【Grant-in-Aid for Scientific Research(S)】
Integrated Science and Innovative Science (Comprehensive fields)

Title of Project: Molecular studies of motor learning and maturation of the cerebellar network

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Research Area : Integrated Science and Innovative Science

Keyword : cerebellum, motor learning, neural network, neural maturation, intracellular signaling

【Purpose and Background of the Research】

The organization and the integrative regulation of the neural network are fundamental subjects for a better understanding of mechanisms underlying brain function and dysfunction. The cerebellum is the key neural substrate that controls motor coordination and learning. The research projects using the reversible neurotransmission blocking (RNB) technique are directed toward the following subjects:

1) how the cerebellar network controls motor coordination and motor learning.
2) how the functional cerebellar network is established in an activity-dependent manner during development.

【Research Methods】

1. Regulatory mechanisms of the cerebellar circuit

We developed a novel RNB technique that allowed us to selectively and reversibly block a particular neural transmission in the neural network and to dissect sequential processes of motor learning at different cerebellar circuits. The mechanisms underlying different processes of motor learning (expression of motor learning at Purkinje cells and acquisition/storage of motor learning at the interpositus and vestibular nuclei) will be investigated by various approaches combining in vivo Ca^{2+} imaging, electrophysiology, molecular biology and microarray analysis of the RNB model mice.

2. Maturing mechanisms of the cerebellar circuit

The cerebellar granule cells mature at the postnatal period. The gene expression in maturing processes is controlled by a master transcription factor via a sequential activity-dependent mechanism involving the stimulation of glutamate receptors, Na^{+} and Ca^{2+} channels and intracellular Ca^{2+} signaling. This investigation will explore the regulatory mechanisms of gene expression and Ca^{2+} signaling in granule cell maturation.

【Expected Research Achievements and Scientific Significance】

1. This project deals with the central theme of brain science as to how neural information is processed and integrated in the neural network and how memory and learning are acquired, expressed and stored by integrative mechanisms of the different neural circuits.
2. The mechanisms that govern maturation of the neural network in an activity-dependent manner largely remain elucive and are being explored in this project.

【Publications Relevant to the Project】

1. Nakanishi, S. Genetic manipulation study of information processing in the cerebellum. Neuroscience 162:723-731(2009)
2. Okazawa, M., Abe, H., Katsukawa, M., Iijima, K., Kiwada, T. and Nakanishi, S. Role of calcineurin signaling in membrane potential-regulated maturation of cerebellar granule cells. J.Neurosci. 29: 2938-2947 (2009)
3. Wada, N., Kishimomto, Y., Watanabe, D., Kano, M., Hirano, T., Funabiki, K. and Nakanishi, S. Conditioned eyeblink learning is formed and stored without cerebellar granule cell transmission. Proc.Natl.Acad.Sci.USA 104: 16690 -16695 (2007)

【Term of Project】 FY2010-2014

【Budget Allocation】 167,400 Thousand Yen

【 Homepage Address and Other Contact Information】
http://www.obi.or.jp/