Molecular Mechanisms for Activity-dependent Elimination of Supernumerary Excitatory Synapses in Developing Cerebellum

1999 Fiscal Year Final Research Report Summary

Molecular Mechanisms for Activity-dependent Elimination of Supernumerary Excitatory Synapses in Developing Cerebellum

Research Project

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10480230

Research Category

Grant-in-Aid for Scientific Research (B)

Allocation Type

Single-year Grants

Section

一般

Research Field

Neuroscience in general

Research Institution

Kanazawa University

Principal Investigator

KANO Masanobu Kanazawa University School of Medicine, Professor, 医学部, 教授 (40185963)

Co-Investigator(Kenkyū-buntansha)

TABATA Toshihide Kanazawa University School of Medicine, Assistant Professor, 医学部, 助手 (80303270)
HASHIMOTO Kouichi Kanazawa University School of Medicine, Assistant Professor, 医学部, 助手 (00303272)

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mouse / cerebellum / Purkinje cell / climbing fiber synapse / postnatal development / synapse elimination / NMDA receptor / activity-dependent

Research Abstract

The climbing fiber to Purkinje cell synapse in the cerebellum has been a good model to study cellular and molecular mechanisms of synapse elimination by which redundant connections formed earlier during development are refined. In early postnatal days of rodents' life, most Purkinje cells are innervated by multiple climbing fibers. Then, elimination of supernumerary climbing fibers occurs until the one-to-one relations between climbing fibers and Purkinje cells are attained at approximately postnatal day 21 (P21). This relationship is maintained throughout life. This process has been shown to depend on neural activity involving NMDA receptors (Rabacchi et al., 1991). In the present study, we found that continuous and local application of tetrodotoxin or an NMDA receptor antagonist, MK-801 to developing mouse cerebella

resulted in persistent multiple climbing fiber-innervation in about 40% of Purkinje cells. We also demonstrated that blockade of NMDA receptor-mediated neural activity in the cerebellum during P15-P16, but not before nor after this period, caused persistent multiple climbing fiber innervation. as well as motor discoordination. The NMDA receptor blockade did not cause apparent change in cerebellar morphology and basic synaptic properties. Our results suggest that the NMDA receptor-dependent climbing fiber synapse elimination is achieved during this critical period, and its disruption leads to persistent impairment of cerebellar function. By using gene deletion technique in mice, we have demonstrated previously that the signal transduction involving metabotropic glutamate receptor subtype I (mGluR1), the α subunit Gq (Gαq), phospholipase Cβ4 (PLCβ4) and protein kinase Cγ(PKCγ) is required for climbing fiber synapse elimination during the third postnatal week that coincide with the critical period revealed in the present study. We assume that neural activity along the mossy fiber-granule cell-parallel fiber pathway activates mGluR1 and the following cascade in Purkinje cells that is required for elimination of supernumerary climbing fibers.▲ Less

Research Products (28 results)

All Other

All Publications

[Publications] Miyata, M.: "Corticotropin-releasing factor plays a permissive role in cerebellar long-term depression"Neuron. 22. 763-775 (1999)

[Publications] Tsubokawa, H.: "Elevation of intracellular Na^+ induced by hyperpolarization at the dendrites of pyramidal neurons of mouse hippocampus"J. Physiol. (London). 517. 135-142 (1999)

[Publications] Hashimoto, K.: "Impairment of AMPA receptor function in cerebellar granule cells of ataxic mutant mouse Stargazer"J. Neurosci.. 19. 6027-6036 (1999)

[Publications] Ohno-Shosaku, T.: "Heterosynaptic expression of depolarization-induced suppression of inhibition (DSI) in rat hippocampal cultures"Neurosci. Res.. 36. 67-71 (2000)

[Publications] Matsuzawa, M.: "Formation of hippocampal synapses on patterned substrates of a laminin-derived synthetic peptide"Eur. J. Neurosci.. (in press). (2000)

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[Publications] Hashimoto, K.: "Neural Development./ Electrophysiological evidence that Gαq is required for climbing fiber synapse elimination during postnatal cerebellar development"Springer-Verlag, Tokyo. 5 (1999)

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