HELLO PSJ

A message to the Journal of Japan Physiology

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Please allow me take this good opportunity to say “hello” to all my friends both old and new.

I started my Brain Sciences career in 1993 at Dr. Okihide Hikosaka’s laboratory, as a graduate student. At that time, most of the members in the laboratory worked on the neuronal mechanism of the procedural learning. I made the muscimol injections into the cerebellar nuclei while monkeys were performing both new sequences and over learned sequences. We found that the animals had a difficulty doing the over learned sequences after the inactivation of the dorsal aspect of dentate nucleus. In contrast, the animals were able to learn the new sequences as quick as the pre-injection animals, in spite of the muscimol injection made into the same portion of the dentate nucleus. Other researchers carried out a series of experiments in the varied areas, including pre-SMA, SMA, and basal ganglia. The results showed that these areas contributed to the sequential hand movements in the separate ways. For example, pre-SMA, SMA, and anterior striatum to the early stage of learning, and poster striatum to the later stage of practice. Overall, during the long-term course of visuomotor sequence learning, the cerebral cortex, and basal ganglia, possibly including cerebellar cortex, initially may work in parallel, but eventually the majority of the skill for sequential movement shifts toward the cerebellar nucleus, perhaps in addition to the posterior striatum.

I left for Dr. James Ashe’s laboratory in 1999. The laboratory belongs to Dr. Apostolos Georgopoulos’ group in Minneapolis. You might immediately imagine how cold it is there. You are absolutely right, in the winter it went to 20 degrees below zero. However, there was not a moment when I felt the freezing factor because the researching front is really hot. That is a pretty big and very active research team in the Neurosciences area with a total of 35 members. The name of this organization was “Brain Sciences Center.” It was generally a department containing members from the University of Minnesota. But it was firmly supported by both the University of Minnesota and the VA Medical Center. The compound was inside of the VA medical center which is a great hospital belonging to the Federal Government. The multiple methodologies offered this research team a great opportunity to examine the brain functions from all sides, including the single neuron recording in monkey, function MRI and MEG in human. In addition to those things, they were preparing the

MEG system in the monkey. Researchers in the Brain Sciences Center came from all over the world, including Europe and Asia, in addition to the United States. As some people already know, Apostolose was from the Greece and James was from Ireland. Most of the members in this group were concentrating on the motor system. I was not an exception.

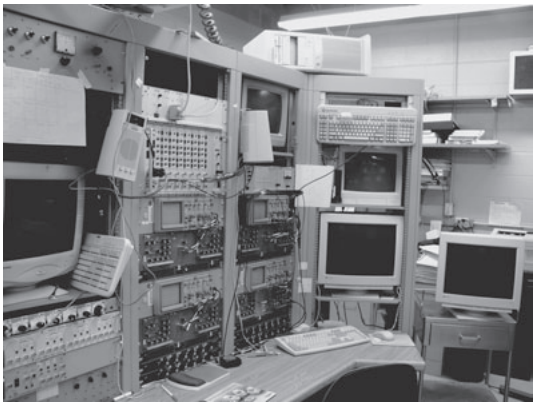
Based on our previous studies, I considered a question another step up. Most of our complex motor behaviors are composed of a small number of simple movements. In other words, we execute the limited kinds of multiple movements in variously specific sequences in order to achieve an unlimited number of volitional goals. Where and how do we generate the sequences in our brain? In the previous studies, we could not get the complete answer to this question, because the hand movements during the task were too fast. Also, the patterns of motions were too complicated to separate the sequence aspect from the movements. Fortunately, the 3 years aboard gave me a better approach.

The main achievement was that, through both a single neuron recording in the monkeys who were well trained by the sequential arm movement task, we found that a single cell in the primary motor cortex responded to its specific sequence, but not the rest of sequences, despite all the given sequences were composed of completely the same components as single movement. Furthermore, the effects of the muscimol injections were quite supportive. These results suggest that the primary motor cortex plays a key rule in generating the sequences.

At this point, we raised a proposal that the neuronal network between the cerebellum and the primary motor cortex, through the thalamus, was critical to the skill of the sequential hand movements. Furthermore, at the stage that the sequential movement, such as playing a piano, became automatic by the repeated practices, the primary motor cortex played a role in the generation of the sequences of hand movements.

So far, I have spent a total of 10 years examining the neuronal mechanism for the sequence control wherever I have been. Achievement was certain, but in order to reach the goal it might take more time. The chief reason is that each sequential movement includes both the hand movements and the eye movements. To understand the role of the oculomotor system in the sequence control, during the last two years before I left Dr. Hikosaka's laboratory, we recorded neuronal activity in the frontal eye field (FEF) and supplementary eye field (SEF) while the monkeys were performing the saccadic sequences. We made it clear that SEF contributed to the generation of saccades in the over learned sequences.

Regarding the neuronal mechanism for the sequence control, had we learned enough about



Brain Science Center—the lab I worked in Minnesota

what we were concerned about now? The answer is "no." We had questions like, where and how do we integrate the two separate parts, hands and eyes, during the sequential movement? This answer is still unclear. To get a solution to this is our next goal. Right now, I am joining Dr. Shigeru Kitazawa's project of artificial cerebellum in Juntenndo University while managing to make the previous study up through the anatomic study with Dr. Masahiko Takada in the Tokyo Metropolitan Institute for Neuroscience.

Before I end, forgive me complaining of the deep feeling about the difficult reality for making any approach in the field. In many ways, it appears to be impossible to fully approach the soul of the life by itself. However, once any progress, even a little, it would be so encouraging and so supportive. Therefore, as long as we don't learn that we have zero hope to make a better approach, we are going to keep challenging.