory signal to the juxtaglomerular cells. Morphologic observations showed that the macula densa is present in the quail as in mammals, but it is absent in the eel. Thus, it is likely that an increase in plasma osmolality itself has a stimulatory effect on plasma angiotensin II as exemplified by the effect of hypertonic sucrose, while plasma angiotensin II was inhibited in the quail but not in the eel after injection of hypertonic NaCl according to the presence or absence of the macula densa.

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EFFECT OF BRAIN MAST CELL STIMULATION ON ADRENOMEDULLARY & -CORTICAL SECRETION AND PLASMA RENIN ACTIVITY. MATSUMOTO, I., HIROSE, T., SHIMADA, T., TANAKA, Y. AND AIKAWA, T. Dept. Physiol., Nagasaki Univ., Sch. of Med., Nagasaki 852

The present study was undertaken to explore whether or not stimulation of brain mast cells by intraventricular(V_{III}) administration of comp.48/80, a histamine releaser from mast cells, affects plasma vasopressin(ADH), plasma renin activity(PRA) and the adrenal secretion of epinephrine(Epi) and cortisol(F) in dogs. After the infusion of comp.48/80, Epi and F markedly, PRA significantly and ADH slightly increased. The increase in Epi and PRA was abolished by splanchnicotomy, but that in F was not affected. In about 2/3 of animals to which ketotifen, a mast cell stabilizer, had been orally administered for one week before the experiment, the increase in Epi and PRA by the administration of comp.48/80 was almost completely depressed. These results suggest the possibility that brain mast cells in the pathophysiological conditions activates the plasma renin activity and the secretion of Epi and F in dogs.

697

REDUCED WATER AND FOOD INTAKE IN THE RAT DURING THE LATE PREGNANCY. HIGUCHI, T., HONDA, K., TAKANO, S. AND NEGORO, H. Dept. Physiol., Fukui Medical School, Fukui 910-11

Body weight of pregnant rats and fetuses increased toward delivery which occurred on day 22 or 23 of pregnancy. However, water and food intake increased until 4-5 days before parturition and declined thereafter, being minimum during the day of delivery. The decrease in the intake of food and water was accompanied by reduced locomotor activity and attenuated output of feces and urine. The reduction of food intake was significantly smaller in the rats ovariectomized on day 18 of pregnancy than in sham-operated controls, but the reduction of water intake was not altered. The amount of water drunk in 30 min after angiotensin II injection (0.2 mg/kg s.c.) was not different among the rats on day 18, day 22 of pregnancy, on day 1 of nursing or on diestrus, but smaller in the rat on proestrus. Present results show that food and water intake, urine and feces output and locomotor activity were reduced during late pregnancy when body weight was still increasing and indicated that the reduction in the intake of food but not of water seems to be induced at least in part by ovarian hormones.

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TAMOXIFEN AND INHIBITION OF GONADAL FEMINIZATION IN THE MALE QUAIL EMBRYOS TREATED WITH ESTROGEN. ARAKI, Y. and YAMAMOTO, N. Dept. of Physiology. Gifu University. School of Medicin. Thukasamachi 40. Gifu 500.

A single injection of estradiol benzoate (Es) (0.002 mg) and double treatment of Es and tamoxifen (T) (0.2mg) were carried out into the yolk sacs of fertilized eggs on zero day stage. The sizes of developping gonads of treated males were measured as the maximal dimension of the transverse sections and compared with those of normal males. Those of the cortexes of left gonads in Es group were about $3x10^{-2}mm^2$ on the ninth day and about $6x10^{-2}mm^2$ on the thirteenth day, and was increased over those in normal or Es+T group (about $1.5x10^{-2}mm^2$ on the ninth day and about $2.5x10^{-2}mm^2$ on the thirteenth day). On the other hand, those of the right entire gonads in Es group were about $5x10^{-2}mm^2$ on the thirteenth day and showed a decrease against those in normal or Es+T group (about $9x10^{-2}mm^2$ on the same stage). Therefore tamoxifen exerts opposite effects to those of estradiol benzoate which reversely favours cortical proliferation and reduces in size of the right gonad.

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POSTNATAL CHANGES OF BLOOD-T_4, RNA, DNA AND TUBULIN BY VARIOUS FETAL THYROID FUNCTIONS. TAKAHASHI, T. SUDO, S., NAKANO, M., MATSUDA, T., OKAMUNE, S. 2nd Dept. of Physiol., Kanazawa Med. Univ., Uchinada, Ishikawa 920-02

Rat fetuses were radio-thyroidectomized (Tx) with [^{131}I]-Na or were injected with DIMIT (L-T_3 analogue) in utero.

Blood T_4 (L-thyroxine) levels were not detected by RIA at one day old, but the level was suppressed in Tx-group at 11 days old. DNA values (per wet wt.) were not changed by Tx- or DIMIT-treatment at one day old, but the values were increased in hypothalamus and cerebellum from 11-day-old Tx-group. Intracellular RNA values (per DNA) were rised in hypothalamus and cerebellum from one-day-old Tx-group, but these were not normalized by fetal DIMIT-supplement to Tx-fetuses. In 11-day-old Tx-group, RNA was reduced in hypothalamus, and it was normalized by postnatal T_4-supplement. Intracellular tubulin contents (per DNA) were increased by fetal DIMIT-treatment in the three brain areas at one day old. Although the content was not changed in Tx-group at one day old, it was decreased by the operation in 11-day-old hypothalamus and it was normalized by the postnatal T_4-supplement.

Fetal abnormal thyroid states were observed to induce delayed effects on DNA, RNA and tubulin metabolisms in brains during postnatal development.

700

VISUALIZATION OF NEUROSECRETORY ACTIVITIES BY A VIDEO CAMERA. TERAKAWA, S. AND NAGANO, M. Dept. Cell Physiol., Nat. Inst. Physiol. Sci., Okazaki 444

Changes in light scattering associated with neurosecretory activities of nerve terminals of frog neurohypophyses and crustacean X-organ sinus glands were measured using a high S/N video camera and a real-time image processor. The time resolution achieved was 33 ms and the spatial resolution was 0.3 μm. With these resolutions, the turbidity of nerve terminals was found to be decreased by about 0.1 - 0.6% (against the background) upon electrical stimulation of the axon. The shape of the response observed on the monitor screen suggested that the response arises from individual nerve terminals and not from smooth muscles possibly contained in the tissue. The response could be reversibly suppressed by cadmium ion and greatly enhanced by tetraethylammonium ion. The technique employed will provide promising methods for elucidating the secretory process including the osmotic swelling, cytoskeletal translocation, and membrane fusion of vesicles.

701

EXTRACELLULAR POTASSIUM INCREASE FOLLOWING ACTIVATION OF NEUROSECRETORY TERMINALS MODULATES EXCITATION-SECRETION COUPLING IN THE RAT POSTERIOR PITUITARY. SHIBUKI, K. & LENG, G.* Dept. Physiol. Jichi Med. Sch. Tochigi 329-04, *AFRC Institute of APGR., Cambridge CB2 4AT, U.K.

Extracellular ionic changes following excitation was studied by ion-sensitive microelectrodes in the posterior pituitary of male Wistar rats *in vitro*. Stalk stimulation with biphasic pulse trains (1 mA peak to peak, 2 ms width, 20 Hz, 5 s) evoked potassium increase by 184±33 % (mean±S.E., n=21). Stalk stimulation (50 Hz, 5 s) also evoked calcium decrease by 10-20 %. To analyse effects of the potassium increase, medium potassium concentration was changed from 0 to 25 mM in 5 mM steps. The potassium and calcium responses evoked by 6 Hz stalk stimulation were the largest at 10 mM and suppressed at lower or higher potassium concentration. Vasopressin and oxytocin secretion evoked by 6 Hz stimulation was inhibited at 10 mM, facilitated at 15 mM and inhibited at potassium concentration higher than 15 mM again. These results suggest that extracellular potassium changes evoked by activation of neurosecretory terminals are large enough to modulate excitation-secretion coupling in the posterior pituitary.

702

A DECREASE IN PLASMA VASOPRESSIN IN RESPONSE TO CLASSICALLY CONDITIONED 'FEAR' STIMULI IN RATS UNDER HYPERTONIC STATES. ONAKA, T., HAMAMURA, M., YAGI, K., Dept. of Physiol., Jichi Med. Sch., Tochigi 329-04

A footshock-induced increase in plasma vasopressin (VP) is suppressed by classically conditioned 'fear' stimuli. The present study aimed to determine whether 'fear' stimuli decrease plasma VP under physiological conditions in male rats. Light and sound stimuli were paired with footshocks (FS) in training session. In testing session rats received light and sound in training cage 2 - 48 h after the training. The testing stimuli given 30 min after an injection of 0.5 M NaCl (2 ml/100 g b.w.) increased plasma ACTH but decreased VP as compared with those in 0 mA-FS control or conditioned but not tested rats. Motor activity was suppressed in conditioned rats during testing. These changes depended on FS intensity and number of training sessions. Light and sound stimuli during intervals between training and testing sessions extinguished these changes. More training trials were needed to produce and fewer extinction trials to extinguish VP changes than ACTH or behavioral changes. Retention time of VP conditioned response is shorter than that of the other responses.

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FOOTSHOCK-INDUCED INCREASE IN TAIL FLICK THRESHOLD: BLOCKING BY VASOPRESSIN ANTAGONIST IN RATS. HAMAMURA M., ONAKA, T., AND YAGI K. Dept. of Physiol., Jichi Med. Sch., Tochigi 329-04

Exogenously administered vasopressin (VP) is known to prolong tail flick (TF) latency to noxious heat (Berson et al., 1983). Electric footshocks (FS) increase plasma VP extremely (Onaka et al., 1986) and lengthen TF latency (Akil et al., 1976). So it is possible that antinociception after FS is due to VP. In male conscious rats the tail surface temperatures were recorded by a thermocouple (0.2 mm in diameter). The temperature at the time when TF occurred was used as the threshold. Intravenously injected arginine-VP (0.32 - 1.6 μg/kg, b.w.) was confirmed to increase the TF threshold in a dose-dependent manner. FS (3 mA, 50 Hz, 1 min) also increased the threshold. Pretreatment with a V1 vasopressin receptor antagonist (d(CH_2)$_5$Tyr(Me)AVP; 0.5 - 50 μg/kg, i.v.) reduced the increase in TF threshold after a VP injection (1.6 μg/kg) in a dose-related manner. The antagonist (5 μg/kg) also blocked the increase of TF threshold after FS. These data suggest that FS-induced increase in TF threshold is due, at least in part, to endogenous VP.

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EFFECTS OF LOCALLY APPLIED OSMOTIC STIMULUS USING A PRESSURE EJECTION SYSTEM ON PARAVENTRICULAR NEUROSECRETORY CELLS IN THE RAT. YAMASHITA, H., OSAKA, T. AND KANNAN, H. Dept. of Physiol., Univ. of Occup. Environ. Health, Sch. of Med., Kitakyushu 807

Single-unit activities were recorded from neurons in the paraventricular nucleus (PVN) of the hypothalamus in urethane-anesthetized rats. Effects of hypertonic (+30 mOsm/kg, by NaCl or mannitol) and hypotonic (-30 mOsm/kg) solutions applied with pressure to the immediate neighborhood of these neurons were studied. Thirteen of 44 identified neurosecretory cells were excited by the local hypertonic stimulus, while the remaining unchanged. Of 43 non-neurosecretory cells, 12 were excited and 2 were inhibited by the local hypertonic osmotic stimulus and one was excited by the hypotonic stimulus. Osmotic responsiveness of the PVN neurosecretory cells supports the idea that release of the neurohypophysial hormones in response to hyperosmotic conditions is mediated, at least partly, by PVN neurons themselves. However, unresponsiveness of a majority (70%) of neurons to this stimulus suggests that elements outside the PVN may play an important role for control of vasopressin and oxytocin release.

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INHIBITION OF VASOPRESSIN SECRETING NEURONS IN THE PARAVENTRICULAR NUCLEUS OF THE RAT HYPOTHALAMUS BY GASTRIC DISTENSION. KANNAN, H., UETA, Y., INENAGA, K. AND YAMASHITA, H. Dept. of Physiol., Univ. of Occup. Environ. Health, Sch. of Med., Kitakyushu 807

Extracellular recordings were performed in rats anesthetized with urethane-chloralose to investigate effects of gastric distension on the neural activity of neurosecretory cells of the paraventricular nucleus (PVN) of the hypothalamus. Approximately one half of phasically firing neurosecretory neurons (7 out of 16 cells) were inhibited by gastric distension. The inhibitory response to the gastric distension was greatly attenuated by severing the left cervical vagus nerve. Distension of the intraperitoneally placed balloon produced no effect. While most of continuously firing cells were unaffected (55 out of 66 cells), 9 continuously firing cells were excited by gastric distension. These data suggest that sensory information originating from the gastric mechanoreceptors inhibits the activity of putative vasopressin-secreting neurons, which is, at least partly, responsible for "early diuresis" following drinking large volumes of water, and also excites certain putative oxytocin-secreting neurons in the PVN.

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EFFECTS OF CORTISOL ON NEURONS IN THE PARAVENTRICULAR NUCLEUS OF THE HYPOTHALAMUS (PVN) IN VIVO AND IN VITRO. KASAI, M., KANNAN, H., UESUGI, S. AND YAMASHITA, H. Dept. of Physiol., Univ. of Occup. Environ. Health, Sch. of Med., Kitakyushu 807

Extracellular recordings were made from 83 neurons in the paraventricular nucleus of the hypothalamus(PVN) in anesthetized rats with urethane and from 147 neurons in the parvocellular division of the PVN in rat brain slice preparations. Iontophoretically applied cortisol excited 10(45%) of 22 tubero-infundibular, 7(21%) of 34 magnocellular and 8(30%) of 27 unidentified neurons tested, and inhibited 1(4%) magnocellular neuron and 3(11%) unidentified neurons in the PVN. In intact rat brain slice preparations, although high concentration of cortisol(10^{-3} M) excited 6(40%) of 15 neurons tested in the parvocellular division of the PVN, physiological dose of cortisol(10^{-5} M) did not affect its basal firing rate. Whereas, in adrenalectomized rat brain slice preparations cortisol(10^{-5} M) inhibited 12(25%) of 47 neurons tested. We concluded that cortisol might have an inhibitory effect on neurons in the PVN which included CRF neurons.

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PARAVENTRICULAR CATECHOLAMINES ARE INVOLVED IN THE PREFEEDING CORTICOSTERONE PEAK IN RATS UNDER RESTRICTED FEEDING. *NOE, Y., HONMA, K., HONMA, S., KATSUNO, Y., HIROSHIGE, T. AND *OIKAWA, K. Dept. of Physiol. Hokkaido Univ. Sch. of Med., *Dept. of Pediat. Dent., Sch. of Dent., Sapporo 060

Male adult rats of the Wistar strain were subjected to restricted daily feeding for 2 weeks. Free-access to food and water was allowed to rats only from 10:00 to 12:00 hr under a light-dark cycle (lights from 06:00 to 18:00 hr). 6-OHDA (2-4 ug dissolved in 200 nl physiological saline) was injected stereotactically into the suprachiasmatic nucleus (SCN), paraventricular nucleus (PVN), ventromedial hypothalamic nucleus (VMH) or lateral nucleus (LH). This treatment reduced the norepinephrine concentration in each nucleus to 10-20 % of the control level. 6-OHDA into PVN suppressed the prefeeding corticosterone peak and that into VMH suppressed the hormone peak partially, while 6-OHDA into SCN or LH had no effect. In contrast, the circadian corticosterone peak was not affected by 6-OHDA injection into PVN or SCN in rats fed ad libitum. These findings indicate that the catecholaminergic mechanism in PVN is responsible for the prefeeding corticosterone peak in rats under restricted daily feeding and that its effect on corticosterone secretion is stimulatory. This mechanism can be separated from that which regulates the circadian corticosterone peak, and seems to be specific for the feeding associated corticosterone secretion.

708

EFFECTS OF NEUROTENSIN (NT) ON PREOPTIC UNIT ACTIVITY AND LH SECRETION. AKEMA, T., PRAPUTPITTAYA, C. AND KIMURA, F. Dept. Physiol. Yokohama City Univ. Sch. Med., 3-9 Fukuura, Kanazawa-ku, Yokohama 236.

Microinjection of NT into the medial preoptic area significantly facilitated the circadian afternoon rise of LH secretion in unanesthetized, ovariectomized estrogen-primed rats. The timing of the afternoon LH rise was not altered by the peptide. In ovariectomized estrogen-unprimed rats, on the other hand, NT did not affect the existing pulsatile LH secretion nor induce an afternoon LH rise. Microelectrophoresis of NT produced both excitation and inhibition in preoptic neurons. However, the unit responses to NT did not differ between estrogen-primed and unprimed rats. Microelectrophoresis of antiserum against NT not only antagonized excitatory and inhibitory actions of NT, but also by itself altered the spontaneous firing rate of some NT-sensitive cells. These results suggest that the preoptic NT may regulate neural activities involved in the LH release mechanism which undergoes the circadian clock under the influence of estrogen.

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INHIBITION BY EXTRACELLULAR Na^+ REPLACEMENT OF GRF-INDUCED GH SECRETION FROM RAT PITUITARY CELLS. KATO, M. AND SUZUKI, M. Dept. Physiol., Inst. Endocrinol., Gunma Univ., Maebashi 371

To further clarify the ionic mechanism of actions of growth hormone (GH) releasing factor (hGRF) on GH secretion, the involvement of extracellular Na^+ was studied in perifused dispersed rat anterior pituitary cells. The removed pituitaries were dispersed with 0.5% trypsin and then mixed with Bio-Gel P2 and packed in a perifusion chamber. The perifusion flow rate was 1.2 ml min^{-1}. Replacing extracellular Na^+ with mannitol or $Tris^+$ suppressed hGRF- and di-butyryl cyclic AMP (dbcAMP)-induced GH secretion. The peak responses to a 2 minute application of 1 nM hGRF were 165.0±5.6 ng ml^{-1} (normal medium, mean±SE), 21.2±1.4 ng ml^{-1} (mannitol substituted medium) and 18.0±1.7 ng ml^{-1} ($Tris^+$ substitution). GH secretion induced by dbcAMP was also suppressed by Na^+ replacement to less than 50% of that in normal medium. However, 30 mM KCl-stimulated GH secretion was not markedly affected by replacement of Na^+ with either compound. Tetrodotoxin was ineffective on both hGRF- and excess K^+-induced GH secretion. cAMP production by hGRF was not greatly affected by replacing extracellular Na^+. Thus, extracellular Na^+ plays an important role in hGRF-induced GH secretion, especially in the process after the cAMP production. The involvement of cAMP-sensitive Na^+ and Ca^{2+} channels is speculated on in relation to hGRF-induced GH secretion.

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EVIDENCE FOR AFFERENT INPUTS FROM THE UTERUS TO HYPOTHALAMIC MAGNOCELLULAR NEURONS IN THE RATS. AKAISHI, T.,ROBBINS* A.,SAKUMA, Y. AND SATO, Y. Dept. Physiol., Niigata Univ. Sch. of Med., Niigata 951.(A.T., SAK.Y.), Dept. Physiol., Tokyo. Inst. of Gerontol., Tokyo 173 (R.A., SAT.Y.).

To study the role of the perception of afferent inputs from the uterus in control of the oxytocin release, the effects of uterine distension and somatic stimuli were examined in the activity of magnocellular paraventricular (PV) neurons. Extracellular action potentials were recorded from the ovariectomized and estrogenized female rats under urethane anesthesia (1.0 g/kg, i.p.). Forty-eight PV neurons with a tonic firing pattern were antidromically identified by electrical stimulation of the neurohypophysis. Both uterine and vaginal distension evoked the excitations in the firing activity in 33% of the PV neurons. Cutaneous pinching of hindpaw activated 39%, inhibited 11% neurons tested. Poststimulus time histograms constructed for responses to the stimulation (3/25 Hz) of the sciatic, hypogastric or pelvic nerve showed excitatory responses in 80%, 55% and 30% of PV neurons, respectively. These data indicate that the uterine afferents to a specific group of PV neurons may be involved in the hypogastric and pelvic nerves. The uterine mechanoreceptors may play a certain part in the regulation of oxytocin release in the female rat.

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EFFECTS OF LEUMORPHIN ON THE MIDBRAIN CENTRAL GRAY NEURONS IN FEMALE RATS. Koyama,Y., Oomura,Y. and Nishino,H Natl. Inst. Physiol. Sci., Okazaki, 444

Leumorphin has various kinds of biological functions, one of which is its involvement in rat lordosis. As this behavior is mediated by the axis from the hypothalamus, ventromedial nucleus (VMH) and the medial preoptic area (MPOA), through the midbrain central grey (MCG) to the gigant cellular nucleus of the medulla (GCN), and leumorphin is found in the hypothalamus and the midbrain, it is important to examine the effects of leumorphin on this lordosis-relevant system. In the present study, effects of iontophoretically applied leumorphin were examined on the MCG neurons classified by the response to the electrical stimulation of the VMH, MPO and the GCN. Twenty-seven ovariectomized, estrogen-primed female rats were used under light urethane anesthesia. Of 78 MCG neurons, 19 (24%) were excited and 9 (12%) were inhibited by the VMH stimulation. The leumorphin had mainly inhibitory effects on the MCG neurons; it caused inhibition in 9 of 28 neurons (32%) responsive to the VMH stimulation and caused excitation in 2 cases (7%). Nearly the same tendency was observed in the neurons responsive to the MPOA stimulation. However, leumorphin had no effects on the firing rates of 15 neurons responded to the antidromic stimulation of the GCN. In some neurons, leumorphin suppressed the excitatory responses to the VMH stimulation without affecting the spontaneous firing rates. The results suggest that leumorphin has some roles in lordosis by changing the firing rate of the MCG neurons or modulating the excitatory inputs from the hypothalamus to the MCG.

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INHIBITOLY EFFECT OF ELECTRICAL STIMULATION OF MIDBRAIN CENTRAL GRAY ON GROWTH HORMONE SECRETION IN THE PENTOBARBITAL ANESTHETIZED RATS. KOIBUCHI, N., KATO, M. AND SUZUKI, M. Department of Physiology, Institute of Endocrinology, Gunma Univ., Maebashi 371

The present study was designed to clarify the topography in the midbrain central gray (CG) and its surrounding area related to the suppression of growth hormone secretion. In pentobarbital anesthetized male rat, a silastic catheter was inserted into the right atrium for blood sampling. 5 μg human GRF (hGRF) dissolved in 0.3 ml saline was injected iv,resulting in a marked increase in plasma GH level from resting value 28.5±7.1 ng/ml (mean±SE) to 686.1±62.0 ng/ml in 10 min after injection. Electrical stimulation (biphasic square wave) was delivered for first 10 min through a chronically implanted bipolar electrode. When the amplitude of stimulation was 500 μA, the hGRF-induced GH secretion was markedly suppressed by CG stimulation. Moreover, the suppression was also observed when the electrode tip was outside of the CG. When the amplitude was 100 μA, the effective area seemed to be more limited. Medial portion of the CG significantly suppressed GH secretion in 20 min and 30 min after the onset of the stimulation. Moreover, electrical stimulation of ventromedial portion of the CG suppressed GH secretion to a greater extent in 10 min, 20 min and 30 min. Prior lesion of periventricular hypothalamic nucleus where the perikarya of major fibers containing somatostatin (SRIF) originate, abolished the suppression by CG stimulation.

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CHARACTERIZATION OF ESTROGEN-SENSITIVE NEURONS IN THE FEMALE RAT HYPOTHALAMUS RESPONSIBLE FOR THE INDUCTION OF LORDOSIS REFLEX. SAKUMA, Y. AND AKAISHI, T. Dept. Physiol. II, Sch. Med., Niigata Univ., Niigata 951

Antidromic action potentials were evoked in neurons in the ventromedial nucleus of the hypothalamus (VMN) following stimulation of the midbrain central gray (CG) in the ovariectomized, female rats under urethane anesthesia. The efferent axons of the VMN in these animals had been selectively disrupted as they leave the nucleus either laterally or caudally. Earlier experiments showed that bilateral parasagittal knife-cuts lateral to the VMN abolish the lordosis reflex; damages confined to the caudal projection of the nucleus had no effect on this behavior. In the posterior-cut animals, estrogen treatment of the ovariectomy significantly lowered antidromic activation thresholds and shortened absolute refractory periods for CG stimulation. Estrogen had no detectable effect on the excitability of cells that survived the lateral cut. Measurement of the extracellular spread of the antidromic action potentials suggested that VMN cells with the lateral projection had larger soma than those with the axons leaving the nucleus in the caudal direction. Histological analyses located antidromically driven cells in the posterior-cut animals in the rostral extremity of the VMN; those in the lateral-cut animals were scattered throughout the VMN.

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SPONTANEOUS ELECTRICAL ACTIVITIES IN CULTURED MAMMARY EPITHELIAL CELLS. ENOMOTO, K., MAENO, T. AND OKA, T. Dept. of Physiol., Shimane Med. Univ., Izumo 693

Electrophysiological measurements of the membrane potentials of mouse mammary epithelial cells in primary culture revealed the presence of spontaneous-oscillating-hyperpolarizing potentials in cells incubated with epidermal growth factor. The hyperpolarizing potentials were 5-20 mV in amplitude and about 10 sec in duration. The peak height of the response was reduced by hyperpolarization, and the input membrane resistance decreased during the response. The response was probably due to activation of K^+ channels. The latency period for the epidermal growth factor induction of the hyperpolarizing potential was approximately 3 hr. In contrast, insulin induced spontaneous-depolarizing potentials that were about 5 mV in amplitude and 1 sec in duration. The depolarizing potentials were attributed to activity of ion channels, since the peak height was dependent on the membrane potential and the depolarizing potential was accompanied by a decrease of input membrane resistance. The time lag for the induction of the depolarizing potential was 6-12 hr. Other hormones involved in mammary cell differentiation, such as cortisol and prolactin, neither induced the depolarizing potentials nor changed the induction of depolarizing potential by insulin. In addition, other growth factors, such as nerve growth factor and fibroblast growth factor, elicited no electrical activity.

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SPLEEN FIBRINOLYTIC PROTEINASE ACTIVITY IN PREGNANT AND PUERPERAL MICE. HORIE, N., WADA, Y. AND OKAMOTO, U. Dept. Physiol., Fac. Nutr., Kobe-Gakuin Univ., Kobe 673

Variation of a spleen fibrinolytic activity was examined in pregnant and puerperal mice. The weight of the spleen, the plasma fibrinogen level, the leukocyte count, activated partial thromboplastin time, prothrombin time were also measured. Before the delivery (the height of fetus > 1.5cm), the fibrinolytic activity was enhanced nearly three times compared with that of the control. The fibrinolytic activity was completely inhibited with diisopropyl fluorophosphate, phenyl-methyl sulfonyl fluoride, p-nitrophenyl p-guanidino-benzoate, N-tosyl-L-phenyl-alanine chloromethyl ketone or soya-bean trypsin inhibitor, but was not inhibited with tranexamic acid, aprotinin, lima-bean trypsin inhibitor, chicken ovoinhibitor, antipain, chymostatin, cysteine or EDTA. These data showed that the fibrinolytic enzyme was a serine proteinase and a chymotrypsin-like proteinase, but was not plasmin. We demonstrated by immuno-blotting assay that the proteinase hydrolyze not only fibrinogen, but also plasminogen.

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CATECHOLAMINE RELEASE FROM ADRENAL GLAND EVOKED BY BRADYKININ AND ACETYLCHOLINE

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Properties of the catecholamine (CA) release evoked by bradykinin (BK) and acetylcholine (ACh) from rat adrenal gland were investigated by means of perfusion technique. Wistar rats, weighing ca. 400g, were anesthetized with sodium pentobarbital. Left adrenal gland was isolated and perfused with a modified Krebs solution (MKS) equilibrated with 100% O_2. The gland was stimulated with MKS containing 100nM BK or 100μM ACh. The secretion ratio of norepinephrine (NE) to epinephrine (E) with BK was lower than that with ACh (NE/E=0.039±0.023 for BK, n=10, and 0.24±0.10 for ACh, n=11). CA release evoked by BK was slightly inhibited and that by ACh was profoundly suppressed in Ca^{2+}-free medium in the absence of EGTA. CA release evoked by BK was also profoundly suppressed in the Ca^{2+}-free medium containing 1mM EGTA. Ketamine (100μM) and lidocaine (1mM) did not depress the BK-evoked CA release, while they inhibited the ACh-evoked CA release. The results indicate that an entry of extracellular Ca^{2+} is necessary for the CA release evoked by both BK and ACh, and that differential mechanisms may exist in the Ca^{2+} entry with each stimulation.

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TEMPERATURE DEPENDENCE OF THE THORACIC DUCT LYMPH FLOW IN THE RAT DURING ACUTE HEAT STRESS. YAMADA, S., KUBO, M. and HAYASHIDA, Y. Dept. of Systems Physiol., Univ. Occup. Environ. Hlth, Kitakyushu 807.

To quantitate the change of the regional lymph flow into the thoracic duct in the conscious rats during acute heat stress, we collected the thoracic duct lymph every 15 min and measured the colonic temperature every 5 min using a thermocouple. We found decrease of the thoracic duct lymph flow depending on the rise of the colonic temperature. As the colonic temperature was kept raised by 1 ℃, 2 ℃ and 3 ℃ using a infrared lamp, the decrease of lymph flow into the thoracic duct was 18%, 30% and 45%, respectively. To elucidate the decrease of lymph flow into the thoracic duct, 1) we calculated the redistribution of the regional lymph into the thoracic duct by the equations reported previously(Jpn. J. Physiol., 34, 575, 1984), and obtained 13% increase of the lymph flow from skin and 6% decrease from the visceral organs by the increase of 1 ℃ of the colonic temperature(Jpn. J. Physiol., 36, 619, 1986); 2) we continuously recorded the splanchinic nerve activity in the conscious rats during heat stress. The splanchinic nerve activity increased as the colonic temperature rose. The change of the symphathetic nerve activity in the visceral organs accords with the redistribution of the regional lymph into the thoracic duct during acute heat stress.

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PYROGENIC RESPONSE IN PIKA (WHISTLE RABBIT). KOSAKA, M., OHWATARI, N., FUJIWARA, M., TSUCHIYA, K., YU-JEN FAN, NAKAMURA, K., F.J. YANG AND P.G. RIWA Dept. of Environment. Physiol., Inst. of Trop. Med., Nagasaki Univ., Nagasaki 852

Pika's better heat conservation ability has been due to its higher metabolic rate, poor heat dissipation through panting and smaller ear surface area. Althought its very sensitive to narcotics, it responds poorly to ip LPS pygogen. In this experiment 9 pikas (mean BW:262.2g) reared at 22°C were subjected to iv LPS pyrogen 0.1μg/body in the environmental chamber (temp 28°C and 60% r.h.). Throughout the experiment the animals were unrestrained in cages with thermister probe insitu deep in rectum and fixed. 15 minutes prior to iv pyrogen injection, rectal temperature (Tre) and respiratory rates (RR) were recorded every 5 minutes, and there after every 10 minutes. The LPS pyrogen evoked a monophasic fever (mean peak Tre:40.23°C, mean ⊿T:0.73°C ± 0.3°C) which persisted for 70 minutes after a mean latent period of 20 minutes. RR from precontrol rate of 108 c/min to 100 c/min at the peak of fever and to low 92 c/min at the end of the pyrexia. It was observed that the pika developed piloerection and shivering during the rising phase of the fever. The animals kept recumbent on the abdomen and chest with both extremities stretched. Occasionally they licked their body but mostly they had minimal movements during the pyrexic period. These observation show that Pika can elicit fever with iv pyrogen but the heat loss mechanisms differ from those of albino rabbits.

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CUTANEOUS SYMPATHETIC VASOMOTOR ACTIVITIES IN HEAT ACCLIMATED RABBITS. FUJIWARA, M., OHWATARI, N., TSUCHIYA, K. & KOSAKA, M. Dept. of Environment. Physiol., Inst. of Trop. Med., Nagasaki Univ., Nagasaki 852

The physiological changes that occur during heat acclimation were measured in six albino rabbits which had been reared at 30°C (Ta) and 60% (RH) for 24 weeks continuously. During the experiment Ta was changed at a rate of 0.5°C/min. The rectal temperature (Tre) change during Ta shift was 1.1 ± 0.2 (Mean ± SD) in the Heat acclimated rabbits compared to 1.6 ± 0.3°C in the control. The mean threshold level of Ta at which vasodilation of the ear began was 27.5 ± 1.2°C in the heat acclimated series compared to 25.0°C in the controls. Conversely, vasoconstriction occured at 21.8 ± 3.3°C in the former compared to 14.7 ± 2.9°C in the later group. It is suggested that during heat acclimation there is a shift of the threshold temperature at which vasodilatation or vasoconstriction occurs. This is to prevent changed of the core temperature. Further, under general anaesthesia (Nembutal 20mg/kg ip) there was no difference in the thresholds in the two series. It confirms that physiological changes in heat acclimation is through neuronal mechanisms influenced by anaesthesia sympathetic vasoconstrictor tones among the groups were measured after IV administration of α adrenergic blocker (phentolamine mesylate 3mg/kg). At the same Te, there was greater vasodilation in the control than in the acclimated group, suggesting that vasoconstrictor tone is different between heat acclimated and non acclimated even at the same Ta.

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HEAT-INDUCED VASOCONSTRICTION IN THE FINGER AND LOCAL THERMAL SENSATION. HIRATA, K., NAGASAKA, T. AND NUNOMURA, T. Dept. Physiol., Sch. Med., Kanazawa Univ., Kanazawa 920

The effect of local heating on the relationship between local thermal sensation and finger blood flow (BF) was studied. Both hands were immersed in water at a temperature (T_w) of 35°C. T_w for the heated hand was raised by steps of 1°C every 10 min from 35°C to 43°C, while T_w for the control hand was kept at 35°C. Local thermal sensation sharply increased concomitantly with rising of the local skin temperature (T_{loc}) for the first few minutes of each local heating period, then gradually returned and adapted to a new level of the sensation at each T_{loc}. Finger BF in the control hand (BF_c) was essentially constant. Finger BF in the heated hand (BF_h) decreased in the first few minutes and then returned toward the previous values at T_{loc} of 38°C - 41°C. At the T_{loc} of 42°C and 43°C, BF_h increased after an initial transitory decrease. The changes in BF_h were correlated negatively with concomitant dynamic changes in local thermal sensation. However, the heat-induced vasoconstriction was inhibited during mental calculation test inspite of rising T_{loc}. The present results suggest that the decrease in finger BF in the heated hand relates to the dynamic response characteristic and to the perception of the local thermal sensation at T_{loc} above core temperature.

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CORRELATION BETWEEN OPIOID AND NEUROTENSIN EFFECTS ON THERMOREGULATION. Kubo, K., Tsuzuki, S. and Sasaki, T. Dept. of Bioregulation, Inst, for Med. Gen., Kumamoto Univ. Med. Sch., Kumamoto 862, Japan.

Influences of intra-third ventricular injection of β-endorphin (ED, 1 μg) or naloxone (1 μg) on the effects of intraventricular injection of neurotensin (NT, 10 μg) on body temperature and oxygen consumption were studied in the rats in the thermoneutral (Ta 23°C) and cold (Ta 5°C) environments. In the neutral environment, NT induced a fall in rectal temperature which was associated with a decrease in oxygen consumption and a rise in tail skin temperature, while ED induced a rise in rectal temperature with an increase in oxygen consumption and naloxone did not any change. However, the NT-induced hypothermia was enhanced and inhibited by ED and naloxone respectively, if NT was injected 10 minutes after either injection of ED or naloxone. On the other hand, in the cold environment, both ED and NT induced hypothermic responses. The hypothermia after consecutive injections of ED and NT was greater than those observed after injection of ED or NT alone. It thus appears exogenous ED and probably endogenous opioid systems antagonized with naloxone act to modulate the NT effects on the central thermoregulatory mechanisms.

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DUAL PROCESSES FOR FEVER DEVELOPMENT AND ACUTE PHASE RESPONSE. MURAKAMI, N., MORIMOTO, A., WATANABE, T. AND MYOJIN, T.* Dept. Physiol., Yamaguchi Univ. Sch. Med., Ube, Yamaguchi 755

Recently, it was proposed by us (J. Physiol., 383) that there are dual structures for producing fever where are laid inside and outside the blood-brain barrier (BBB). Endogenous pyrogen (EP) which is a potent factor for producing fever, also mediates a series of host defence responses, i.e. the acute phase response (APR). In the present paper, the acute phase response which includes changes in plasma concentration of iron, zinc, copper and fibrinogen and in the number of white blood cells, was compared between monophasic, biphasic and monotonic fever (ICV fever). Eventually, among various variables of APR the plasma copper concentration is mainly controlled and the plasma fibrinogen concentration is partly controlled by the central action of EP. The remains are resulted from the action of EP on other targets and tissues than the brain. These results indicate that there exist at least two separate mechanisms in the APR production inside and outside the BBB.

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FEBRILE RESPONSE TO RECOMBINANT HUMAN INTERLEUKIN-1 ALPHA IN RABBITS

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Recombinant human interleukin-1α(rhIL-1α, 159 amino acids; MW, 18063 daltons, Dainippon Pharmaceutical Co.) was injected into the lateral cerebroventricle of conscious rabbits (2-3 kg) through chronically implanted cannula. A single dose of rhIL-1α of 100 pg/kg - 50 ng/kg induced a monophasic fever, dose-dependently: core temperature was increased by 0.5 - 2.6 °C. To investigate whether prostaglandins were involved in IL-1α fever, indomethacin (IM), the most potent inhibitor of prostaglandins-biosynthesis, was injected 15 min before rhIL-1α administration, either subcutaneously (sc, 20 mg/kg, in oleum ricini) and/or intracerebroventricularly (icv, 500 ug/rabbit, in 99 % ethanol). IL-1α was injected either intraveously (iv, 3 μg/kg) or icv (1ng/kg). By IM given either sc or icv, fever induced by iv IL-1α was inhibited moderately: and by IM given icv, fever induced by icv IL-1α was inhibited remarkably. By IM administered both sc and icv, fever induced by iv IL-1α was inhibited remarkably. When IM was given sc, fever induced by icv IL-1α was also inhibited remarkably. It is concluded that prostaglandins produced both peripherally and centrally played an impotant role in IL-1α fever.

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BRAIN SITES SENSITIVE TO PROSTAGLANDIN E_2 and $F_{2\alpha}$ FOR PRODUCING FEVER.

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The febrile responses induced by intraventricular or intrapreoptic (bilateral) injections of prostaglandin E_2 (PGE_2) were investigated in the same group of rabbits. Both injections produced dose-dependent fever over the range of 100-2000 ng. The magnitude of febrile responses induced by ventricular injections was significantly greater than those by intrapreoptic injections. This indicates that there exist regions more sensitive to PGE_2 than the preoptic region for producing fever. The effects of microinjection (1 μl) of PGE_2 (50 ng & 100 ng) on the rectal temperature were extensively examined in the 68 brain regions. The preoptic and anterior hypothalamic region, and the ventromedial hypothalamic (VMH) region are highly sensitive to PGE_2. The febrile responses to PGE_2 (50 ng-100 ng) microinjected into the preoptic region were compared with those induced by VMH injection. Fever induced by VMH injection was significantly greater than that by injection into the preoptic region.

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EFFECT OF PROSTAGLANDIN E_2 ON THERMORESPONSIVE NEURONS IN SLICE PREPARATION OF RAT BRAIN STEM.

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The present results show that microinjection of prostaglandin E_2 (PGE_2) into the preoptic and anterior hypothalamic (PO/AH) region, or the ventromedial hypothalamus (VMH) produced the rise in the rectal temperature in rats. Therefore, effect of PGE_2 on the neuronal activity in the PO/AH region and the VMH was investigated after identification of thermoresponsiveness, using brain slice preparations of rats. The present results demonstrate that there exist thermoresponsive neurons in the VMH as in the PO/AH region. Moreover, the neurons in the PO/AH region showed facilitatory response to bath-applied PGE_2, while those in the VMH inhibitory response. When compared the dose-response relationships of the warm-responsive neurons in the PO/AH region with those in the VMH, it was clarified that the warm-responsive neurons in the VMH started to respond to PGE_2 or reached the maximum change in response to PGE_2 at lower dose than those in the PO/AH region.

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RELATIONS BETWEEN LEVER PRESS AND HEAT LOSS BEHAVIOR IN INTRACRANIAL SELF-STIMULATION RATS.

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To investigate the thermal factors which influence voluntary lever press in intracranial self-stimulation (ICSS) rats, we examined effects of tail amputation, wrapping of the tail by heat insulation cloth, and hypothalamic warming on ICSS behavior. Lever press was continued for 1 hr in control experiment, but after tail amputation it was frequently interrupted by heat loss behaviors, such as grooming and body extension. Hypothalamic temperature at the onset of body extension was higher than that at the end of 1 hr lever press in control. Heat insulation experiment showed the same result. Lever press was interrupted by heat loss behaviors during hypothalamic warming. The data indicate that increase in hypothalamic temperature interferes with lever press.

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EFFECTS OF PREOPTIC ANTERIOR HYPOTHALAMIC THERMAL STIMULATION ON NEURONAL ACTIVITY IN THE VICINITY OF THE SALIVATORY NUCLEUS IN RATS.

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In anesthetized rats, preoptic anterior hypothalamic (POAH) warming elicits salivary secretion. Effects of POAH thermal stimulation on firing rates of the neurons around the salivatory nucleus were examined in urethanized rats. Thirty seven out of 102 neurons were responsive to POAH warming and 1 was responsive to POAH cooling. These neurons changed their firing rates in response to efferent signals from POAH because local temperature was little influenced by POAH thermal stimulation. Twenty three out of 37 warm responsive neurons showed dynamic responses when preoptic temperature (Tpo) reached above 38°C. The remaining 14 neurons responded with relatively linear increase in firing rate during Tpo rise. The location of warm responsive neurons distributed in the area 1mm rostral to the salivatory nucleus. These results showed that some neurons in the midbrain receive efferent signals from POAH, facilitated by POAH warming.

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THERMAL RESPONSES OF VENTROMEDIAL HYPOTHALAMIC NEURONS IN VIVO AND IN VITRO.

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Of 44 ventromedial hypothalamic (VMH) neurons recorded in anesthetized rats, 13 were excited by preoptic (PO) warming and/or supressed by PO cooling (W-type). Sixteen were excited by PO cooling and/or supressed by PO warming (C-type). PO thermal stimulation changed VMH temperature also; for 1°C increase or decrease in PO temperature, VMH temperature rose or fell by 0.7°C, respectively. In VMH slice preparations, where neurons were isolated from PO area, 32 out of 47 neurons were W-type and only one neuron was C-type. These thermal characteristics were retained in Ca^{++}-free/high Mg^{++} perfusate, suggesting inherent thermosensitivities of VMH neurons. These results suggest that neuronal excitation by PO cooling observed in the anesthetized rats was not due to a direct effect of temperature on the VMH neurons, but should be brought about by synaptic inputs to the VMH area, probably from PO and other hypothalamic area.

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EFFECTS OF INTERFERON$_\alpha$ ON THE PREOPTIC THERMOSENSITIVE NEURONS IN VITRO.
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Along the line of studies on the neuronal responsiveness to immune transmitters, we investigated the effects of the local application of recombinant human interferon$_\alpha$ (IFN α) on the unit activity of thermosensitive and thermally insensitive neurons in the tissue slices of preoptic hypothalamus of rats. The perfusion of IFN$_\alpha$ ($10-10^4$ units/ml) decreased the activity in about 70% of warm- and cold-sensitive neurons and 25% of thermally insensitive neurons. However, some cold-sensitive neurons were excited by lower dose of IFN$_\alpha$. The neuronal responses to IFN$_\alpha$ were preserved in a Ca^{2+} free/high Mg^{2+} solution, and therefore the effects are taken as being postsynaptic. The simultaneous application of sodium salicylate could not block the effects of IFN$_\alpha$ in 11 of 12 warm-sensitive neurons, but naloxone antagonized the suppressing effect of IFN$_\alpha$. These neuronal responses to IFN$_\alpha$ are consistent with our findings on the initial poikilothermia and the hyperthermia observed in the rat after intrahypothalamic injections of large and small amounts of IFN$_\alpha$ respectively. The results, taken in conjunction with the previous finding (Blalock and Smith, 1981) that human IFN$_\alpha$ binds to opiate receptors of mouse brain, suggest that IFN$_\alpha$ exerts thermoregulatory effects, at least partly, by the action on the opiate receptors of preoptic thermosensitive neurons.

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CONVERGENCE OF THERMAL, OSMOTIC AND BLOOD PRESSURE SIGNALS ON PREOPTIC NEURONS.
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The effects of local thermal stimulation and changes in arterial blood pressure and/or hepatoportal osmotic stimulation were studied on the activity of preoptic (POA) neurons in urethane anesthetized rats. Changes in blood pressure by less than 15mmHg induced by intravenous injection of vasoactive drugs (phenylephrine, nitroprusside) or the reversible withdrawal of blood altered the activity of thermosensitive neurons (53/80, 66%) and thermally insensitive neurons (51/170, 30%). The neuronal responses were abolished by baro/volume receptors denervation. The major pattern of responses to a fall in blood pressure was the activation of warm-sensitive neurons (37/65) and the suppression of cold-sensitive neurons (6/15). The neuronal responses are appropriate to the hypothermia or the suppression of shivering during hypotension, which are considered to have an adaptive value during large blood loss. Infusion of 3%NaCl, 9%mannitol or water into the hepatoportal vein changed the activity of thermosensitive neurons (14/24, 58%) and thermally insensitive neurons (6/47, 13%). Decreased activity to hyperosmotic stimuli in warm-sensitive neurons (9/20) indicates that the decrease in heat dissipating responses during dehydration is a centrally mediated phenomenon.

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RESPONSES OF PREOPTIC THERMOSENSITIVE NEURONS TO THYROTROPIN RELEASING HORMONE AND CYCLO (HIS-PRO).
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In urethane anesthetized rats and brain slice preparations, a total of 319 neurons in the preoptic hypothalamus (POA) were studied for the responsiveness to changes in local temperature and application of TRH and its metabolite, cyclo (His-Pro). Drugs were applied electrophoretically by the use of multibarrelled microelectrode in the *in situ* study or by perfusion in the slice experiment. Application of TRH decreased and increased the activity of 45 warm-sensitive neurons and 30 warm-sensitive neurons respectively. Of 29 cold-sensitive neurons, 15 (52%) neurons were excited and 5 (17%) were suppressed by TRH. TRH did not affect 82 (50%) of 164 thermally insensitive neurons and the remaining 44 and 38 neurons were excited and suppressed respectively by TRH. On the other hand, cyclo (His-Pro) had no discriminating effects on the 129 POA neurons studied depending on their thermosensitivity in both *in situ* and *in vitro* preparations. Perfusion of Ca^{2+}-free solution did not abolish the responses to TRH and cyclo (His-Pro) in the POA tissue slices, and therefore the responses were taken as being postsynaptic.

The results are consistent with the previous finding that TRH produces a hyperthermia by increased heat production and decreased heat loss in the rat, but do not support the hypothermic effect of cyclo (His-Pro) after intrahypothalamic injection.

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POSSIBLE ROLES OF CENTRAL VENOUS PRESSURE IN THE TERMINATION OF DRINKING
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Dogs are known to consume almost the exact amount of water needed to replace their fluid loss within a few minutes of access, and called early drinker. In order to examine the mechanisms of termination of drinking in dogs, blood volume (BV), plasma sodium concentration ([Na]) and central venous pressure (CVP) were measured continuously for 60 min after fluid intake. After dehydration for 48 h (9.3 % of b.w.), chronically implanted catheters were connected to the extracorporeal curcuit and CVP transducer, and dogs were allowed to access to tap water or 0.9 % saline. Complete (tap water) or temporary (saline) satiation occured within 2 min without showing any changes in BV and [Na], and the satiation was accompanied with a rapid increase in CVP by 6 mmHg. In the case of tap water intake, CVP declined gradually to the control level at 20-30th min. Systemic BV and [Na] began to change at 7th min after the cessation of drinking. In the case of saline, CVP stayed at the elevated level and oscillated with the successive fluid intakes without any change in [Na]. These results suggest that atrial baroreceptor is involved in the body fluid regulation by drinking behavior, and when a threshold in CVP is exceeded, the drinking induced with hyper-osmolality is terminated.

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DIFFERENCE IN REHYDRATION PROCESS DUE TO THE SALT CONCENTRATION OF DRINKING WATER IN RATS. OKUNO, T., YAWATA, T., NOSE, H. AND MORIMOTO, T. Department of Physiology, Kyoto Prefectural University of Medicine, Kyoto 602

Drinking water with different salinity were provided to thermally dehydrated rats and the rehydration processes were compared. Rats were dehydrated by about 8% of body wt exposing to a hot environment(36C, 20% RH) for 6-8 h. Dividing them into 5 groups, one of tap water, 0.2%, 0.45%, 0.9% or 2.0% NaCl solution was given ad libitum, and the amount of fluid consumption, urine volume and urinary output of Na and K were measured every 30 min for 16 h and the balance of water and cations were determined. Both 0.9% and 0.45% groups could rehydrate within 3 h and positive water and cation balances were observed thereafter, which were corrected by kidney function after about 10 h. Tap water group could rehydrate only about 80%, and lost cation further due to water diuresis. 2.0% NaCl group could not rehydrated although cation balance was positive. 0.2% NaCl group took about 10 h to rehydrate. These results indicate that there is a certain range of sodium concentration with which rats can rehydrate after thermal dehydration.

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EFFECTS OF STIMULATION OF NUCLEUS RAPHE MAGNUS ON GAMMA DISCHARGE ACTIVITY IN RATS. SATO, H. 2nd Dept. of Physiol. Nagoya City Univ., Sch. Med., Nagoya 467

Electrical stimulation of the nucleus raphe magnus(NRM) caused a marked inhibition of cold-induced shivering, and it was suggested this effect was mediated via the ascending or descending pathway of the NRM(Hinkel et al., 1983). The present study was undertaken to clarify that gamma motoneurons which are essential to the neural mechanismus of cold shivering participated in such an inhibition of shivering. To eliminate the influences from the higher center via the ascending pathways of the NRM, the bilateral hypothalamus were electrically lesioned. Effects of raphe stimulation on the spontaneous discharge activity from a single gamma efferent were examined in the urethane-anesthetized rats. Most(88%) of the 40 gamma units studied were completely inhibited by raphe stimulation, and only a few(12%) facilitated. In some experiments, it was observed that such an inhibitory response of gamma motoneurons due to raphe stimulation was blocked by serotonin antagonist(p-chlorophenylalanine 10mg/kg, i.p.). The result suggests that the gamma motoneurons receive the serotonergic descending projections of the NRM.

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INHIBITORY EFFECT OF HINDLIMB MUSCLE- AND SOLE SKIN-AFFERENTS ON COLD SHIVERING IN THE PIGEON PECTORAL MUSCLE.

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One of the authors (S.N.) showed previously that cold shivering in the pectoral muscle was inhibited immediately after onset of treadmill exercise in pigeons. In this study, we examined the roles of hindlimb muscle-afferents and sole skin-afferents in this inhibition.

Cold shivering was induced by spinal cord cooling. EMG activity of the right and left pectoral muscles was monitored as an indicator of cold shivering. When cold shivering steadily continued, a hindlimb muscle or sole skin was stimulated electrically.

Electrical stimulation of the hindlimb muscle or sole skin inhibited cold shivering. In the case of the skin stimulation, latency to the onset of inhibition and recovery time to the pre-stimulation level were longer than those of the muscle stimulation. The inhibition started prior to the increment of hindlimb muscle EMG activity when a flexor reflex was induced by strong stimulation to the sole skin. This suggests direct involvement of skin-afferents as well as muscle-afferents in the inhibitory effect on cold shivering.

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RELATIONSHIP OF FINGER BLOOD-FLOW TO ESOPHAGEAL AND TYMPANIC TEMPERATURES DURING EXERCISE

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To find whether finger blood-flow (BF) was correlates better to esophageal temperature (T_{es}) or to tympanic membrane temperature (T_{ty}), the relationship between finger BP to each temperature was compared during exercise at 50% VO_2max for 40 min in male subjects. Finger BF was measured by venous occlusion plethysmography using temperature compensated mercury-in-Silastic strain-gauges. At an ambient temperature of 25°C, the exercise increased finger BF, T_{es} and T_{ty} in proportion. However, the relationship of finger BF to T_{es} showed a bend below which the slope of the regression line of the relationship was slower. Above the bend the slope was steeper. On the contrary, the relationship of finger BF to T_{ty} did not show such a bend and fitted a single regression line. The results confirm the hypothesis that finger vascular tone during moderate exercise correlates better with T_{ty} than T_{es} in man.

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TYMPANIC MEMBRANE TEMPERATURE AND EFFECT OF FACE FANNING ON EXERCISE PERFORMANCE.

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This study examined the effect of face fanning on maximum enduramce performance in man. Six male subjects exercised on bicycle ergometer with wind blown in face (4m/sec) and without at increasing work rate until exhausion. Exercise with face fanning was longer performance time than control condition. At the onset of exercise, Tty decreased slightly, then rose continuously until exhausion. The maximum change in Tty and Ts (forehead and femoral region) during exercise with face fanning was lower than those in control codition, whereas Tre was not different in both condition. At maximum levels the HR, $\dot{V}O_2$ and O_2 pulse in face fanning were decreased in comparison with those in control condition. These results shows that improved endurance performance in face fanning might be related to a decreased thermal load to the brain.

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PHYSIOLOGICAL STRAIN OF AGED MEN DURING HEAT EXPOSURE. K. SHIRAKI, S. SAGAWA, K. MIKI, AND M. K. YOUSEF. Dept. Physiol. Sch. Med., Univ. Occup. Environ. Hlth., 807 Kitakyushu, and Desert Biol. Res. Cent., Univ. Nevada, Las Vegas, NV 89154 USA

Six old (61-73 yr) and ten adiposity-matched young (21-39 yr) men were exposed, while sitting, to 40°C and 40% relative humidity for up to 130 min. Continuous measurements of sweat responses, esophageal (Tes) and skin (Tsk) temperatures, and heart rate (HR) were recorded. Other variables measured once every 5 min included cardiac output (CO), blood pressure (BP), and forearm blood flow (FBF). Old men exhibited a higher threshold Tes for sweating, however, there was no significant difference in the time required for the onset of sweating. Once sweating began sweat rate/min and sweat rate/ΔTes were similar in both age groups. Changes in Tsk, HR, and CO were the same during heat exposure in young and old men. However, the response of FBF to the increase in Tes and forearm Tsk was significantly lower in the elderly, suggesting a retardation of the vasodilation reflex to heat exposure in the elderly. The data suggest that the higher risk of the resting aged in hot environments is not a consequence of inadequate sweat gland activity but may be associated with retardation of the vasodilation reflex which prevents effective transfer of heat produced internally to outside and result in greater heat storage.

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SWEATING RESPONSES TO CHANGNES IN CENTRAL COMMAND DURING ISOMETRIC MUSCLE CONTRACTION. OHNISHI, N., OGAWA, T., SUGENOYA, J., YAMASHITA, Y. AND IMAMURA, R. Dept. of Physiology, Aichi Medical University, Nagakute 480-11

Application of vibration to the patellar ligament during isometric knee extension reflexly reinforces excitation of the extensor muscle and thus reduces central command required to achieve a given tension, Contrarily, the same maneuver during isometric knee flexion increases the central command. In the present study, effects of the tonic vibration reflex (TVR) on sweating with subjects performing sustained isometric knee extension and flexion (approximately 5% of maximal voluntary contraction), respectively, by essentially the same methods as used by Goodwin et al. (1972). Forearm sweat rate was measured continuously during an isometric effort at specified tensions with and without TVR. Isometric efforts caused an increase in sweat rate, the degree of which tended to decrease with TVR during knee extension, and tended to increase with TVR during knee flexion, with considerable individual variations. These results suggest that irradiation of the descending central command to the central mechanism of thermal sweating takes place during voluntary muscular contraction in man.

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CHANGE IN SWEATING ACTIVITY FOLLOWING HEMODIALYSIS. SUGENOYA, J., OGAWA, T., YAMASHITA, Y., OHNISHI, N., IMAMURA, R. Dept. of Physiol., Aichi Med. Univ., Nagakute, Aichi 480-11

We previously demonstrated, by the analysis of characteristics of sweat expulsions, that sweating suppression due to thermal dehydration may be caused mainly by an elevation of threshold temperature for central sudomotor activity, but failed to determine whether the primary factor responsible for the elevation is an increase in plasma osmolality (PO) or a decrease in plasma volume (PV). In the present study we examined the characteristics of sweat expulsions before and after the hemodialysis (HD) in 4 patients with chronic renal disease. Forearm sweat rates, core temperature and skin temperatures were measured under various conditions of hot environment before and after HD. The PO level was markedly lowered and the estimated PV was decreased after HD. In 3 patient, the regression line relating the rate of sweat expulsions (Fsw) to mean body temperature shifted upward, or to the left, following HD, indicating that the threshold temperature for central sudomotor activity was lowered after HD. The regression line relating the sweat rate to Fsw showed no apparent shift after HD except a case. It was suggested that an increase in PO plays a predominant role in elevating the threshold temperature for central sudomotor activity in thermal dehydration.

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EFFECTS OF HYPOTHERMIA ON ACh-INDUCED CONTRACTION OF ISOLATED RAT ILEUM.
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Gastrointestinal motility is generally activated when animals are subjected to cold environment and cold stimulation. To analyse this cold-induced enhancement of gastrointestinal motility, we investegated the effect of hypothermia on acetylcholine(ACh)-induced contraction of isolated rat ileum. The amplitude of ACh-induced contraction of the ileum was enhanced at medium temperatures lower than normal body temperature. Maximum enhancement was achieved between 30 and 25 ℃. This enhancement of contraction was observed in two mediums with different buffer systems whose pH change differently in a thermal gradient. Therefore, changes in medium pH were not essential for this effect of hypothermia. ACh-induced contraction was also enhanced by hypothermia in ileum preparations treated with tetrodotoxin. Thus, changes in activities of the enteric nervous system due to temperature changes failed to contribute to this enhancement. It is concluded that ACh-induced contraction of the rat ileum is enhanced in temperature range lower than normal body temperature due to subcellular mechanism which follows an excitation of muscarinic receptors.

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FEVER INDUCED IN RABBITS BY INTRAVENTRICULAR INJECTION OF RABBIT AND HUMAN SERUM ALBUMIN. NAKAMORI, T., MORIMOTO, A., WATANABE, T. AND MURAKAMI, N. Dept. Physiol., Yamaguchi Univ. Sch. Med., Ube, Yamaguchi 755

Intraventricular injection of rabbit and human serum albumin, and rabbit endogenous pyrogen produced dose-dependent fevers in rabbits. The pyrogenicity of albumin was less than one-twentieth of the pyrogenicity of endogenous pyrogen. Fevers induced by ventricular albumin were significantly suppressed by intraventricular injection of indomethacin, while subcutaneous injection had no effect. Ventricular endogenous pyrogen induced several of the acute phase responses, i.e. decreases in the plasma concentration of iron and zinc, and increases in both the plasma concentration of copper and the white blood cell count. Albumin induced none of these responses. It is concluded that fever induced by ventricular albumin is processed by prostaglandins synthesized within the central nervous system. However, ventricular albumin does not induce any variables in the acute phase response.

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INFLUENCE OF HYPOTHALAMIC TEMPERATURE ON THE ACTIVITY OF THE THALAMIC NEURONS RESPONDING TO SKIN-COLD STIMULATION. SAKATA, Y., WATANABE, T., MORIMOTO, A. AND MURAKAMI, N. Dept. Physiol., Yamaguchi Univ. Sch. Med., Ube, Yamaguchi 755

Responses of the thalamic neurons to cold stimulation of skin were examined electrophysiologically in rats. The responses of the neurons to skin cooling (a range of 33 to 18°C at skin temperature) were classified into two groups; the switch-like response in which the activity abruptly increased with a narrow range (less than 0.5°C) of skin temperature and the graded response in which the activity gradually increased with a wide range (0.5-6.0°C) of skin temperature. Furthermore, the activity in 2/3 of the thalamic neurons to the skin cooling was affected by the hypothalamic cooling (38-34°C) or warming (38-42°C). The response of the thalamic neurons responding to skin cooling was reduced during the hypothalamic warming. During the hypothalamic cooling the thalamic neurons responded with overlapping effect of the response to the skin cooling on the increased base level of the activity.

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RISE OF DEEP BODY TEMPERATURE DURING TREADMILL EXERCISE IN RATS. TANAKA, H., ISHIKAWA, Y. AND NAKAYAMA, T. Dept. of Physiol., Osaka Univ. Med. Sch., Kita-Ku, Osaka 530

Deep body temperature rises during exercise in man with increase in exercise intensity. Opinion varies, however, if the same applies to rats. Using a treadmill especially designed for stable low speed running, present study examined changes in rectal(T_{re}), tail, skin temperature(T_t) and evaporative water loss during rat's treadmill exercises at 55~95% $\dot{V}O_2$ max for 30 min at an ambient temperature of 24°C. T_{re} at the beginning of T_t rise increased to 39°C with increase in exercise intensity to about 75% $\dot{V}O_2$ max. Total evaporative water loss during exercise for 30 min increased with increase in exercise intensity. T_{re} at the end of exercise showed higher level proportionately with increase in exercise intensity and reached the maximum 38.5°C at 75% $\dot{V}O_2$ max. The data proved that treadmill exercise in rats is a useful model to investigate thermoregulatory mechanism during exercise.

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EFFECTS OF PROGESTERONE ON THERMOSENSITIVE NEURONS IN PREOPTIC SLICE PREPERATIONS. TSAI, C.L., MATSUMURA, K. AND NAKAYAMA, T. Dept. of Physiol., Osaka Univ. Med. Sch., Kita-ku, Osaka 530

The single neuronal activities in preoptic (PO) slice preperations from both male and female rats were recorded and examined for their resposes to 3 μM or 30 μM progesterone (P). Of 31 warm sensitive neurons, 19 (61.3%) were inhibited, 5 (16.1%) were excited by P and 7 (22.6%) did not respond to P. Of 26 thermally insensitive neurons, 4 (15.4%) were inhibited, 3 (11.5%) were excited by P and 19 (73.1%) did not respond to P. Of 4 cold sensitive neurons, 3 were inhibited and one was excited. Onset latency of inhibitory effects of P was 8.3±6.0 min (Mean±SD) and only half of neurons inhibited recovered in about 30 min. Neither sex-difference nor dose-dependency on P was associated with a significant difference in the number of responding neurons. In conclusion, that P inhibits most of PO warm sensitive neurons directly or indirectly via local neuronal circuit in the slice.

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EFFECTS OF CARBON DIOXIDE ON PREOPTIC THERMOSENSITIVE NEURONS IN VITRO. MATSUMURA, K., AND NAKAYAMA, T. Dept. of Physiol, Osaka Univ. Med. Sch., Kita-ku, Osaka 530.

Effects of carbon dioxide (CO_2) on the firing rates of preoptic thermosensitive neurons were examined in rat brain slice preparations. The perfusing medium was saturated with gas mixtures consisting of 90% O_2 and one of various concentrations (5 %, 6.3%, 7.5%, and 10%) of CO_2 balanced with N_2. The medium containing 5% CO_2 was used as control. Most preoptic neurons were inhibited during application of a high CO_2 medium. An excitatory effect of CO_2 on a small number of neurons was also significant, although this was weak and transient compared to the inhibitory effect. Thermosensitivities of the neurons did not correlate with their CO_2 sensitivities. The influence of CO_2 tended to be more evident at higher temperatures. We conclude that the direct effect of CO_2 on preoptic thermosensitive neurons as well as on thermally insensitive neurons is mainly inhibitory.

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EFFECTS OF INTERFERONα ON THE BODY TEMPERATURE OF RATS.
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Recent findings indicate that the immune system and the central nervous system communicate with each other. We have demonstrated that chemical signals originating from the immune system such as interleukin-1, muramyl dipeptide and interferonα (IFNα) may modulate the activity of thermosensitive neurons in the preoptic and anterior hypothalamus (PO/AH) thereby causing changes in thermoregulatory responses. This study concerns with the effects of IFNα on the deep body temperature of rats. Injection of lower doses ($10-10^4$units) of IFNα into the PO/AH or the third ventricle produced a hyperthermia of about 0.8-1.5°C, but injection of higher doses (over 10^5units) of IFNα produced a poikilothermia which was followed by a hyperthermia (about 1.0-1.5°C). Naltrexone (3mg/kg, IP) blocked the initial poikilothermia and the early rise in body temperature after injection of large and small amounts of IFNα respectively, but not the later rise in body temperature in both cases. Acetaminophen (25mg/kg, IP) inhibited the later rise in body temperature. The results, together with our findings on the responsiveness of PO/AH thermosensitive neurons to IFNα (Hori et al., 1987), suggest that the initial changes in body temperature to intracerebral IFNα may by mediated, at least party, by binding of IFNα to the opiate receptors of the PO/AH thermosensitive neurons and the later rise in body temperature may be due to the local release of prostaglandins.

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INVOLVEMENT OF PONTINE AND MEDULLARY RETICULOSPINAL NEURONS IN THE COLD-INDUCED SHIVERING AND MUSCLE TONE.
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A total of 181 and 103 neurons in the pontine and medullary reticular formation (pRF and mRF) were studied for the responsiveness to changes in temperatures of local brain sites, preoptic hypothalamus and skin in urethane anesthetized rats. Of these, 32 pRF and 38 mRF neurons were identified as reticulospinal (RES) neurons by antidromic stimulation given to the ventrolateral and ventromedial funiculi of the spinal cord. Local thermosensitivity was found in 59 % and 77 % of pRF and mRF neurons respectively. While pRF contained predominantly cold-sensitive neurons (77 % of locally thermosensitive neurons), locally warm-sensitive neurons were more frequently (64 %) found in the mRF. There was a high degree of convergence of cold and warm signals from the hypothalamus and the skin on pRF and mRF thermosensitive neurons, respectively. Such convergence of thermal signals from these 3 different sites was more frequently found among RES neurons than among non-RES neurons. Almost all the pRF and mRF neurons responding to hypothalamic temperature responded to electrical stimulation of preoptic hypothalamus. The results, in conjunction with our findings that the cold-induced shivering was abolished by local anesthetization of pRF, suggest that pRES neurons were involved in the control of cold-induced shivering and muscle tone.

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THERMALLY INDUCED ACTIVITIES OF THE RUBROSPINAL NEURONS AND THE MIDBRAIN RETICULOSPINAL NEURONS IN THE RAT.
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Unit activities of 142 neurons in the nucleus ruber (RB) and 182 neurons in the midbrain reticular formation (mRF) were investigated during thermal stimulation of midbrain, preoptic hypothalamus and skin in the urethane-anesthetized rat. Of these, 36 and 15 neurons were identified by antidromic stimulation of spinal cord as rubrospinal (RBS) and reticulospinal (RES) neurons, respectively. Responsiveness to midbrain temperature (Tmb) was found in about 35% of RBS neurons and 43% of mRES neurons. While RB warm-sensitive neurons outnumbered slightly RB cold-sensitive neurons, cold-sensitive neurons were more frequently (35%) found in the mRF than warm-sensitive neurons (8%). There was a high degree of convergence of cold signals from hypothalamus and skin on the mRF Tmb cold-sensitive neurons, particularly in RES neurons having Tmb cold sensitivity. On the other hand, RBS neurons showed various combinations of responsiveness to temperatures of different sites. Microinjection of procaine (1μg) into the mRF in lightly anesthetized rats decreased or completely abolished the cold-induced increase in muscle tone and shivering without changes in cardiovascular and respiratory parameters, but the injection into the RB had not effect. The results suggest that mRES neurons are involved in the control of thermoregulatory muscle tone and shivering.

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AVA CONTRIBUTES TO HEAT-INDUCED VASOCONSTRICTION OF THE FINGER. NUNOMURA, T., NAGASAKA, T. AND HIRATA, K. Dept. Physiol., Sch. Med., Kanazawa Univ., Kanazawa 920

We have observed that finger blood-flow decreases when the hand is heated locally to temperatures above the body core temperature. This study was designed to elucidate which vessels, arteriovenous anastomoses (AVAs) and/or capillaries, participated in this heat-induced vasoconstriction in the finger. Blood-flows in the finger were measured simultaneously by laser Doppler flowmetry which is known to detect blood-flow of superficial vessels mainly capillaries, and by venous occlusion plethysmography in a warm environment (35°C, 40% rh). One hand was immersed in a water bath the temperature of which (T_w) was raised every 10 min by steps of 2°C from 35°C to 43°C. Finger blood-flow measured by venous occlusion plethysmography decreased at T_w of 39°C and 41°C. In contrast, blood-flow measured by laser Doppler flowmetry increased steadily with raising T_w from 37°C to 43°C. The results suggest that the decrease in finger blood-flow in response to local heating may be limited to AVAs, and capillaries may not contribute to this heat-induced vasoconstriction of the finger.

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THERMOREGULATORY RESPONSES TO INTERNAL AND EXTERNAL HEAT STRESS IN HEAT-ACCLIMATED RATS. SHIDO, O. AND NAGASAKA, T. Dept. Physiol., Sch. Med., Kanazawa Univ., Kanazawa 920

Heat loss and metabolic responses to heat stress were tested in male rats acclimated to either 24 (C), 29 (H1) or 32°C (H2) for 14 days. In a direct calorimeter set at 24°C, the rats were subjected to internal heating (IH) with an intraperitoneal heater (6.5 $W \cdot kg^{-1}$) or to external warming (EW) by a raising water jacket temperature surrounding the chamber ($0.19°C \cdot min^{-1}$). Nonevaporative heat loss (R+C+K) during EW was computed by canceling heat transfer to the chamber. The resting hypothalamic temperature (T_{hy}) and the threshold T_{hy} for the tail skin vasodilation (T_{th}) increased according to the rise in acclimated temperature. The amount of increase in T_{hy} due to heat stress was the greatest in C-rats. During IH, the responses of R+C+K and thermal conductance (k) to the change in T_{hy} were not different among the groups. In H2-rats, however, EW enhanced the response of k to the increase in T_{hy} beyond T_{th}. IH signigficantly reduced heat production (M) only in H2-rats. During EW, M significantly decreased in all groups of rats. However, the reduction of M continued longer in H1- and H2-rats than C-rats. These results suggest that heat acclimation affects not only the metabolic response to heat stress but also the gain of heat loss mechanisms when peripheral thermal input is increased in rats.

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STUDIES ON HEAT ACCLIMATIZATION (REPORT IV) — CONTINUOUS MEASUREMENT OF THERMAL SWEATING IN TROPICAL INHABITANTS —. YU-JEN FAN, KOSAKA, M., OHWATARI, N., NAKAMURA, K., YAMAUCHI, M., G.J. YANG, C.M. CHEN AND P.G. RIWA Dept. of Environment. Physiol., Inst. of Trop. Med., Nagasaki Univ., Nagasaki 852

Measurement of sweat rates in tropical and Japanese subjects were conducted in the environmental chamber. Two plastic capsules (30mm diameter and 30mm high) with connections to hygrometer recorder and nitrogen gas flow were used. These capsules were firmly fixed onto the chest and abdominal wall with a liquid adhesive (celloidin). Continuous measurement of humidity in the capsules were recorded by Hygrometer (H211 TAKARA Instruments Co.). Blood pressure, skin and oral temperatures were also recorded. The results show that the tropical subject had a lower sweat rate than Japanese sportsman. Both had a higher oral temperature after the first heat challenge but later showed increased sweat rates with shorter onset times. These findings are consistent with our previous experimental results in which we found out that tropical subject (N=12) had a longer onset time (Mean 11.6 min) and higher rise of oral temperature (0.045°C/min Δt:0.24-0.29°C) compared with Japanese sportsman who had a shorter onset time 8.6 min and lower oral temperature increase (0.035°C/min, Δt:0.18-0.19°C). The experimental modalities used in these investigations may be utilized in further determination of physiological mechanisms of heat acclimatization.

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AUTONOMIC NERVOUS TONE IN HEAT ACCLIMATED RATS. TSUCHIYA, K. Dept. of Environment. Physiol., Inst. of Trop. Med., Nagasaki Univ., Nagasaki 852

Male Wistar rats (5-8 months old) were used in this study. Heat acclimated rats (30°C, 50% r.h. for 3 months) and controls reared at 24°C, 50% r.h. for similar period, were kept in metal wire cage (5 x 5 x 15cm) in the climatic chamber. ECG, rectal temperature (Tre) and tail skin temperature were recorded continuously 90 min before and 60 min after drug administration. Atropine sulfate (1mg/kg,i.p.) or propranolol hydrochloride (8mg/kg,i.p.) were administred. Before drug administration the HR was 405 ± 7 beats/min (Mean ± SE, N=8) at 25°C and 328 ± 10 beats/min (N=4) at 30°C in the control group. The HR in the heat acclimated group was 423 ± 9 beats/min (N=4) at 25°C and 363 ± 6 beats/min (N=4) at 30°C, respectively. The autonomic nervous tone was expressed as the ratio of the HR change due to drug injection to the calculated intrinsic HR (Lin and Horvath, 1972). The parasympathetic tone (PT) and sympathetic tone (ST) were 15.0% and 30.9% at 25°C and 24.4% and 21.0% at 30°C in the control group, respectively. In the heat acclimated group, the PT and ST were 9.1% and 32.9% at 25°C and 18.5% and 18.8% at 30°C, respectively. In both groups PT was greater while ST was lower at 30°C compared with those at 25°C.

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HEAT LOSS RESPONSES TO IRRADIATION WITH ARGON LASER ON RABBIT'S CENTRAL THERMOSENSITIVE TISSUES. OHWATARI, N., KOSAKA, M., FUJIWARA, M., TSUCHIYA, K., YU-JEN FAN AND NAKAMURA, K. Dept. of Environment. Physiol., Inst. of Trop. Med., Nagasaki Univ., Nagasaki 852

To clarify the thermal effect of Argon laser to rabbit's brain, analysis of brain surface temperature influenced by irradiation with Argon laser on brain surface was performed, and the used powers of laser were 40, 60, 100 and 150mW and the diameter of glass fiber was 0.4mm. The results obtained, suggest that Argon laser is fit to heat a micro-area in the brain and it easily controls temperature and heating area. In 15 rabbits, nine points including the preoptic area (POA), posterior hypothalamus (PH) and reticular formation (RF) in the brain were irradiated with Argon laser at 100mW for 5 min. Heat loss responses (panting and vasodilation) were markedly induced at POA. During heating of POA, rectal temperature decreased 0.39 ± 0.04°C, because that ear skin temperature and respiratory rate increased 6.6 ± 0.6°C and 121 ± 10min^{-1} (Mean ± SE). All these values of thermoregulatory responses were significant (t-test:$p < 0.05$). In 3 rabbits, the same nine points were locally heated with Argon laser at 40, 60, 100, 150mW for 4 - 10 min. Heat loss responses were induced in heating of POA at 60mW, and those of RF were induced at 150mW. The volume area of 40°C to 42°C of RF was 19 times compared with that of POA, when the onset of vasodilation was initiated at the ear skin. This suggests that thermoregulatory capability per unit volume concerned with POA is 19 times larger compared with that RF.

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EFFECTS OF DIFFERENT TYPES OF CLOTHING ON THERMOREGULATORY RESPONSES AND CLOTHING TEMPERATURE IN MAN AT SUPINE REST. JEONG, W.S. AND TOKURA, H. Div. Environ. Sci. Human Life, Grad. Div. Human Culture, Nara Women's Univ., Nara 630

In order to elucidate the thermophysiological role of the body core-shell ratio changed by different garments, we tried to compare the human thermoregulatory responses when man wore different two types of clothing, i.e., one which was covering the whole body area and the other which was covering only the central body area. The experiment was performed for 160 min with six healthy males at an ambient temperature of 10°C and a relative humidity of 50 %. Major results showed that core and trunk skin temperature were maintained higher when only the central body area was covered with garments, as compared to the whole body area covered. It might be suggested that these different responses are ascribed to the redistribution of blood flow caused by the difference of the body core-shell ratio between the two types of clothing.

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PHASE RESPONSE OF LOCOMOTOR ACTIVITY RHYTHM IN LAMPREY AND REESTABLISHMENT OF THE CIRCADIAN RHYTHM BY PINEAL TRANSPLANTATION.
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Free-running locomotor activity rhythm of lamprey phase-shifted by light pulse (2 h, 50-80 lux). Removal of both eyes did not change the direction of the phase shift (delay or advance). However, the amplitude of the phase shift changed, i.e. the phase delay became large and the phase advance became small after the operation. This indicates that the eye biases the sensitivity of phase response to light pulse. The circadian locomotor activity rhythm is abolished by pinealectomy. Pineal organ was transplanted to the pinealectomized lamprey that showed no circadian rhythm. It was implanted into the connective tissue just above the pineal cavity of the neurocranium that had a cut resulted from pinealectmy. Four out of seven lampreys reestablished the circadian locomotor rhythm, indicating that the pineal transplantation synchronizes the oscillators to circadian period.

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CIRCADIAN RHYTHM OF BODY TEMPERATURES AND OF HEART RATES IN RABBITS.
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Circadian rhythms of the temperatures in the hypothalamus, abdominal cavity and ear love and of the heart rates were studied under conscious and unrestrained state using 6 male rabbits. Each temperature was measured using chronically implanted thermisters together with the room temperature and their mean values of 50 data for each 5 sec were printed out in every minute by a personal computer. Heart rates in the 20 sec period for temperature measuring were counted visually from ECG records. Each body temperature falls from early morning, is at relatively lower level in daytime and rises from evening to night. The mean heart rate was significantly lower in the D period than in the L period. Most of the interrelations between each of the body temperatures and heart rate in each L and D period showed a positive correlation and higher coefficients were obtained between the ear lobe temperature and the heart rate. Cross-correlation analysis revealed that the changes of the heart rate is advancing in temporal sequence by 1 to over 20 min from every body temperature change.

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BODY TEMPERATURE RHYTHMS IN THE BLINDED OR INTACT RATS UNDER THE LIGHT-DARK CYCLE AND UNDER THE CONTINUOUS DARK.
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To know the oscillatory mechanism underlying the circadian body temperature rhythm, rectal temperature measured intermittently for 2 hr intervals were examined. Freerunning-body-temperature-rhythms were recognized not only in the blinded rats under the light-dark cycle, but also in the intact one under the continuous dark. Simultaneously measured circadian rhythm of locomotor activity (Animex) were well correlated with that of the body temperature keeping a phase differences of 1-3 hr, though their levels examined throughout a circadian period were not correlated. When the relationships of body temperature and activity rhythms were precisely analyzed for the component of cicadian rhythm (ultradian rhythm), the ratio of the events having a positive correlation and negative one was 3:2. From these results, even the rats were handled and inserted a mercury thermometer at the measurement of them, intermittent recordings of body temperature were considered to be verified to analyze the circadian rhythm of them.

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HUMAN CIRCADIAN RHYTHMS IN A TEMPORAL ISOLATION UNIT: CIRCABIDIAN RHYTHM AND BRIGHT LIGHT PULSE. HONMA, K., HONMA, S. AND *WADA, T. Dept. of Physiol., Hokkaido Univ. Sch. of Med., *Coll. of Med. Technol., Sapporo 060

Sleep and rectal temperature rhythms were measured in two subjects who spent 3 weeks in an isolation unit without knowledge of time. A sleep rhythm of one male subject became circabidian (about 48 hr day) 3 days after the start of isolation. A sleep episode was cancelled on every second day, so that his subjective day consisted of a 40 hr wakefulness and a 10 hr sleep. He took 3 meals every "day". On the other hand, the circadian temperature rhythm was kept throughout. The circabidian rhythm in sleep-wakefulness persisted 3 cycles. When a bright light pulse (3 hr, 5,000 lx) was introduced at the early subjective day, the temperature rhythm phase-advanced and the circabidian sleep rhythm returned to be circadian. One week later, the sleep rhythm became circabidian again after the light pulse applied at the late subjective day. This time, the circabidian rhythm persisted only one cycle. A similar circabidian sleep rhythm appeared in one female subject who had been free-running with a circadian fashion until a birhgt light pulse was given at the middle subjective night. In this case, sleep was lengthened to 14-18 hr with a short nap. The rectal temperature rhythm remained to be circadian. It is concluded that the transition from circadian to circabidian or vice versa in sleep-wakefulness cycle is triggered by a bright light pulse.

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RHYTHMS WITH CIRCADIAN PERIOD APPEARED IN SCN LESIONED RATS BY METHAMPHETAMINE. Honma, S., Honma, K. and Hiroshige, T. Dept.Physiol.,Hokkaido Univ.Sch.Med.,Sapooro 060

We reported a robust activity rhythm appeared in SCN lesioned rats by methamphetamine. The rhythm had a circadian period but did not entrain to the light-dark cycle. The present experiment was done in order to know whether similar rhythms appeare in other physiological functions. Materials and Methods Wistar female rats were lesioned in the SCN electrolytically. A loss of the circadian rhythmicity was examined by mathematical analyses. Methamphetamine was administered by disolving into drinking water. Spontaneous locomotor activity was monitored by an Animex. Wheel-running activity, feeding and drinking behavior were also monitored in some rats. Blood samples for the plasma corticosterone determination were obtained from the tail of freely moving rats at 4-h intervals for 48 h. Deep body temperature was continuously monitored telemetrically. Results Rhythms with a circadian period appeared in all functions examined. Rhythms in the wheel-running, feeding and drinking were all in the same phase. Fluctuation of body temperature corresponded with locomotor bouts. Plasma corticosterone level increased prior to the onset of locomotor activity and decreased during the latter half of the active period. Conclusion Behavior, temperature and corticosterone rhythms with a circadian period appered in SCN lesioned, methamphetamine treated rats. The phase relation among them was similar to that of circadian rhythms in intact rats.

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EFFECT OF KETAMINE ON CIRCADIAN RHYTHM. YAMAOKA, S., AND YOSHIDA, N.*, Dept. Physiol., Saitama Med. Sch. Saitama 350-04

The circadian susceptibility rhythm to anesthetics is well documented in various animal species. But very little is known concerning the effect of anesthetics on circadian behavioral rhythmicity. And it has been found the several drugs(such as diazepam) affecting the phase shift of circadian rhythm. We examined the effect of anesthetics (nembutal=pentobarbital sodium, ketamine) on circadian rhythms(sleep-wakefulness and wheel-running)and their phase shifts in male Sprague-Dawley(SD) eye-enucleated rats. EEGs from frontal cortex, dorsal 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. The nembutal anesthesia indicated the slight decrease of 1hr PS amount within 3hr after EEG alertness, and did not show any changes in 1hr SWS amount and circadian phase and period. On the other hand, the ketamine anesthesia indicated the marked decrease of 1hr PS and SWS amount for 3 to 4 hours after EEG alertness and then the significant increase of 1hr SWS amount for 2 to 3 hours, the phase shift in the acrophase of PS and SWS, and the different phase response curves from diazepam. From these results, it is suggested that the ketamine anesthesia may affect directly the circadian oscillator systems, but not in the nembutal anesthesia.

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SLOW FLUCTUATIONS OF SPONTANEOUS ACTIVITIES IN HIPPOCAMPAL AND THALAMIC NEURONS DURING SLEEP-WAKING CYCLES AND SEROTONERGIC ROLE

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Spontaneous activities of hippocampal pyramidal neurons and thalamic relay neurons of head-restrained cats have been recorded to investigate wheter there exist slow fluctuations in neuronal activities during paradoxical sleep (PS) or not. The result shows that the slow fluctuations, ranged from 0.5 s to 50 s, are prominent during PS as shown in the mesencephalic reticular formation (MRF) neurons.

We previously investigated causes of the slow fluctuations with crosscorrelation analysis, which could not explain them successfully. In this study, neuronal activities were recorded, to clarify the same problem, both during the phase without serotonin by parachlorophenylalanine administration (PCPA phase) and during the phase with a serotonin agonist under the condition of PCPA pretreatment (5MeODMT phase). The results show that the slow fluctuations during PCPA phase were prominent and similar to those during PS. Whereas, none of slow fluctuations were observed during 5MeODMT phase like during SWS. It is highly probable that pause of serotonergic system during PS leads to the fluctuations of neuronal activities in low frequency band.

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SEROTONERGIC AND CHOLINERGIC MECHANISMS OF SLOW FLUCTUATIONS IN SPONTANEOUS ACTIVITY OF HIPPOCAMPAL THETA CELLS

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Spontaneous activity of hippocampal theta cell of head-restrained cats were recorded during natural sleep-waking cycles and during serotonin-depleted states induced by p-chlorophenylalanine (PCPA). During PS and PCPA-induced insomnia, the theta cells exhibited slow-fluctuations (0.01-0.1 Hz) in their spike density. Furthermore, the slow fluctuations during PCPA-induced insomnia were suppressed by both serotonin agonist (5MeODMT) and choline antagonist (atropine sulfate).

During PS and PCPA-induced insomnia, not only the theta cell activity, but also theta wave frequency and ponto-geniculo-occipital (PGO) wave showed slow fluctuations. These three fluctuations were correlated with one another. Therefore, these results suggest that the slow fluctuations in the theta cell activity may be physiological (during PS) and pharmacological (during PCPA-induced insomnia) expressions of the removal of serotonergic influences, and that these fluctuations may be activated and/or maintained by cholinergic mechanisms including PGO generators.

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SLOW FLUCTUATIONS OF SPONTANEOUS ACTIVITIES IN MIDBRAIN RETICULAR FORMATION NEURONS DURING PARADOXICAL SLEEP

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During paradoxical sleep (PS) in the head restrained cat, neurons in the midbrain reticular formation (MRF) spontaneously fire with spectral densities inversely proportional to frequency (the 1/f spectrum) of at least 0.1-1.0 Hz. In order to ascertain whether slow fluctuations are similarly observed during different PS episodes in a MRF neuron, we recorded spontaneous neuronal activities during 3 PS episodes in each of 19 MRF neurons. During every PS episode each neuron fired with almost comparable spectral densities: the 1/f spectrum. The slope of the spectral curve with logarithmic plots for a frequency band (0.1-1.0 Hz) was calculated by means of the least mean-square analysis. The pooled mean slope ($\pm$S.E.) for all 57 spectrums was 0.96 ($\pm$0.23), and in 70% of them the slope ranged between 0.7 and 1.3. These results confirmed that the spontaneous activities of MRF neurons during PS definitely show the 1/f fluctuations as a whole. Moreover there existed neurons whose slope was different from each others irrespective of episodes, which might indicate functional and morphological differences of the MRF neurons.

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CHARACTERISTICS OF NON-PARAMETRIC ENTRAINMENT OF A CIRCADIAN CELLULAR PACEMAKER.
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Responsiveness of the circadian behavioral rhythm in a cell population of Paramecium to regimens of various "complete" photoperiods and "skeleton" (PPs) photoperiods has bee previously examined. The present study focuses "bimodality" of the rhythm in the PPs of 12 with morning pulse and evening pulse (both 2 hours x 1000 lux) separating 12 hours each other. The rhythms steadily entrained to the PPs of 12 were subjected to continuous darkness (DD) after either a morning pulse or an evening pulse. Both cases showed a clear free-running oscillation with a circadian period, initiating immediately after the morning pulse or the evening pulse and exhibiting a maximum 12 hours after each pulse. The results manifest the bimodality that the Paramecium cells are simply "reset" equally by either of the morning or evening pulses to their new circadian time 0 and subsequently initiate their endogenous circadian oscillations. This describes, for the first time, an important character of circadian cellular pacemakers as non-parametric entrainment as predicted in theory, and provides a basis for understanding the hierarchical structure of the animal circadian system.

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HYPOTHALAMIC MULTIPLE UNIT ACTIVITY DURING SLEEP-WAKING CYCLE IN CATS.
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Multiple unit activities (MUA) were recorded in chronic cats during waking (W), slow-wave sleep (SWS) and paradoxical sleep (PS). MUA data were sampled from 280 sites in the brain stem ranging rostrally from the diagonal band of Broca to the pontine tegmentum caudally. A great majority of MUA (199 out of 280) showed high discharge rates during W and PS in comparison with during SWS. In the brain stem caudal to the preoptic area, almost all of MUA (189 out of 211) had reduced firing rates during SWS and none of them showed the opposite tendency. On the other hand, 15 MUA records showing an increased firing rate during SWS were obtained from the preoptic area (13) and diagonal band of Broca (2). It is unlikely that the diagonal band of Broca plays an essential role for inducing SWS, because their activity increased remarkably also during locomotor behaviors. The preoptic sites showing increased activities were specifically localized in the medial portion running parallel along the wall of the third ventricle at a distance of about 1 mm. It was reported that destruction of the medial preoptic area caused a decrease in the amount of SWS. Therefore, it is suggested that the medial preoptic area is involved in mechanisms inducing SWS.

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EFFECTS OF EXERCISE ON URINARY EXCRETIONS OF PURINES IN MAN. HADANO,S., OGASAWARA,M.,MIKAMI,T.,GOTO,H.,SAITO,A.,KASUGAI,A.and ITO,A. Institute of Health and Sports Science,Tsukuba Univ.,Sakuramura,Niiharigun,Ibaraki 305

To investigate the effects of exercise on urinary excretions of purines in man , we performed exhaustive exercise test on bicycle ergometer , and determined the changes in purine metabolites levels in venous blood and urine. 8 healthy male subjects who were given allopurinol,an inhibitor of xanthine oxidase, before exercise participated in this study. Results were summarized as follow ; 1) Uric acid excretion decreased significantly from 30 minutes to 1 hour after exercise,and recovered to basal level until 3 hours after exercise . 2) Xanthine excretion decreased at 30 minutes after exercise, and increased thereafter. 3) Hypoxanthine excretion increased significantly from 30 minutes to 3 hours after exercise . 4) Inosine excretion did not change except for one subject. These observations suggested that the effects of exercise on the renal handlings of hypoxanthine and inosine were different from those of uric acid and xanthine.

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CHANGE IN RENAL FUNCTION FOLLOWING EXHAUSTIVE EXERCISE. SUZUKI,M.,SHIOTA,M.,MATSUBARA.S. AND IKAWA,S. Dept. Lab. Med., Jikei Univ., Sch. Med., Nishishinbashi Minatoku,Tokyo 105

In a previous report, a dilution of the urine was observed 30 min after exhaustive exercise(post-exercise diuresis). The present study was carried out to investigate the factors inducing post-exercise diuresis. Fifty-two healthy males were subjected to exhaustive exercise on a treadmill. The urine volume(UV), urinary osmolality(Uosm), urinary excretions of Na, K, Cl, inorganic phosphate(Pi) and lactate(LA) were observed before and after, and 30 min and 60 min after exhaustive exercise. Urine volume significantly decreased from the resting value of 0.47 to 0.26 ml/min immediately after exercise, and increased by 0.11 ml/min($p<0.001$) following exercise. Uosm decreased from the initial level of 1014 to 807 mOsm/kg·H_2O 30 min after exercise. This decrease in Uosm was accompanied with decreases in urinary Na, UN and Cl concentration. The decrease in urinary Cl concentration was especially remarkable, and a 2.0-fold decrease in Na was observed at 30 min after exhaustive exercise, whereas urinary lactate and Pi concentration increased by 54.5 and 52.9 mM/l, respectively. The magnitude of the post-exercise diuresis was significantly correlated with the increases in LA and Pi concentrations, and decrease in Cl concentration. The results suggested that the post-exercise diuresis might be induced by increase of nonreabsorbable or poorly reabsorbable solute(lactate or inorganic phosphate) in the nephron.

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EFFECT OF EXERCISE-TRAINING ON THE MEMBRANE FLUIDITY OF RAT ADIPOCYTE PLASMA MEMBRANES. IZAWA, T., [1]KOMABAYASHI, T., [1]TSUBOI, M., [2]SUDA, K. AND KOSHIMIZU, E. Exercise Physiol. Lab., [1]Dep. of Pharmacol., Tokyo Coll. Pharmacy, [2]Kochi Jr. Coll.

The membrane fluidity in adipocyte plasma membranes from exercise-trained rats was measured using fluorescence polarization spectroscopy at physiological temperature. Moreover, total cholesterol and total phospholipids content in adipocyte plasma membranes were also measured. The adenylate cyclase activity induced by (-)-isoproterenol above 10 uM was significantly greater in exercising group than in control. Neither total cholesterol nor total phospholipids content of plasma membranes from exercise-trained rats was significantly altered. The DPH fluorescence polarization and the calculated microviscosity tended to decrease but marked changes were not observed at physiological temperature. However, it would be premature to conclude that exercise-training could not affect the membrane fluidity of adipocyte plasma membranes. Further studies are needed with much more sampling.

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CHANGES IN LIPID COMPOSITION OF STATICALLY TRAINED MUSCLES.
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To clarify quantitative and qualitative changes in lipid composition in muscular hypertrophy, wire net griping training was loaded to rats by prolonging gradually the time. There were not significant changes in body and soleus muscle weights between control and trained groups, but gastrocnemius muscle was significantly larger in training group than in control group and decreases of the TG, PE, and PC and increase of the CL signifi-cantly caused. In soleus muscle, linoleic acid composition of the TG and CL and stearic acid compositions of the PE and PC significantly increased, despite of being no changes in the muscle weight. Central mitochondrial protein increased by the training with increases of the PE and PC and these unsaturated fatty acids significantly increased, but in peripheral mitochondria, linoleic acid composition of the CL and stearic acids of the PE and PC significantly increased. These results indicate that stati-cally muscular training cause significantly quantitative and qualitative changes in lipid composition in the hypertrophied muscle and influences on subcellular lipid composition, mitochondrial fractions.

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PLASMA AND AORTIC LIPIDS IN OLD EXERCISED RATS. FURUI, H., HASHIMOTO. M., HARA, T. AND MASUMURA, S. Dept. Physiol., Shimane Medical Univ., Izumo, Shimane 693

To study whether exercise protects from vascular lipid accumulation with age, we measured plasma and aortic lipids in old exercised rats. In this study, female Wistar rats, 98 weeks of age were grouped into NE and TE. NE was non-exercised group. TE was treadmill exercise animals. The levels of total cholesterol(Total-C), high density lipoprotein cholesterol(HDL-C), low density lipoprotein cholesterol(LDL-C), triglyceride(TG), and phospholipid(PL) in the plasma and/or aortae were determined using enzyme kits. The chylomicron cholesterol and very low density lipoprotein cholesterol (ΔC) concentrations were computed by the difference between the values of Total-C and (HDL + LDL)-C. In the groups of NE and TE, the levels of HDL-C and aortic lipids were unchanged. However, in the TE animals, the concentrations of Total-C, LDL-C, ΔC, TG and PL were decreased by 16.2 - 46.0 % ($p<0.05$). In this case, we found the following:

Total-C = 0.5790 HDL-C + 0.4483 LDL-C + 1.407 ΔC + 49.15
PL = 0.7243 HDL-C + 0.6390 LDL-C + 1.844 ΔC + 81.93
TG = 3.116 LDL-C + 7.030 ΔC - 75.84

Thus, decreased levels of Total-C, PL and TG in the TE group were originated from the decrements of LDL-C and ΔC. The present results suggest that physical activity, from an old age, participates in reduction of lipids in plasma, but not in aortae.

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EXERCISE AND COLD STRESSES AND γGTP. OHNO, H., YAHATA, T. AND KUROSHIMA, A. Dept. Physiol., Asahikawa Medical College, Asahikawa 078

There are very few reports about the change of γGTP under physical exercise as compared with other enzymes, such as CK, AST, and LDH. The aim of the present study was to estimate the effects of physical exercise on both the activity and concentration of γGTP in men and rats. Experiments with men: The effects of 10-week running training (over 5 km, 6 times/week) on plasma activity and concentration of γGTP were investigated on seven previously sedentary healthy male students. After training the resting plasma γGTP concentration decreased to half, whereas the γGTP activity did not vary significantly. Experiments with rats: Fifteen male Wister strain rats were exercised by swimming until exhausted with a weight equal to 3% of their body weight in water at 34-36 ℃. The γGTP activity in the extramicrosomal fraction of the liver was increased after swimming, suggesting an increase in the in vivo permeability of the microsomal membrane. On the other hand, the γGTP concentration did not change definitely. In addition, we determined the influences of chronic cold exposure on liver γGTP in rats. As a result, it appeared that long-term cold exposure stabilizes the membrane of the liver microsomes. These results suggest that immunoreactive γGTP dose not always correlate with the enzyme activity and that exercise and cold adaptation affect liver microsomal membrane stability.

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Lactate metabolism in rats during 40 min of recovery after strenuous exercise

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Metabolism of lactate was investigated in male Wistar rats (185～259g,n=5) after strenuous running to exhaustion at the speed of 80～110 $m.min^{-1}$, lasting 122 sec in mean value. Immediately after the exercise, 5 $\mu Ci.200g^{-1}$of [U-^{14}C] lactate was injected into aorta through an indwelling catheter. Expired gas was collected during recovery. After 40 min of the exercise rats were sacrificed. Blood lactate concentration immediately after the exercise was 18.6 ±1.2 mM (Mean ±SE) and was 4.2 ±0.5 mM at 40 min of recovery. Glycogen content in muscle had not returned to resting level(2.7±0.7 $mg.g^{-1}$,gastrocnemius). During 40 min of recovery 20.4 ±2.0 % of ^{14}C injected was expired as $^{14}CO_2$. No significant incorporation of ^{14}C into tissue glycogen was found. The incorporation of ^{14}C into tissue was greatest in muscles of lower limb. The concentrations of ^{14}C in plantaris, liver, kidney, heart and blood were 63.2±5.6, 44.0±7.7, 30.7±4.1, 31.1 ± 5.4 and 17.9 ±4.2 $dpm.mg^{-1}$, respectively. It was calculated that at least 20 % of ^{14}C was in skeletal muscle involved in running movement at 40 min of recovery. It was suggested that skeletal muscle might be the main cite of lactate removal after strenuous exercise.

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EFFECTS OF PHYSICAL EXERCISE ON CHOLESTEROL SYNTHESIS IN VIVO IN STROKE-PRONE HYPERTENSIVE RATS.

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The purpose of this study was to determine whether voluntary exercise would increase levels of endogenous cholesterol biosynthesis in stroke-prone spontaneously hypertensive rats(SP-SHR). The study was initiated when the animals were 47-51 days of age after which they were assigned to either activity or sedentary cages. The active group ran an average of 1-4 km/day intermittently for 8 weeks. In order to measure the rate of cholesterol biosynthesis in vivo, the rats were injected with 15μCi of [1- ^{14}C]-acetate per 100g body weight into the intraperitoneal, and the incorporation of radioactivity into cholesterol in the major organs were examined 60 minutes after the injection. The level of total serum cholesterol was significantly higher in the active rats than in the sedentary control rats. The hepatic cholesterol synthesis increased by three fold which was significant($p<0.01$) in the active rats, however it did not normalize[sedentary control(C)=658±326;active(A)=1860±1094 cpm/mg cholesterol] while their intestinal cholesterol synthesis significantly($p<0.05$) decreased(C=3858±1800;A=2386±877 cpm/mg cholesterol). The incorporation of acetate into heart, kidney and spleen were similar between active and sedentary control groups.

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CARDIAC OUTPUT USING A THERMODILUTION METHOD DURING EXERCISE IN CONSCIOUS DOGS.

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Cardiac output using a thermodilution method was measured during treadmill running. Four dogs weighing 14-21 kg were anesthetized with pentobarbital(25 mg/kg). Five % glucose solution(0°c, 5 ml) was injected through a catheter inserted in the pulmonary artery. The treadmill running speed was increased gradually from 1 to 4 miles/hour during 15 min. Cardiac output in conscious state was larger than that of anesthetized state. Heart rate increased about 195% of the control value at the end of exercise. Cardiac output also increased about 205% and then returned to the control level within 7 min after the exercise. It is concluded that the increase of heart rate plays an important role in the increase of cardiac output during exercise. Therefore, the thermodilution method is useful for the measurement of cardiac output during exercise.

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EFFECT OF AGING UPON THE INFORMATION OF COMMON CAROTID ARTERY DUE TO SUBMAXIMAL EXERCISE.
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The purpose of the study was to elucidate the blood flow of the head during exercise by observation of blood flow of common carotid artery, which should be related with the cerebral blood flow. The observation was made by an ultrasonic quantitative measurement system(QFM), and non-invasive measurements could be made on blood vessel diameter, blood flow velocity and blood flow rate. The exercise was 10 min. running on a treadmill of 3° inclination and the running speed was regulated in each subject according to the results of preliminary experiment with reference to PWC170. The thermal conditions were regulated at 36°C in warm, at 23°C in normal and at 10°C in cool environments. The subjects were healthy men of young ages and middle ages. The blood flow rate, blood flow velocity and diameter of common carotid artery, respectively showed a significant increase due to the exercise, and a positive correlation with the heart rate changes. Moreover, the increase was conspicuous in case of warm environmental conditions. But the changes in the middle age group were markedly smaller than those in the young group. The increase of circulatory resistance with aging was presumed the decrease of elasticity of arterial wall and the restriction of blood flow of the head.

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THE CORRELATION BETWEEN HEART RATE AND SPECIFIC APPLIED FORCES IN THE UNDERWATER
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The upper limit of specific applied forces by diver's fin kick was examined in underwater(26 °C). The performance rate (%) of the specific applied forces below 6.5 Kg and beyond 7.0 Kg was 80 - 100 % and 0 -40 % . The correlation between heart rate and specific applied forces was given linearly below the 6.5 Kg.
This indicates that the upper limit of the specific applied forces was 6.5 Kg.

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CHARACTERISTICS OF EMG ACTIVITIES ON THE LEG AND THE RESPIRATORY MUSCLES DURING STATIC AND DYNAMIC EXERCISES.
SHIMOSHIKIRYO, K., MURO, M., YONA, M., NAGATA, A., AND SUNAMOTO, H. Toho Univ. Sch. Med., Tokyo 143

The purpose of the present study were to evaluate electromyogram on the respiratory muscles during static and dynamic voluntary exercises; and to see whether neural effects on the respiratory muscles could be related to fatigue quadriceps muscle. Six female and seven male subjects participated in these experiments. Static exercise was sustained the fraction of maximal voluntary contractions(50%MVC) with knee extension, and was continued during constant force. Dynamic exercise was cycled with the step load at 150 watts for male 100 watts for female. EMG of the right vastus lateralis(m.VL) and of the right intercostales(m.IC) were picked up with miniture surface electrodes(ø=4mm). IEMG of m.VL during static exercise was increased. However, IEMG of m.VL during dynamic exercise was observed to be little unchanged. On the other hand, IEMG of m.IC during both experiments were increased on the time courses significantly. Moreover, mean power frequency(MPF) on m.VL during static and dynamic exercises were sifted to lower and higher frequency band, respectively. MPF of m.IC were observed to be little unchanged. These results were suggested that a neural safe-guard mechanism of intercostal muscles would be still affecting existence in the central nervous system, and then activities of respiratory muscles were maintained approximatly, even though the limb muscle would be fatigued overall, during muscular voluntary exercise.

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TREATMENTS OF PHYSICAL EXERCISE AND OXYGEN INSPIRING ON WHOLE FATIGUE.

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Sixteen subjects volunteered for the experiment, and exercised vigorously on three running speeds two times per one trial with 15 min interval. After vigorous exercise, four treatments were applied to recover from fatigue or exercise stress. Four treatments consisted of (I)oxygen inspiring and stretching exercise on the triceps sureas, (II) oxygen inspiring, (III) stretching exercise, and (IV) rest only without any treatments. Inspiring oxygen-content was about 28% (PO_2) and 8% (PCO_2) and flow velocity was about 12m/sec. Stretching exercise was practiced on the condition of 80 angle degrees of the ankle during five minutes. Resting only were without any special preciptions used as control treatment. Generally some treatments are called to be the active rest, and only to be the passive rest for relieving fatigue. Treatments and running stress were considered fixed and subjects random. The analysis of variance (ANOVA) was applied for effects of treatment, running stress time and interaction of both elements. The F-ratio of treatments effects and running stress were evaluated at the 0.01 or 0.05 levels in three cases statistically. Interactive effects between treatments and running stress did not appear significant F-ratio every measurements (p 0.05). However, results of ANOVA among the four treatments and the running stress established a statistically significant difference of blood contents, metabolism and ventilation of oxygen, respectively.

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CHARACTERISTICS OF WALKING PATTERN OF JAPANESE ADULT MEN.

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To discuss the characteristics of the walking pattern of Japanese adult men, various stride features and shoulder rotation were measured during treadmill walking and compared with those of Caucasian. Several gait components related systematically and significantly with height. Step length showed the greatest value in the tall subjects and the least in the short subjects. Conversely, cadence and sagittal rotation of the shoulder showed the least value in the tall subjects and the greatest in the short subjects. However, when the gait components were normalized to body height, the differences were not significant. In comparison with Caucasian, it was found that Japanese males walked with the shorter step length and the higher cadence, even when the differences in body height were taken into account. Therefore, it seems likely that these differences of the walking patterns are attributed to not only the body height or the leg length but also the flexibility of the hip joint, the length of iliofemoral ligaments, and the degree of experience in walking at high speeds.

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The effects of training with endurance running and jumping for long period on bones and muscles.

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In order to investigate the effects of training on working muscles and bones, endurance running (30 $m.min^{-1}$, 60 min, 6 days a week)and jumping training (30 cm height, 50 times, 6 days a week) were carried out for 16 weeks in male Wistar rats. Body weight in running group (RG,n=11) and in jumping group (JG, n=5) were significatly higher than that in control group (CG,n=7). Wet weights of leg muscles(gastrocnemius, plantaris, EDL, tibialis anterior) in RG were significantly lower that those in CG, but those in JG were about the same as those in CG. When expressed as per body weight, those in JG and RG were significantly higher than those in CG. No significant difference was found in weight of femur among the three groups. Leg bone weight in JG (1174.9±12.5 mg, mean ±SE) was significantly higher than those in CG (1102.3±15.4 mg) and in RG(1120.9 ±16.2 mg). Using roentgenogram, it was suggested that the width and density of cortical bone tended to be greater in JG than those in CG and RG. It was concluded that the jumping training seemed to have greater effects on leg bone than the running training. There seemed specific effects of training with jumping on bones and working muscles.

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CHANGES IN SKIN TEMPERATURE ON ACTIVE MUSCLE DURING ARM EXERCISE. KASHIMURA, O. AND UEDA, G. Dept. Environmental Physiol., Shinshu Univ. Sch. of Med., Matsumoto, 390

To observe the skin temperatures of the forearm and upper arm during the dynamic and static arm exercises, a thermistor thermometer was used.

The experiments were carried out in an experimental room with air temperatures of 18 ℃ and 32 ℃.

Changes in upper arm skin temperature on the biceps were remarkably observed during the dynamic and static exercises. There were fewer changes in forearm skin temperatures on the extensor and flexor muscles.

Among three longitudinally - placed measurement - sites on the upper arm, both proximal and distal points were widly different from the mean skin temperature of three points during all exercises at 18 ℃ air temperature.

The result of measurement suggested a statistically significant correlation ($p<0.001$) between the center point of skin temperature and the mean skin temperature on biceps.

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DEVELOPMENT AND APLICATION OF A METHOD TO DETERMINE MYOGLOBIN(MB) CONTENTS IN A VERY SMALL QUANTITY OF MOUSE SKELETAL MUSCLES. NAKATANI, A., ENOKI, Y. AND KAWASE, M. Second Dept. Physiol., Nara Med. Univ., Kashihara, Nara 634

A new method was developed to determine Mb contents in as least as 5 mg of murine skeletal muscles. The method was a modification of Reynafarje's spectroscopic technique and was based on Soret absorptions at 416 and 422nm of the muscle extract. Mb contents in the skeletal and cardiac muscles increased with age and were widely different from muscle to muscle. The contents in most of 13 muscles examined at the 30th week of age were less than 0.5 mg/g wet muscle, but the cardiac,soleus and gracilis muscles showed an exceptionally high value of 1.5 mg/g. The relative content of one muscle to the other was the same independent of differences in age,strain and sex. Young mice (5 wk-old) were endurance-trained by a gradual load-increment program on treadmill for 10 weeks (5 days/wk),but the training had no effect on the Mb contents. No substantial alteration of the contents was also observed in the limbs immobilized by plaster-fixation for 4 weeks.

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CHANGES IN CREATINE KINASE ISOENZYMES OF SKELETAL MUSCLE,HEART, AND SERUM BEFORE AND AFTER EXERCISE. WATANABE,M. AND INOUE,N. Dept.Exercise Physiol Sch. Educa.,Tokyo Gakugei Univ.,Tokyo 184

The purpose of this study is to clarify whether acute exercise induces the changes of creatine kinase (CK) isoenzymes composition of muscle and serum. Female 34 Wistar strain rats were used in this study and run on motor-driven treadmill for 1 hour. The soleus (Sol), the extensor digitolum longus (EDL), and heart were excised, homogenized, After centrifugation, supernate and serum were used in the assay of CK isoenzymes composition (CK-MM, -MB, -BB). Before and after running CK isoenzymes of both Sol and EDL had no significant changes. At least running didn't induce CK-B subunit synthesis and hybridization of CK-MB. Serum CK-MB % did't increase after running. So the origin of serum CK-MB elevation may not be skeletal muscle and acute exercise induced heart CK isoenzyme composition. If serum CK-MB elevated after exercise in untrained subjects, the origin of CK-MB might be heart and not skeletal muscles.

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SEX DIFFERENCES IN BASAL METABOLIC RATE AND PHYSIOLOGICAL RESPONSES DURING PUBERTAL BOYS AND GIRLS. TSUJITA, J., HORI, S.,* TANAKA, N.,** AND MAYUZUMI, M.*** *Dept. of Physiol. Hyogo Coll. of Med. **Kyoto Sangyo Univ. ***Mukogawa Women's Univ.

Measurements of basal metabolic rate and physical characteristics, observation of the physiological responses during exercise were made on 30 pubertal boys (between the ages of 12 and 13 Group B) and 30 pubertal girls (between the ages of 11 and 12, Group G). Exercise was performed on a bicycle ergometer at a cycling rate of 50 rpm for 20 min. in a room at 20°C with 70% relative humidity. The subjects warmed up for 5 min. at zero load, and then the work load was increased by 0.5 every 5 min. up to 1.5 kp. There were great individual differences in basal metabolic rate per body weight or body surface area and physiological responses during exercise. The decrease of basal metabolic rate per body weight accompanied by aging was observed in Group G. Individual differences in physiological responses during exercise were somewhat greater in Group G than in Group B. Sex differences in physiological responses during exercise and skinfold thickness increased after menophania.

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CHANGES OF THE BEARD GROWTH RATE INDUCED BY EXERCISE AND ITS DEPENDENCE ON AGING. ONO, M., Dept. of Physiol., Jikei Univ. Sch. of Med., Tokyo 105

The relation between daily beard growth rate and the frequency of exercise during the period between 38 and 57 years old of the author's age was presented at the 56 Annual Meeting of this Society in 1979. The result suggested that high frequent jogging in the morning inhibited the daily beard growth. However, the recent result obtained between 58 and 65 years old showed the opposite effect of the frequent jogging on the beard growth rate. High frequent jogging (4-5 times per week) which caused exercise-induced arrhythmia increased the beard browth rate, and low frequent jogging (about once per 5 days) decreased it. The seasonal variation study of the beard growth showed that the beard growth rate increased as atmospheric temperature rised. This suggested that exercise might change skin temperature and influence the beard growth. The opposite effect of frequent jogging on the beard growth rate observed at different ages suggests that high frequent jogging influencing the beard growth rate might cause the exercise-induced arrhythmia.

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CHARACTERISTICS OF PIKA AS HIGH-ALTITUDE ADAPTED ANIMAL.
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Pika, the genus Ochtona, caputured at Quinhai areas in China, 2,300 m (HL), n=13, 3,300 m (HM), n=15 and 4,460 m (HH), n=14 above sea level, were studied in August 1986. The body weight ranged from 90 to 150 g. Among the items measured, the pulmonary pressures Ppa indicated especially lower values, 13.1 ± 2.8 mmHg at HL, 15.7 ± 2.2 mmHg at HM and 17.2 ± 2.3 mmHg at HH, compared with rats which indicated 24.1 ± 3.4 mmHg at HL. The raio of (RVW) to the left ventricular weight (LVW) for Pikas was 0.225 ± 0.037 at HL though that of rats was 0.38 ± 0.034 at HL. The ratios were greatest for mice and rats captured at various heights in Japan, moderate for Clethrionomys-mice, and lowest for pikas. As for the erythrocytes, the hematocrit (Ht) values at HL were 37.4 ± 3.9 % for Pikas and 53.4 ± 5.2 % for rats. These lower values of Ppa, the ratio RVW/LVW and Ht indicate more efficient adaptability of Pikas to high altitudes compared with other groups of rats.

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LEFT VENTRICULAR FUNCTION AT REST AND DURING SUBMAXIMAL WORK UNDER ACUTE HYPOBARIC HYPOXIA. KIKUCHI, K., ASANO, K. and KIKUCHI, Y.*, Lab. for Work Physiol., Inst. Health & Sports Sci., and *Dept. Bioeng., Inst. Basic Med. Sci., University of Tsukuba, Ibaraki 305

The M-mode echocardiography and systolic time intervals methods were applied to nine healthy male subjects for evaluation of left ventricular function under acute hypobaric hypoxia from 4,000 m to 6,500 m simulated altitude. The relationship between cardiac function and plasma catecholamine excretion was also examined. At rest, end-diastolic diameter showed a tendency to decrease and a significant decrease in end-systolic diameter at over 4,000 m was observed. The mVcf and ejection fraction(EF) were significantly increased with increase of altitude at over 4,000 m. A significant correlation was observed between mVcf and plasma catecholamine levels. These results suggested that the left ventricular function was enhanced by the acute exposure to hypobaric hypoxia and the enhanced cardiac function was well related to the excretion of catecholamine. The changes in EF and PEP/LVET ratio during work suggested that the cardiac function was enhanced from SL to 5,000 m. On the other hand, left ventricular function during work at 6,000 m tended to be deteriorated.

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Changes in the turnover rate of catecholamines in the rats brain tissues during chronic exposure to simulated high altitude. OSADA,H., ※ TAJIMA,F., ※NAKAMURA,A., Aeromedical Lab.,JASDF., Tachikawa, Tokyo190., KONDOU,Y., ※BAN,T. and YURUGI,R., Natl. Defense Med. College, Tokorozawa, Saitama359.

Rats were exposed to simulated high altitude of 18,000ft for 3 weeks (23 ℃± 1 ℃, fed ad libitum). And norepinephrine(NE) concentration and the turnover rate of norepinephrine in various rats brain (Frontal lobe, Cortex, Cerebellum, Striatum, Thalamus, Hypothalamus, M. oblongata + Pons and Mid brain) regions were studied. NE content in separated eight regions of brain tissues were determined using with electrochemical detection technique. The turnover rate of NE were assesed after blocking catecholamines synthesis with DL- α-methl-P-tyrosine methylester(α-MPT, Aldrich). The total NE content of rat brain showed a transient fall at 1 d of the hypoxic exposure, which recovered to the sea level control after 3 d of the exposure and maintained this level for the rest of the experimental period. The NE content in each brain region also decreased transiently, especially Hypothalamus, M.oblongata + Pons and Mid brain showed significant fall at 1 d of the exposure. The turnover rate of NE in each brain region had similar temporary decrease at early stages of hypoxia. These results indicated that hypoxia caused a distinct transient decrease at eary stage of hypoxia, which seemed to be associated with a significant alternation of NE metabolism.

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CORRELATION BETWEEN HYDROXYL RADICAL AND LIPID PEROXIDATION WITH POST-EXPOSURE TO HYPERBARIC OXYGEN

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Hydroxyl radical resulted in significant increase at 24hrs of post-exposure of rabbits to 100% oxygen at 4ATA for 60min, 176.5 ± 47.2%.
Superoxide dismutase(SOD) activity under hyperbaric condition at 4ATA for 60min revealed significant decrease to 29.8% at zerotime and increased to 45.9% versus control at 72hrs of post-exposure.

In vitro experiments were performed by monitoring cholesterol in lipoprotein subclasses on human venous whole blood and plasma alone exposed to 100% O_2 at 5ATA for 60min. The fraction of damaged LDL in plasma, obtained from the whold blood, was elevated markedly to 2.3 fold more than Air Control at 24hrs of post-exposure. Autoxidation of egg lecithin phosphatidylcholine dispersed in water produced hydroxyl radical at the same exposured condition and was found to reach maximum level at 24hrs of post-exposure.

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INVOLVEMENT OF PTH IN ALTERED Ca·P METABOLISM UNDER HIGH ALTITUDE EXPOSURE IN MAN.

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Previously we reported that a slight increase in serum PTH may involve in altered Ca metabolism under high altitude exposure in man. Present investigation was carried out to confirm the postulation. Twenty one adult subjects were exposed to simulated 6,000m altitude. Serum level of total Ca and Ca^{2+} was elevated significantly, while serum P was markedly decreased. Urinary excretion of both Ca and P decreased. Though the elevation of serum PTH by the exposure was not significant statistically, urinary cAMP adjusted by creatinine and glomerular filtration rate increased. These results suggest that increased secretion of PTH may partly be involved in altered Ca and P metabolism under altitude exposure.

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CHANGES OF BLOOD CELLULAR COMPONENTS IN HYPER-GRAVITY EXPOSURE.

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Male golden hamsters (8-10w) were loaded with hyper-gravity (-2Gx,-3Gx, -10Gx)with spatial disorientator at Gifu Univ. Blood samples were collected by heart puncture immediately after loading. Numbers, frequency distributions and physiological functions of blood cells were investigated. Hyper-gravity exposure caused various shifts of particle size distribution curves of erythrocytes like previously reported changes in platelets. The serum concentration of erythropoietin was slightly decreased. However, counts of erythrocytes,leucocytes and platelets did not show remarkable changes. Platelet function in vitro were impaired as the same experiment in vivo. This results suggests that hyper-gravity exposure experts a direct influence upon blood cells and confirms our previous reports that short term hyper-gravity exposure impaired platelet function and blood samples formed fragile clots.

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EFFECTS OF AGING ON MUSCLE SYMPATHETIC NERVE ACTIVITY UNDER WEIGHTLESSNESS SIMULATED BY WATER IMMERSION. MANO, T., SAITO, M., IWASE, S., KOGA, K., ABE, H. AND MATSUKAWA, T. Dept. Aerospace Psychol., Res. Inst. Environ. Med., Nagoya Univ., Nagoya 464

We have already reported that muscle sympathetic nerve activity (MSA) is strongly suppressed in young human subjects under weightlessness simulated by water immersion. In the present study, the effects of aging on the suppressive response of MSA induced by water immersion were analyzed in 7 human subjects ranging in age between 19 and 61 with prior informed consent. The changes of MSA, recorded by a tungsten microelectrode inserted into the tibial nerve at the popliteal fossa in standing subjects were observed during head-out water immersion. In all subjects, MSA was suppressed during stepwise water immersion, in proportion to the rise of the immersion level up to the neck. MSA was also markedly suppressed at the initial phase of the immersion up to the neck, then increased slightly in 30 minutes, but still remained suppressed moderately in the course of prolonged head-out immersion until 150 minutes. These suppressive responses of MSA were age-dependent, being remarkable in younger subjects and less prominent in elderly ones. In conclusion, the suppressive response of MSA under weightlessness seems to be reduced by aging.

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THE ROLE OF FASTIGIAL PRESSOR RESPONSE TO FAST REPEATED HEAD-UP AND HEAD-DOWN TILTING IN ANESTHETIZED RATS. TERADA, N., KOYAMA, S.*, HORIUCH, J., TAKEUCHI, T. 2nd.Dept.Physiol., Yamanashi Med. Col., Tamaho, Ymanashi 409-38 and *2nd Dept. Physiol., Shinshu Univ. Sch. of Med., Matsumoto, 390

The interaction between fastigial nucleus and baroreceptor reflexes in cardiovascular adjustments during repeated head-up and head-down tilting (±90°) was studied in anesthetized rats. In both intact and vagotomized animals, percent changes in the systemic blood pressure(SBP) during head-up tilting of 30 cycles per min (HUT) did not differ significantly from pre-tilting level. . However, SBP fell significantly after either sino-aortic denervation or pretreatment with phenoxybenzamine. Bilateral lesions in the fastigial nucleus (FN) produced a decrease in SBP during HUT in all groups. Following head-down tilting of 30cpm (HDT), percent changes in SBP increased, depending on buffering effects of baroreceptors. FN-lesion produced similar increases in SBP in all groups. These results indicate that the role of FN in the cardiovascular adjustment during HUT is more predominant than HDT, interacting with activation of peripheral baroreceptors.

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ANALYSIS OF THE POSTURE CONTROL SYSTEM FOR TRACKING MOVEMENT.
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The dynamics of posture control in humans during body tilting fore and aft were investigated. The subjects stood with Romberg's position on the force plate was instructed to track the target spot displayed on the CRT with the other spot revealed a position of the center of gravity. For periodical rectangular target movement the delay of tracking response shortened with increasing frequency (0.05-0.8 Hz). In some subjects, it was found even a phase lead in 0.6-0.8 Hz. Over 1.0 Hz the delay was again prolonged. Tracking response to lower frequency (0.05-0.2 Hz) and random target movement, showed a characteristic feature such as initial counterswing followed by overshoot and holding a plateau. For random frequency, the peak latency of counterswing and overshoot was almost constant. A peak to bottom (v.v.) time measured between a counterswing and a overshoot was longer for periodical frequency of 0.05-0.1 Hz than for random frequency. From these results, it is expected that for periodical target movement of low frequency as well as high frequency, the predictive factors concern with a control of periodical body movement.

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POSTURAL CONTROL OF FISH DURING PARABOLIC AIRCRAFT FLIGHT.

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Three kinds of goldfish, namely: normal, unilaterally labyrinthectomized and bilaterally labyrinthectomized, 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.

Normal goldfish showed a diving response during the hypogravity period of parabolic flight. Bilaterally labyrinthectomized goldfish displayed a dorsal light response (DLR) more prominent during the hyporgravity than during normal 1 G and hypergravity. The unilaterally labyrinthectomized goldfish also showed a DLR. During hypogravity, however, tilting behavior about the fish's longitudinal body axis toward the operated side was observed even for the light from the top. 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 ROTATING CHAIR STIMULATION ON H-REFLEX.

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The objectives of this study were to elucidate the effect of passive horizontal body rotation on the spinal reflex activity in man. METHODS. Eight healthy 20 to 26 aged males were used as experimental subjects. Each of them was seated on a rotating chair with eyes covered. The soleus H-reflexes from right leg were evoked by 1 msec electrical pulse applied cutaneously onto the popliteal nerve every 3 seconds, and recorded continuously before, during and after the 40 seconds rotation(15 rpm) of the chair. RESULTS. 1. Four of the subjects showed no unsound symptoms during rotation, expect for a brief dyscomfort or light dizziness. In these subjects, the H-reflex was increased in amplitude during, and sometimes after, the rotation. 2. Two subjects were very sensitive to rotation, and got immediately pallor and nausea. The H-reflex was suppressed by rotation. 3. The rest provided no change of H-reflex at all. Their symptoms appeared to be intermediate between both mentioned above. CONCLUSION. The results suggested that the vestibulo-spinal interaction elicited by passive body rotation is modified different susceptibility to motion sickness.

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EFFECTS OF LINEAR ACCELERATION ON THE DORSAL LIGHT RESPONSE OF THE GOLD FISH.

WATANABE, S. and TAKABAYASHI, A., Res. Inst. Environmental Med., Nagoya Univ., Nagoya 464.

We have already reported elsewhere, that the linear acceleration applied on the X or Y axis of the gold fish produces a pitching response or a rolling response respectively. In this experiment we aim to clarify how the dorsal light response (DLR) modifies the rolling response caused by linear acceleration. Three kinds of gold fish were prepared which were composed of a normal group (11 fish), an unilateral labyrinthectomized (U-LT) group (7 fish), a bilateral labyrinthectomized (B-LT) group (6 fish). A tightly closed fish tank filled with water and provided with an oxygen supply unit was divided into three small chambers. One fish from each of three groups was put separately into chamber. The behavior of the fish was recorded by a 8 mm video-camera facing the fish in the tank, and analysed from pictures on a display unit. The rolling response caused by the acceleration of Y axis (Y accel.) was found in the B-LT as well as in the normal and U-LT. The threshold of the rolling response of the B-LT was higher than in the normal and U-LT. The DLR of B-LT was also modified by Y accel., as found in the normal and U-LT. These results imply that not only the vestibular organ but also the other somatosensory organs such as the lateral line organ and the swimming bladder play an important role on the postural control. This study is performed in collaboration with R. von Baumgarten and J. Wetzig in Mainz University.

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CROSS SPECTRAL ANALYSIS OF LOW FREQUENCY BODY SWAY DURING UPRIGHT STANDING IN MAN. INAMURA, K.*, MANO, T.**, IWASE, S.** Fac. of Liberal Arts, Shizuoka Univ., Shizuoka 423, and Res. Inst. Environ. Med., Nagoya Univ., Nagoya 464

The purpose of the present study is to clarify the origin of low frequency body sway during upright standing in humans. Subjects were 2 healthy males of 18 and 23 yrs old. The center of foot pressure (CFP) was measured as an indicator of body sway. Heart rate (HR), intrathoracic blood volume (ITB) measured by impedance plethysmography, muscle sympathetic nerve activity (MSA) to the soleus (Sol) recorded by microneurography, surface electromyograms (EMG) of the Sol and the tibialis anterior (TA), leg volume (LV) measured by strain gauge plethysmography, and venous pressure at the dorsum pedis (VPF) were observed simultaneously. In the course of prolonged upright standing, HR, and LV tended to increase, while ITB tended to decrease. The power spectral analysis revealed low frequency components of about 1 min periodicity ranging from 0.01 to 0.02 Hz in all of the above-mentioned parameters, except in EMG of TA. Cross correlations between CFP and MSA, VPF or LV showed higher values than those between CFP and other parameters. From these results, it is concluded that the body fluid is shifted downward during upright standing in humans, and the low frequency components of CFP sway with the period of about 1 min may be related to the sympathetic nervous and hemodynamic regulatory mechanisms of the body fluid shifts against gravity.

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THE EFFECTS OF SIZE OF THE VISUAL FIELD ON BODY SWAY DURING OPTOKINETIC STIMULATION. ICHIKAWA, M., HASHIBA, M., TAKABAYASHI, A., SAKURAGI, S., MORI, S. and WATANABE, S. Toyota College of Technology, Toyota 471, Dept. Otorhinolaryngol. Nagoya City Univ. Sch. of Med., Nagoya 467 and Dept. Aerospace Physiol., Res. Inst. Environ. Med. Nagoya Univ., Nagoya 464.

As a fundamental investigation to make better our understanding about postural stabilization under a microgravity environment, we examined effects of visual field size on the body sway during vertical optokinetic stimulation. Healthy subjects in a Romberg standing posture on a force plate were tested for the anterior-posterior sway, with one eye covered and the other eye restricted in the visual field (20, 30 and 40 deg) by a centrally holed spectacle. The optokinetic stimulus-velocity was increased in each condition gradually up to 60 deg/sec in 30 sec and this speed was kept for the next 60 sec. The downward optokinetic stimulation was applied at 1 m apart from the subject's eyes. The subjects was instructed to gaze a fixation point throughout the stimulation. All subjects inclined anteriorly during the stimulation. The body inclination increased in proportion to the size of visual field; the smallest inclination at 20 deg of the visual angle. It was suggested that the visual factor for posture stabilization might be affected mainly by the peripheral vision.

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A DORSAL LIGHT TILT REACTION AND CEREBELLAR ACTIVITY OF CARP DURING PARABOLIC-FLIGHT MICROGRAVITY. MORI, S., WATANABE, S., TAKABAYASHI, A., TAKAGI, S., SAKAKIBARA, A. and USUI, S. Dept. Aerospace Physiol., Res. Inst. Environ. Med., Nagoya Univ., Nagoya 464, and Dept. Inform. & Computer Sci., Toyohashi Univ. Technol., Toyohashi 440

In order to confirm dominant light-dependency of fish under weightlessness, together with possible changes in brain activity, the dorsal light tilt reaction of an intact and labyrinthectomized carp and electrical activity of the cerebellum under parabolic-flight microgravity were examined. The present experiment belongs to prelimary experiments for the Spacelab-J FMPT project. A compact aircraft (Mitsubishi MU-300) carrying two jet engines produced a microgravity of less than 0.05 Gz for about 20 seconds in each parabolic flight. The behavior could be analyzed only for the intact carp and the brain activity only for the labyrinthectomized carp, individually during several parabolas. A completely light-dependent reaction of the intact carp with a rather high speed of the tilting was similar to but not identical with that of a labyrinthectomized carp on the ground. A power spectrum analysis of the cerebellar activity showed enhancement of power at the frequency ranges below 8 Hz and between 12-25 Hz.

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RELATION BETWEEN PHYSICAL FITNESS AND ORTHOSTATIC TOLERABILITY ON 6 HOURS WATEWR IMMERSION.
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Studies on orthostatic tolerance during hypodynamics exposure, seem to be important in space medicine, in connection with the selection and training of astronauts and payload specialists. Orthostatic tolerance to a passive 90° head up tilt was studied in 31 healthy male subjetcts on 6 hours head out water immersion exposure. Their ranges in age and $\dot{V}O_2max$ were 18-24 years and 42-70 ml/kg/min. When the subjects were exposed to a 90° head up tilt and supine position before and after head out water immersion exposure, positive correlation was found between blood pressure and heart rate. As a result of head out water immersion exposure, there were an increase in diastolic blood pressure and mean blood pressure, and a decrease in pulse pressure and heart rate although there was no major fluctuation in systoric blood pressure. From the viewpoint of $\dot{V}O_2max$, orthostatic pulse pressure showed the most remarkable decrease at about $\dot{V}O_2max$ 54 ml/kg/min indicating low orthostatic tolerability. Urine volume during head out water immersion exposure increased in all of the subjects, especially in the subjects whose $\dot{V}O_2max$ is at about 64ml/kg/min. In the subjects with low orthostataic tolerablitity, the increase in urine volume may be due to a decrease in circulating blood volume.

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DEEP BODY TEMPERATURES CHANGE BY COLD GAS INHALATION UNDER HYPERBARIC HELIUM ATMOSPHERES (31bar EQUIVALENT TO 300m OF SEA WATER DEPTH)
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Deep body temperatures: tympanic membrane(Tty), rectal(Tre), 2 esophageal (25cm and 40cm from the nostrils: respectively Tes25, Tes40) were measured during 20min of Cold Gas Inhalation (CGI. inspired gas temperature was between 5°C at 300m and 15°C at 0m) and 20min of recovery at sitting rest under hyperbaric helium-oxygen environment(from 32m to 300m of depth) on four normal subjects. At 300m depth, the time lags of deep body temperature decrease from the start of CGI were respectively 25sec for Tes25, 3min for Tes40, 4min for Tty and 6min for Tre. And their magnitudes of decrease at the end of CGI from its start, the subjects ventilated ambient gas 31.5°C at 300m and 25°C at 0m, were 4°C for Tes25, 1°C for Tes40, 0.6°C for Tty and 0.3°C for Tre. We conclude that the capacity of the nasopharynx and upper airways to completely condition inspired cold gas is not sufficient and the cold gas inhalation gives considerable influences to the deep body organs (brain, lung and heart) in hyperbaric helium-oxygen environment.

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CHANGES IN RENIN, ALDOSTERONE AND ADH SECRETIONS UNDER HELIUM HYPERBARIC ENVIRONMENT.
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Causes of diuresis under helium hyperbaric environment have not been fully understood. We studied changes in renin(PRA), aldosterone(Ald) and anti-diuretic hormone(ADH) secretions by measuring both their basal levels in the early morning and their changes in the tilting test from supine position to standing, making a comparison between 1 and 31 ATA. At 31 ATA, ADH secretion decreased while PRA and Ald increased in the early morning. In the tilting test, ADH showed a slight increase at 1 ATA but no consistent tendency at 31 ATA. PRA increased at 1 ATA but the increase was more marked at 31 ATA. Ald showed no significant change at 1 ATA and no consistent tendency at 31 ATA. These results suggest that the suppressed ADH secretion is intimately related to hyperbaric diuresis in spite of the concurrent increase in PRA.

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ECG CHANGES OF HAMSTERS UNDER HYPERGRAVITY CONDITION

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In hypergravity conditions (-Gz; from tail to head direction), ECGs of anaesthetized hamsters with sodium amobarbital were sampled for 16 seconds every two minutes and were averaged 100 ms before and 412 ms after R wave by using computer to calculate P-Q intervals (P-Q). Under 4G and 6G conditions, R-R intervals (R-R) decreased transiently during the rising phase of G and in the earlier phase of the steady G conditions. On the other hand, P-Q increased in spite of such shortening of R-R. However, the R-R intervals lengthened in the later phase of the steady G conditions. In these conditions, P-Q increased monotonously while R-R increased and then decreased to less than the initial levels. In several cases, P-Q continuously prolonged even after 6 minutes of G-exposure. The different behaviors between P-Q and R-R were more significant in 6G than 4G exposure. The P wave often formed two peaks during the hyper G exposure. During 8G and 10G exposure, similar phenomena as in 4G or 6G were observed, but with more severe arrhythmia; that is, QRS waves without P waves. In those instances, unlike the R-R and P-Q in 4G and 6G, P-Q showed significant shortening in spite of the prolongation of R-R.

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EFFECTS OF CEREBELLECTOMY ON CARDIO-VASCULAR SYSTEMS IN HYPER-GRAVITY CONDITION.

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We studied cardiac changes of decerebellated hamsters in hyper-gravity conditions. The cerebellum was aspirated off one or two days before trials. Hamsters were anaesthetized with sodium amobarbital (125mg/kg i.p.) and were centrifuged with -Gz acceleration (2,4 and 6G). Heart rate (HR), Stroke volume (SV) and Cardiac output (CO) were measured. 1) In the control group, HR increased during the increasing phase of G exposure, but HR decreased during steady phase. In the decerebellated group, HR slightly increased during whole phases of exposure. 2)In the control group, SV decreased during early phase of exposure but continued to increase more than the initial value in the late phase of exposure and post exposure period. In the decerebellated group, SV kept smaller values (85% in 4G and 6G) and did not return to the initial value even in the post exposure period. 3) In the control group, the percent values of CO were smaller than those of SV. That is, during the late phase of exposure, CO decreased from the initial value to 95-100% (4G), and 90-95% (6G) levels. In the post exposure period CO took 110% in 4G and 105% in 6G exposure. In the decerebellated group, the rates of change were similar for CO and SV. CO took 85% of the initial value during the steady phase of 4G and 6G exposure.

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THE RIGHT AND LEFT COMPARISON OF COLD VASOOSCILLATION AT RABBIT'S EARLOBES.

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The similarity of cold reaction patterns between the right (R) and the left (L) rabbit-earlobe vessels (artery:A, vein:V) was investigated. The stimuli ranged from 5 to -20 ℃ in 25 to 30 ℃ room temperature. For the total 54-hr survey of 7 rabbit's at four sites RA, RV, LA, LV, the vasomotor activities between R and L were more similar in central arteries than in posterior marginal veins, and in younger rabbits than in older rabbits. When vasoactive drugs were applied, the right activity dominant type remained in general, the same tendency after the drug administration, and vice versa.

For each vasoactive wave, sometimes the right dominant was followed by the left dominant, continuing to change the dominant side alternately. The one side waves were occasionally fused in one wave on the other side, forming a longer period such as two to three times. Phase shift between the both sides rarely occurrs in the order of 10 to 20 sec. In general the similarity of the wave period is greater than that of the amplitude. Even if the both sides show a similar activity level, one side can reveal the greater activity when the stronger cold stimuli are applied. The pattern similarity changes in the time course spontaneously or artificially.

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METABOLIC AND ENDOCRINE MECHANISMS IN COLD ACCLIMATION UNDER VARIOUS CONDITIONS OF COLD EXPOSURE. KUROSHIMA,A., YAHATA,T. AND MURAZUMI, K. Dept. of Physiol., Asahikawa Medical Coll., Nishikagura, Asahikawa.

Intermittent cold exposure (5 ℃, 6hr/day, 4 wk)(ICE) effected the same extent of cold adaptability as assessed by cold tolerance and nonshivering thermogenesis as continuous cold exposure (5 ℃, 4 wk)(CA) in rats. Food intake was less in ICE than in CA, while the increase in body weight was greater in the former than in the latter. Increase in adrenal weight was greater in CA than in ICE, but brown adipose tissue(BAT) weight increased similarly the both groups. The plasma glucocorticoid level did not differ among WC, CA and ICE under resting state (after about 18 hr at 25 ℃ for CA and ICE). Acute cold exposure (-5 ℃) markedly increased these levels similarly in all groups. The resting plasma glucagon levels were the same among the groups. Acute cold exposure elevated plasma glucagon, but the increase was smaller in CA than in WC and ICE. BAT glucagon level was higher in CA and ICE than in WC, and acute cold exposure elevated the tissue glucagon levels to the same extent in all groups. These results indicate that short daily cold exposure induces the same extent of cold acclimation as continous cold exposure, although the length of total cold exposure in ICE was one forth of CA. It was also suggested that glucocorticoid and glucagon are involved in both CA and ICE, but cold acclimation develops under less energy requiring state in the latter.

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BROWN ADIPOSE TISSUE (BAT) GLUCAGON IN COLD AND IMMOBILIZATION STRESS. YAHATA, T. AND KUROSHIMA, A. Dept. of Physiology, Asahikawa Medical College, Nishikagura, Asahikawa 078

In order to evaluate role of glucagon in BAT function under cold or stress, the changes in immunoreactive glucagon (IRG) of BAT and plasma as well as uptake and metabolism of radioactive glucagon (^{125}I-G) in this tissue were studied in rats. IRG per g fresh tissue was higher in the dorso-cervical (DC) BAT than in the interscapular (IS) BAT. In warm nonstressed controls (WC), acute cold exposure (-5 ℃, 15 min)(CE) or stress (immobilization, 30 min)(AS) elevated IRG of both sites of BAT as well as plasma. In both repetitively immobilized rats (3 hr/d, 4wks)(ST) and cold acclimated animals (CA), the resting levels of BAT IRG, but not plasma one, were higher than WC. CE caused elevation of plasma IRG, but not BAT IRG in ST as well as CA. AS did not affect IRG levels in both plasma and BAT in CA, while shorter immobilization stress (15 min) elevated IRG in both plasma and DC BAT, but decreased that in IS BAT in ST. Cold acclimation did not influence ^{125}I-G uptake by BAT, but rather resulted in less ^{125}I-G level in plasma and liver. The present results suggest that BAT is a target tissue for glucagon to cause nonshivering thermogenesis in response to cold or stress and that turnover of glucagon is enhanced by cold acclimation.

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FATTY ACID COMPOSITION OF BROWN ADIPOSE TISSUE FROM RATS REARED IN COLD FOR MANY GENERATIONS. OGAWA,K., OHNO,T.* AND KUROSHIMA, A.** Lab. of Physical Education, Hokkaido Tokai Univ.; Lab. of Nutrition Physiol., Hokkaido Univ. of Education*; Dept. of Physiol., Asahikawa Medical Coll.**, Asahikawa.

Nonshivering thermogenic capacity was previously found to be greater in rats reared in cold for many generations(CG) than in usual cold-acclimated rats(CA). In order to know metabolic feature of CG, fatty acid(FA) composition in lipid fractions of thermogenic tissue, brown adipose tissue(BAT), were examined in CG (reared in cold for 25 generations). Triglyceride: In CA saturated FA(SA) increased, and monounsaturated FA(MU) and unsaturation index(UI) decreased. In CG MU increased, and SA and polyunsaturated FA(PU) decreased. Whole phospholipid(PL): In CA SA, PU and UI increased, and MU decreased. In CG SA increased and MU decreased. Arachidonic acid(AA) increased in both CA and CG. Cardiolipin(CL): FA composition was also examined in specific PL, CL localized in mitochondrial membrane. CL possessed more linoleic acid and PU, and higher UI than whole PL. In this specific PL fraction AA increased in both CA and CG, and UI increased in CG.

These results suggest that FA desaturation of CL in BAT is closely associated with an enhanced nonshivering thermogenesis induced by cold.

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EFFECTS OF REPETITIVE IMMOBILIZATION STRESS AND COLD ACCLIMATION ON THE CATECHOLAMINE TURNOVER OF BROWN ADIPOSE TISSUE(BAT) AND ADRENOCORTICAL HORMONE SECRETION. MURAZUMI, K., YAHATA, T. AND KUROSHIMA,A. Dept. of Physiol., Asahikawa Medical College, Asahikawa 078

Repetitive immobilization stress(ST) causes cross adaptive effect to cold through an enhanced nonshivering thermogenesis(NST) (Kuroshima et al., 1984). The present study was undertaken to evaluate roles of sympathetic activity of thermogenic tissue, BAT, by measuring its noradrenaline(NA) turnover and adrenocortical secretion by measuring plasma corticosterone(CS) and deoxycorticosterone(DOCS) in the stress- and cold-induced NST of rats. Both ST and cold acclimation elevated BAT NA turnover as assesed by blocking NA synthesis with α-methyl-p-tyrosine. In repetitively immobilized rats(STR) and non-stressed warm controls(WC) acute immobilization stress as well as acute cold exposure increased BAT NA turnover, while in cold-acclimated rats(CA) only acute cold exposure resulted in an increased NA turnover. In WC acute stress and acute cold exposure caused marked increases of CS and DOCS. In STR these responses were potentiated, while in CA they were not influenced. Thus it was suggested that increased sympathetic activity of BAT is involved in cross adaptation between stress and cold, and repetitive immobolizatin stress could enhance NST via an enhanced responsiveness of adrenocortical secretion to stress and cold.

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COLD ADAPTATION PARAMETERS, OXYGEN CONSUMPTION AND PELT WEIGHT, IN RED-BACKED VOLES. YANAGIDAIRA,Y. AND UEDA,G. Dept. of Environmental Physiol., Shinshu Univ. Sch. of Med., Matsumoto, 390

Fifty five red-backed voles (Clethrionomys andersoni) were captured by live traps at Mt. Yatsugatake (alt 2,400 m) throughout September to December. The voles in Nagano are only distributed at subalpine and alpine forest zones. Cold adaptation parameters in the voles were compared with those of wood mice (Apodemus argenteus) which are broadly distributed in Japan. The oxygen consumption ($\dot{V}O_2$) and rectal temperature (TR) were measured at 0, 10, 20, 30℃ in a climatic chamber. The weights of brown fat (BAT), body fat (BF) and pelt were also measured.

Results. The $\dot{V}O_2$ in response to 0℃ for voles indicated maximal values (6.37 ± 0.36 ml/g/hr) in December, whereas minimal values (4.43 ± 0.40 ml/g/hr) were obtained in September. The relationship between the $\dot{V}O_2$ and the environmental temperature (ET), where the voles live, showed a significant inverse correlation ($r=-0.64$, $p<0.05$). The relative pelt to body weight captured in November was greatest ($8.48 \pm 0.08\%$) and lowest ($6.85 \pm 0.25\%$) in September.

The coefficient of correlation between pelt weight and ET was $r=-0.73$ ($p<0.05$). There were significant inverse correlations between ET and the weights of BAT or BF.

From these, the voles were proved to be better adapted to cold than wood mice.

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DISRUPTION OF MEAL PATTERN AND PROGRESSION OF OBESITY IN ZUCKER RAT. OOKUMA,K.FUKAGAWA,K.SAKATA,T.YOSHIMATSU,H.FUJIMOTO,K.AND *SHIRAISHI,T. Faculty of Med.Kyusyu Univ.,Fukuoka *Tokai Univ.,Kanagawa

Zucker obese rats have been reported to eat much amount of food during light period as well as during the dark.To analyze their light-dark cyclicity in feeding and its effect on development of obesity,from the point of meal disruption,changes in ingestive and ambulatory patterns were investigated at age of 12,23 and 30 weeks.The nocturnal pattern of feeding,drinking and ambulatory activity disappeared with the progress of obesity in Zucker obese rats,was unaffected in lean littermates.Light-dark cycle of meal size in the obese had already disappeared in 12 weeks of age and cyclicity of meal frequency was lost in 30 weeks of age.These findings indicated that progress and maintenance of obesity in Zucker rats resulted from loss of meal cyclicity which appeared differently in developmental stages of obesity in addition to their potent hyperphagia.

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EFFCTS OF LOW-ENERGY DIETS ON PROTEIN METABOLISM OF OBESE PATIENTS STUDIED WITH [^{15}N] GLYCINE. OI, Y., OKUDA, T., KOISHI, H., AND NAMBU*, S. Faculty of the Science of Living, Osaka City Univ.,*National Cardiovascular Center.

The effect of low-energy diets on protein metabolism in terms of the metabolic pool, active protein pool, and active and inactive protein synthesis rates were studied by use of [^{15}N] Glycine in five obese patients (percentage of ideal body weight: 120-190%). The results suggested that protein metabolism in obese patients was not maintained with less than 70g of protein daily when energy intake was restricted to 1100kcal/day.

Therefore obese patients need enough protein intake for protein metabolism when energy intake is restricted for reduction of body weight.

AUTHOR'S INDEX

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〔お知らせ〕

第9回日本学術会議内分泌学研究連絡委員会シンポジウム

—神経内分泌機能の生理学的解明への展望—

主　催：日本学術会議内分泌学研究連絡委員会
後　援：日本内分泌学会　同神経内分泌分科会
日　時：昭和62年10月30日(金)午前10：00～17：30
会　場：日本学術会議講堂（1階）
東京都港区六本木7-22-34　電話 03-463-6281
世話人：鈴木光雄（群馬大学内分泌研究所）
前橋市昭和町3-39-15　電話 0272-31-7221-Ext. 2715

プログラム

挨　拶　日本学術会議会員内分泌研究連絡委員長
東京女子医大　鎮目和夫

座　長　北大，医，第一生理　広重　力

1. 隆起漏斗系ドパミン神経細胞のドパミン生合成の調節　横浜市大，医，第二生理　有田　順　貴邑富久子

2. TRH ニューロンの局在と機能
群馬大，内分泌研，生理　石川巧一　鈴木光雄

座　長　自治医大，第二生理　八木欽治

3. 視床下部のバゾプレッシンニューロンに関する神経回路網の電気生理学的解析
高知医大，第二生理　桃　秀人　田中淳一　斎藤英郎

4. 乳汁射出反射の神経機能の調節因子
福井医大，生理　根来英雄

5. 心房性 Na 利尿ホルモン(ANP)とアンギオテンシンIIの視床下部ニューロンに対する *in vitro* の作用の研究　産業医大，第一生理　山下　博

座　長　順天堂大，医，第二解剖　新井康允

6. Synthesis of specific proteins and RNA in the hypothalamus stimulated by estrogen in relation to reproductive behavior
The Rockefeller University　Donald W. Pfaff

7. 視床下部の性分化と雌雄の性行動
新潟大，医，第二生理　佐久間康夫

8. エストロゲンの摂食抑制機能
九州大，医，第一生理　大村　裕　鍋倉淳一

9. 総合討論

閉会の挨拶
内分泌学研究連絡委員会委員
群馬大学内分泌研究所　鈴木光雄

分子細胞学からみた情報伝達シンポジウム

主　催：日本学術会議生理科学研究連絡委員会
後　援：日本生理学会
日　時：昭和62年10月31日(土) 13：30～17：20
場　所：大阪大学医学部附属病院A講堂

プログラム

1. 開会の辞　　日本学術会議会員・生理科学研連委員長　本間三郎
2. シンポジウム　　司　会：久野　宗　中馬一郎
   1) シナプス伝達の可塑性とグルタミン酸受容体
   大阪大，医，高次研　津本忠治
   2) アフリカツメガエル卵母細胞に「移植」された新しいグルタミン酸受容体
   生理研，生体膜　杉山博之
   3) 卵母細胞に発現したセロトニン受容体とその活性化機構
   京都大，医，生理　高橋智幸
   4) ギャップ結合細胞間連絡の制御機構
   広島大，歯，生理　菅野義信
   5) 膜蛋白質の発現機構
   浜松医大，生化・生理研，能動輸送　藤田道也
   総合討論
3. 閉会の辞　　日本学術会議・生理科学研連委員　中馬一郎

なお，当日午前9時30分より阪大附属病院A講堂・B講堂にて第74回近畿生理学談話会が，午後5時30分より恵済団食堂にて合同懇親会が開催されます．合せてご出席下さい．

日本生理学会評議委員　東京医科大学教授　大畑　進君は，昭和62年7月7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．

日本生理学会評議委員　元千葉大学教授　斎藤十六君は，昭和62年7月25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〕

日生誌49巻8，9合併号をお届けします．本号は第69回生理学会大会（千葉大学）の抄録が主な内容となっています．本大会を実り多いものにして頂いた当番幹事の本間教授，本田教授はじめ千葉大学医学部関係各位に改めてお礼を申し上げます．

残暑もまだ厳しいようですが，会員の皆様には新学期も始まり，心機一転，教育に研究に精を出しておられることと思います．筆者は第2回世界神経科学会(IBRO)(ハンガリー，ブダペスト）と第19回ヨーロッパ脳と行動学会（ユーゴスラビア，ノビサド）に出席し，フンボルト大学生理学研究所（東ドイツ，東ベルリン）でセミナーをさせて頂き，約3週間の旅を終えて帰国したばかりです．フンボルト大学生理学研究所はかつてのベルリン大学生理学教室で，お招き頂いたW. Rüdiger 教授の部屋の前の廊下の壁には生理学研究史上有名な J. Müller (1801～1858), E. DuBois-Reymond (1818～1896), H. Helmholtz (1821～1894), G. Fritsch (1838～1927) などをはじめとする同大学の歴代教授および関係の深い教授の写真が掛けられていました．帰国して，すぐ実際に見たベルリン大学生理学教室で，偉大な生理学者達によって行なわれた研究を確かめるために，勝木保次先生が東京医科歯科大学・学長当時にお書きになった「神経生理学における日本人の系譜」(看護技術7月臨時増刊号，第22巻，1976) と豊倉康夫教授監訳「神経学の歴史」(医学書院，1977) を読ませて頂きました．勝木先生の「神経生理学における日本人の系譜」には日本における神経生理学の発展について，イタリアの Galvani (1737～1798), Volta (1745～1827) や Matteucci (1811～1868) の時代からドイツの Müller とその門下生 DuBois-Reymond, Helmholtz などの時代への移行，蘭学とドイツ医学の影響，1869年に大沢謙二博士が東京大学で初めて生理学教授になられたことから，最近までの経緯が見事にまとめられています．しかし，筆者はその1頁から2頁の最初にかけての「神経や筋肉の興奮と電気との関係が知られたのは Luigi Galvani (1786) に始まる．……中略……，カエルの肢筋が風にゆれてピクピクする現象が，今日の電力による文明の源になると誰が思い及んだ事であろうか．誠に興味深いエピソードの一つである．」(原文のまま)という文章に何故か新鮮味を感じました．それもその筈です．昨年11月，J. C. Eccles 卿が富山へ来られた折に，筆者の部屋で多分どの出版社かへの原稿だと思いますが，その何頁目かを開いて，serendipity？serendipity？とおっしゃり，Galvani と Volta の例をあげて，まさに勝木先生と同様のことを話して下さったことが記憶に新しいからです．

本日生誌49巻8，9合併号の多数の抄録を拝見して，今さらながら会員の皆様の研究へのひたむきな態度に敬服させられています．そのような会員の皆様が用意周到な計画に基づく実験により首尾よく当初の目的を達成されるだけでなく，近いあるいは遠い将来に serendipity によるすばらしい発見に恵まれることを願って止みません．　　(小野武年)

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ミニ浸透圧ポンプ



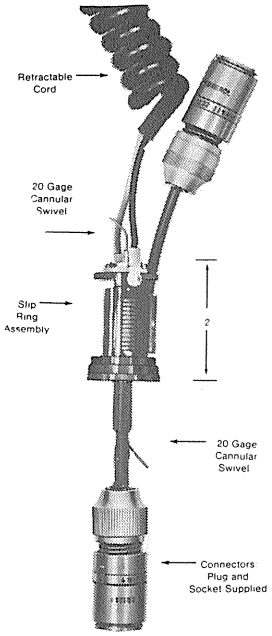
alzet®ミニ浸透圧ポンプは、マウス、ラット、イヌ、サル等の実験動物の皮下、あるいは腹腔内に埋め込むことができ、厳密に制御された流量で薬物を体内に連続注入できる小型自動ポンプです。埋め込み後は体液の浸透圧により、一定流量で連続的に動物体内の全身系又は、脳内、脊髄、静脈等の局部へ目的の薬物をデリバリーできる画期的なポンプです。

モデル		2001	2002	2ML1	2ML2	2ML4
輸液流速(μℓ/hr at 37°C)		1	0.5	10	5	2.5
リザーバー容量 (μℓ)		200	200	2000	2000	2000
サイズ	長さ (cm)	3.0	3.0	5.1	5.1	5.1
	直径 (cm)	0.7	0.7	1.4	1.4	1.4
総容量 (mℓ)		1.0	1.0	6.5	6.5	6.5
重さ (g)		1.1	1.1	5.1	5.1	5.1

日本総代理店 Muromachi
室町機械株式会社 本社 〒103 東京都中央区日本橋室町4丁目3番地 ☎03-241-2444
大阪営業所 〒541 大阪市東区道修町3丁目17 高原ビル ☎06-229-8260

Airflyte Electronics Co.

ELECTRO-CANNULAR SLIP RING



エアーフライト社のカニューラ・スリップ・リングは、動物の脳波を連続的に記録したり、体液を抽出することができ、動物がケージの中で動き回っても、動物に接続されているリード線やプローブはねじれたり、もつれたりすることはありません。
このスリップ・リングは、脳波研究、慢性的カニュレーション、EEG記録、リーション作成、および、これらの関連研究に最適のものです。

●電気的特性 電　流：1μA～1A/ring
電　圧：1μV～115V/ring
絶縁抵抗：500MΩ以上(500V DCの時)

●機械的特性 トルク：
12circuit assembly is less than 1/2in-oz.
including 20 gage swivel
寿　命：10,000,000回転以上
重　量：57グラム以下（リトラクタブルコードを付けない時）

FOR SMALL ANIMAL ELECTROPHYSIOLOGY

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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7T18です。定評ある処理スピードはさらに向上、実装メモリも1M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。また、ルーチン用として各種のアプリケーションプログラムも用意されていますので、臨床から基礎研究まで幅広い対応が可能です。

多チャネル高速データ処理装置

シグナルプロセッサ 7T18

明日の健康と福祉を守る

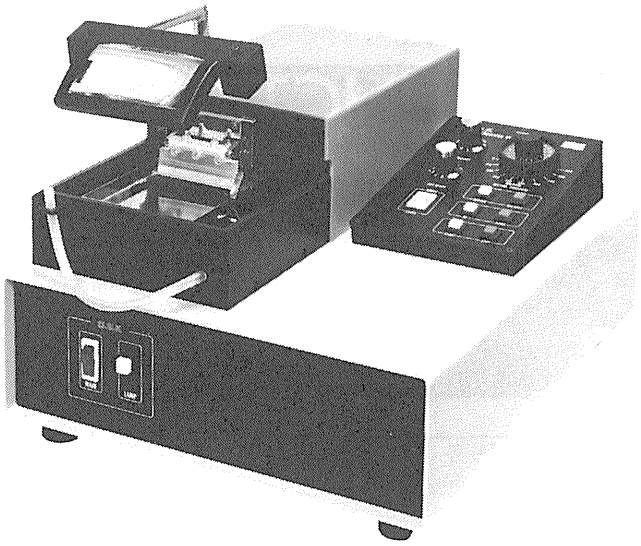
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D.S.K

新鮮脳のスライス作製に！

Automatic



未凍結切片作製装置

マイクロスライサー

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

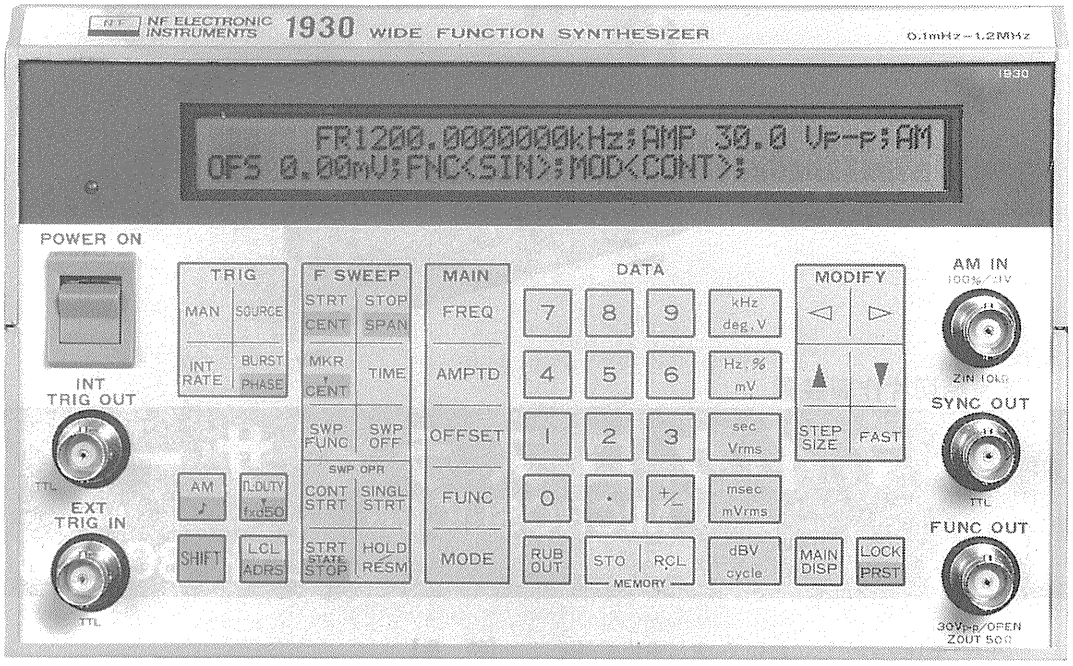
NF ユニーク&オリジナル
NF ELECTRONIC INSTRUMENTS

時代を抜いた。

信号源の新しい波。

1930

WIDE FUNCTION SYNTHESIZER



■スーパー・コストパフォーマンス。

ファンクションジェネレータ国産第一号からの専門家「エヌエフ」が、最新のノウハウを凝縮・結合させた多機能ファンクションシンセサイザです。ファンクションジェネレータ(FG)の機能とシンセサイザの精度・安定度を同時に実現。しかも価格は従来のFG並み。コンパクトボディから、一まわりも二まわりも大きな信頼性を発振します。

■フルレンジ・フルタイム シンセサイズ。

0.1mHzから1.2MHzの全域にわたって、どんな波形、どんな発振モードでもシンセサイズ。しかも、その周波数確度は5ppm(0.0005%)と驚異的。もちろん、5つの基本波形、多機能スイープ、バースト、ゲート、デューティ可変、AMなど従来のFG高級機種の機能を完備。また、すべてのパラメタはディジタル設定ですから、周波数カウンタや電圧計など計測のための計測は不要です。

●[出力波形・発振周波数] ∿、⊓(デューティ50%):0.1mHz~1.2MHz/∿、⩘、⩗、⊓(デューティ可変):0.1mHz~100kHz/周波数設定:最大11桁、分解能0.1mHz(一定)周期設定可能/周波数確度:$\pm 5\times10^{-6}$/周波数安定度:$\pm 2\times10^{-6}$/年 ●[スイープ] ●[ゲート][トリガ][バースト] ●[AM] ●[GP-IBインタフェース]オプション(1931)

■1933フェイズシフタも用意。

1933フェイズシフタを使用すれば最大6相までの多相信号発生器が実現できます。

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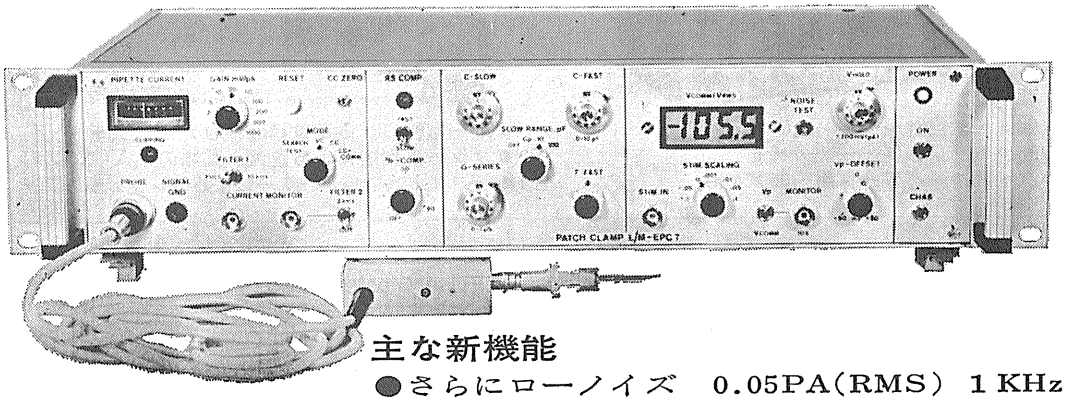
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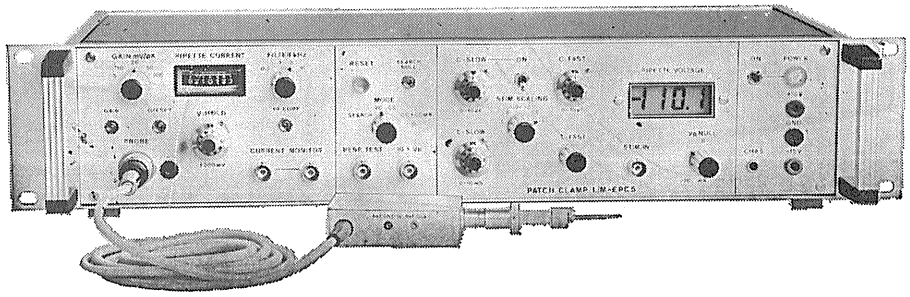
パッチクランプシステム　EPC-7



主な新機能

- ●さらにローノイズ　0.05PA(RMS)　1KHz
  0.30PA(RMS)　10KHz
- ●２レンジ切換　50GΩ　200PA
  500MΩ　20nA
- ●Rs COMPENSATION 1～100MΩ
- ●独自のTRANSIENT CANCEL機能

姉妹機　EPC-5型



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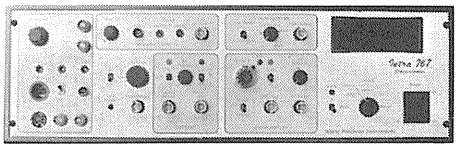
■微小電極用増幅器

Electro 705



- 低ノイズ設計……RS=20 500μV P-P以下
- 超小型プローブ……15g
- バッテリーパワー採用…9V×4ヶ

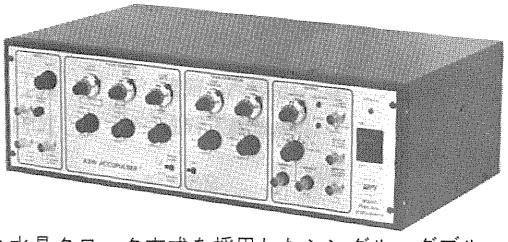
Intra 767



- 単一電極による電位誘導及び定電流通電
- ブレーク機能による色素、薬物の注入(±200V)
- デジタルパネルメーターによるカレントモニター

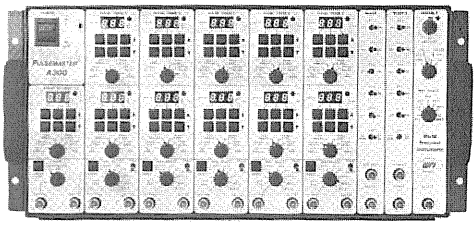
■刺激装置

Accupulser A310



- 水晶クロック方式を採用したシングル、ダブル及びトレインパルスを取り出せる1チャンネル型の刺激装置

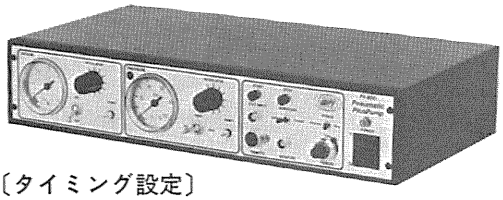
Pulse Master A300



- すべての時間設定をLEDで表示するマルチチャンネル刺激装置
  - インターバルジェネレーター……1，ミキサーチャンネル……2
  - パルストレインチャンネル……5，バリアブルアウトステージ……1

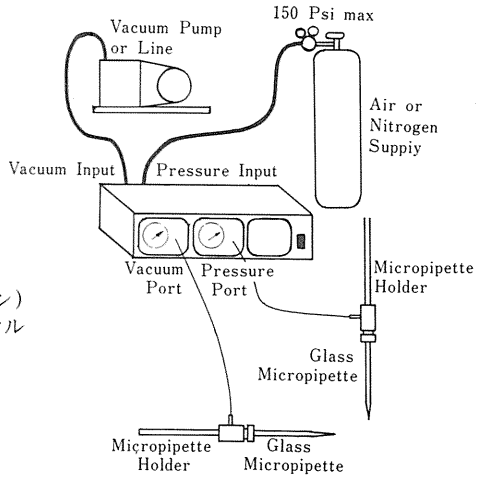
■細胞内／細胞外用マイクロインジェクション 気圧式ピコポンプ

Pneumatic PicoPump PV-820/PV-800



〔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%
外部入力	+5 VTTL-compatible (BNC)
モニター出力	+5 VTTL-compatible(BNC)

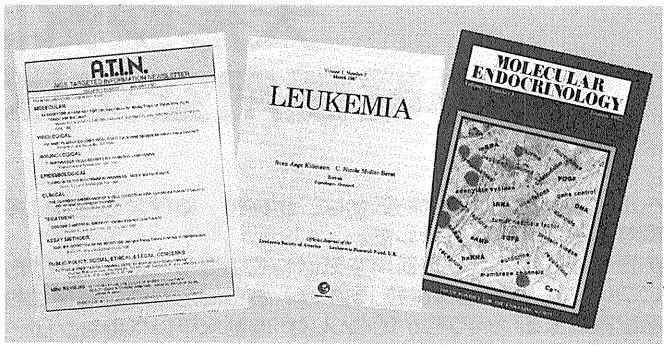


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大阪　大阪市淀川区中島5-7-17（ビップ第2新大阪ビル10F）　☎ 06(308)5732

Williams & Wilkins

エイズ、白血病及び分子メカニズムに関する学術誌群



'87 1月創刊

A.T.I.N. AIDS Targeted Information Newsletter

Managing Editor:Russell E. MacDonald, Ph. D.

AIDSに関する膨大かつ重要な学術文献及び関連ニュースを、世界の代表的な学術雑誌100以上より選択し、論文発表後1ヵ月以内に速報します。
NLMの〝AIDS Update〟は、掲載されるまで5ヵ月を要する点から比較しますと信じられないほどのペースで関連情報を網羅し、速報致します。

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'87 1月創刊

LEUKEMIA

Editors-in-Chief:C. Nicole Muller-Berat, M.D.
Sven-Aage Killmann, M.D.

本誌は、アメリカ白血病協会及びイギリス白血病研究基金の正式機関誌です。白血病及び関連疾病に関する最新で総合的な学術雑誌であり、白血病をより理解する上に必要な抑制、造血について取扱われています。

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'87 1月創刊

MOLECULAR ENDOCRINOLOGY

Editor-in-Chief:E. Bradbridge Thompson, M.D.

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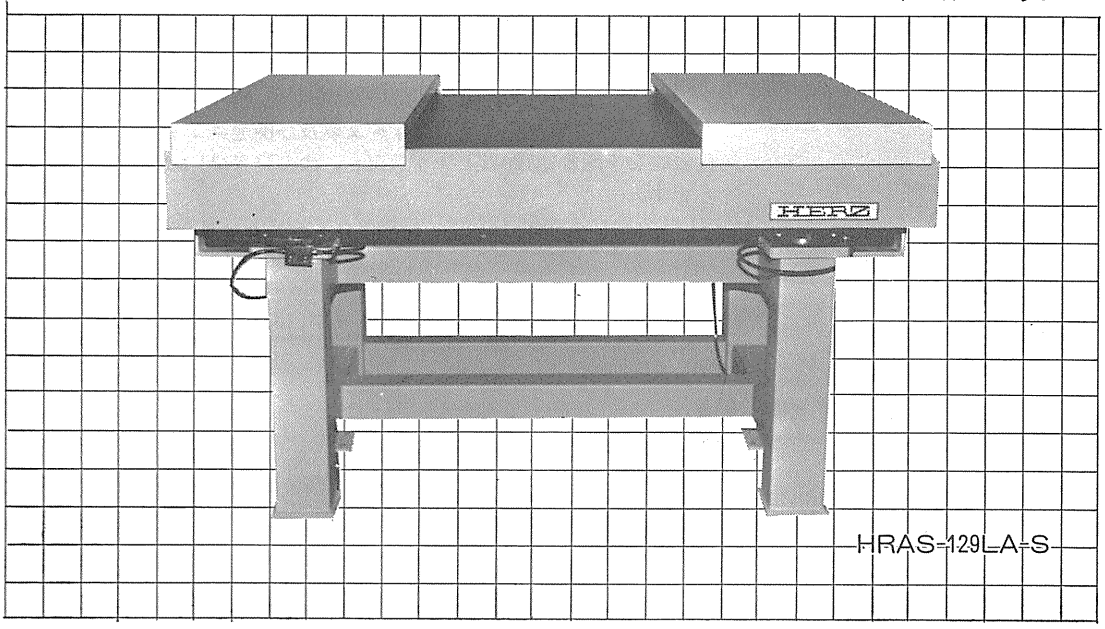
-USACO®-

HERZ

大形空気ばね式防振台
（微小電極用空気ばね式防振台）

ヘルツ大形空気ばね式防振台は、生理学・薬理学の分野に多く使用されている「微小電極装置」を搭載する為に開発されました。

防振性能はレーザー機器用空気ばね式防振台と全く同一であり性能において変わらず、また操作性についても「搭載盤保護枠」を設け、さらに防振性能を損なわぬよう「肘当台」を具備しております。機器配置による「水平アンバランス」は「自動水平レベルセンサー」により自動的に水平を保ちます。



HRAS-129LA-S

仕様

寸法mm

項目 ＼ 形式	HRAS-107LA-S	HRAS-129LA-S
固有振動数	約1.7Hz	
防振方式	HERZ空気ばね	
制振方式	オルフィスによるエアーダンピング	
搭載盤寸法	1000×700	1200×900
外形寸法	1060×800×750	1260×1000×750
搭載可能重量	200kg	
全体重量	130kg	155kg
付属品	肘当台および保護枠（本体に取付）	
その他	空気源は御客様にてご用意ください。	

ヘルツ工業株式会社

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さらに機能充実

メモリオシロスコープ VC-11

■大型7インチCRT

大きくて明るく鮮明な単ガンＣＲＴの採用で見やすさ抜群。

■A/D変換10ビット

分解能の向上により忠実な波形が再現できます。

■専用オプション群でグレードアップ可能

■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。

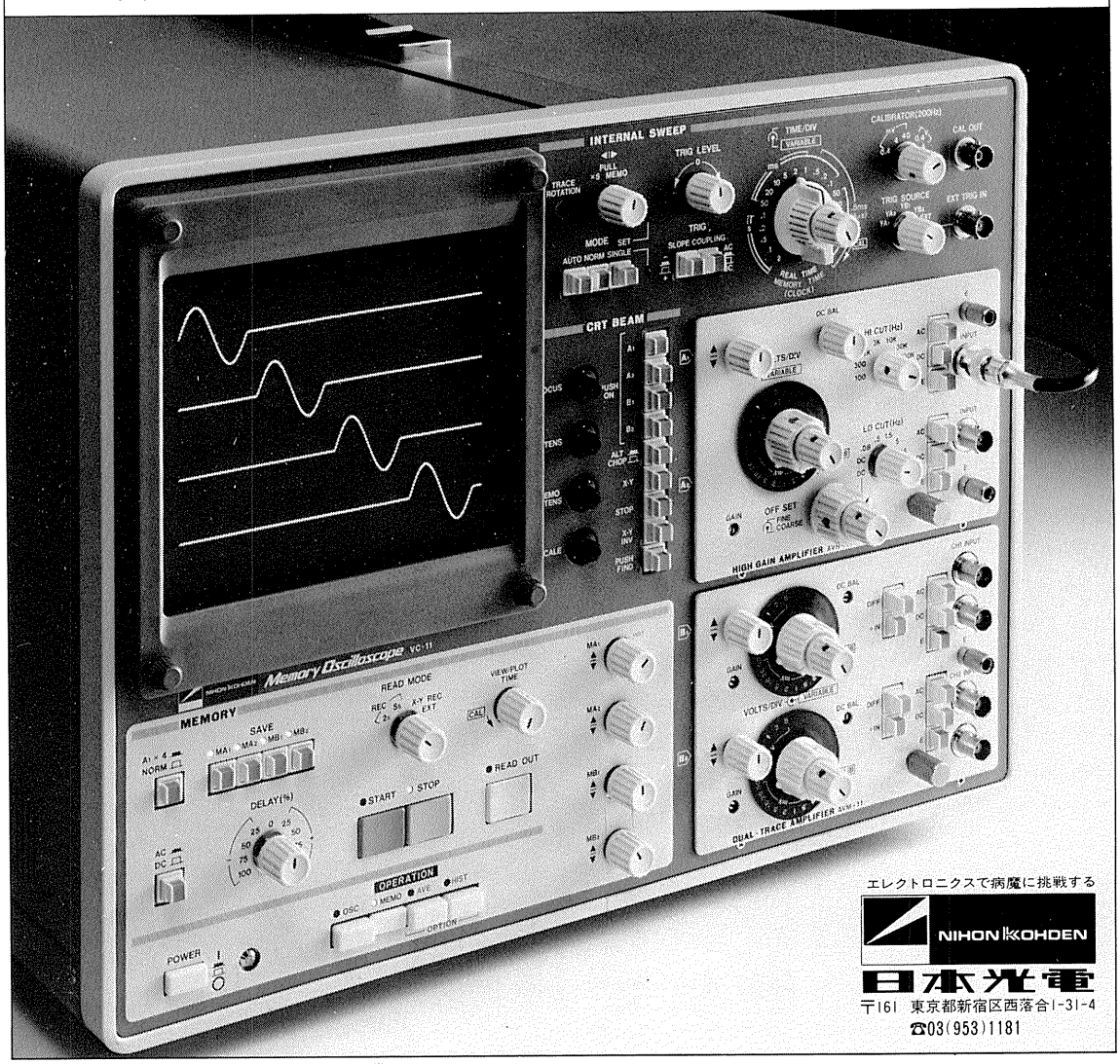
■メモリ読み出し時のX軸拡大可能(×5)

波形の細部を拡大して観測することができます。

■パソコン用インターフェイス内蔵

パラレルインターフェイスを内蔵。
オプションでRS－232Cも用意。

- 反応加算、ヒストグラム解析装置：アベレージ(4ch)、ヒストグラム(1ch)
- ディスクメモリ装置：記憶容量(100 画面　3.5インチフロッピ)
- データ収録用インターフェイス



エレクトロニクスで病魔に挑戦する

NIHON KOHDEN

日本光電

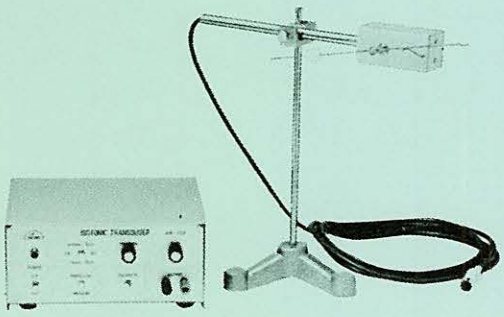
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KN-259 生体用変位計 PAT,P



トランスジューサーと増幅器からなる，微少変位測定装置です。これまでキモグラフィオン・ヘーベルを用いて行なっていた測定を電気的測定におきかえることにより，取扱いの簡便さ，再現性および信頼性を高めました。

測定範囲	0～50mm（±25mm） （中心軸より100mmの時）
分解能	無限大
最大摩擦トルク	50mg・cm以下
直線性	±3％
出力インピーダンス	5KΩ以下
校正器	10mm 極性切換スイッチ付

理化学器械・基礎医学器械・実験動物飼育機械器具・薬学研究器械・医科器械一般

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