［課程－２］

審査の結果の要旨

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Developmental synapse elimination is crucial for a proper maturation of synaptic circuitry. I studied the effect of the knockdown of Fndc3b in Purkinje cells in the cerebellum on the climbing fiber to Purkinje cell synapse elimination in mice. The following results were found:

1 – Electrophysiological analysis on acute cerebellar slices showed that climbing fiber synapse elimination was impaired in Fndc3b-knockdown Purkinje cells compared to control Purkinje cells at postnatal day 19 (P19) to P30.

2 – Electrophysiological analysis during development indicated that Fndc3b was involved in climbing fiber synapse elimination from P8 (during the early phase of climbing fiber synapse elimination), and that Fndc3b negatively regulated synaptic strength of climbing fiber synapses from P12.

3 – Fluorescent in situ hybridization showed that Fndc3b mRNA was expressed the most at P9, during the early phase of climbing fiber synapse elimination.

4 – Immunohistochemical analysis demonstrated that elimination of climbing fiber terminals from Fndc3b-knockdown Purkinje cell soma was impaired and that the translocation of the strongest climbing fiber onto the dendrites of Purkinje cells was also impaired by the knockdown of Fndc3b.

5 – Electrophysiological and Immunohistochemical analysis indicated that Fndc3b did not affect the distribution of parallel fiber synapses or their function.

6 – Fndc3b did not affect the distribution of inhibitory synapses or morphology of interneurons.

To summarize, these results suggest that Fndc3b promotes elimination of redundant climbing fibers from the Purkinje cell soma during the early phase of climbing fiber synapse elimination, negatively regulates climbing fiber synaptic strength and facilitates translocation of the strongest climbing fiber along Purkinje cell dendrites.