【Grant-in-Aid for Specially Promoted Research】

Biological Sciences

Title of Project : Cerebral spine synapses and exocytosis studied with two-photon microscopy

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Research Area : Neuroscience

Keyword : Synapse, cerebral cortex, neural plasticity, functional imaging, neuroendocrinology

【Purpose and Background of the Research】

It is widely accepted that high-order functions of the brain, particularly, the cerebral cortex, represent our cognition and mind. Recent functional brain imaging has revealed detailed localizations of various brain functions to respective regions of the cortex, indicating that various forms of perception, emotion and executive functions are caused by operation of the neuronal networks of respective brain regions. Neurons extend long axons to numerous other neurons in the brain, and form extensive neuronal networks, where electrical signals in axon are transmitted to the next neurons via “synapse.” These electrical activities, however, exist even in unawakened animals, and they cannot simply account for the states of the awake brain.

We have revealed that synapses in the cerebral cortex change their shapes when their connectivity changes. Such motile synapses (spine synapses) are particularly well developed in the cerebral cortex. The motility of synapses can be induced by synchronous firing of neurons which represent the coherent operation of neuronal circuits. The motility can be long-lasting, and leave their traces, in a manner consistent with memory formation. A neuron in the cerebral cortex possesses thousands of spine synapses, and their motility can encode highly diverse states than neuronal electrical activity.

We will further clarify the cellular bases of the motile synapses, and visualize and manipulate the neuronal motility in awake animals (mice).

【Research Methods】

Cortical synapses are visualized by the two-photon microscope both in vitro and in vivo. We further use and develop optical stimulation to investigate the motility of synapses, such as caged-compounds for neurotransmitters, and genetically encoded probes (PA-GFP, ChR2, OptoXR and PA-smallGs). These methods will allow us to introduce large scale modification of synapses to assess their effects on animal behaviors. We will also visualize the motilities of synapses in awake mice, and study their dependence on vigilance, stimulus selectivity, etc. The consequence of synapse motility will be also assessed on the exocytotic functions of the presynaptic terminals. This is to test the existence of non-classical interaction of synapses. Finally, we will examine abnormal motilities of synapses in animal models for psychiatric disorders.

【Expected Research Achievements and Scientific Significance】

Our study will clarify whether neuronal motilities, in addition to neuronal electrical activity, play essential role in high-order brain functions. If these motilities influence the neuronal network activity, we may have new insight into functional localization of high-order brain functions in specific regions of the brain.

【Publications Relevant to the Project】

Matsuzaki, M., Honkura, N., Ellis-Davies, G.C.R. & Kasai, H. (2004). Structural basis of long-term potentiation in single dendritic spines. *Nature* 429:761-766.

Tanaka, J., Horiike, Y., Matsuzaki, M., Miyazaki, T., Ellis-Davies, GCR & Kasai, H. (2008). Protein synthesis and neurotrophin-dependent structural plasticity of single dendritic spines. *Science* 319:1683-1687.

【Term of Project】 FY2009-2013

【Budget Allocation】 430,900 Thousand Yen

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