News Release

Title

Identification of novel molecular mechanism for memory

Key Points

○The present study identified that Girdin is crucial for memory.

○ Our findings suggest that Akt-dependent NR2B phosphorylation through the phosphorylated Girdin, which is associated with synaptic plasticity in the hippocampus underlying memory formation.

○It is possible that Girdin phosphorylation may contribute to cognitive dysfunction in neuropsychiatric disorders.

Summary

Synaptic plasticity in hippocampal neurons has been thought to represent a variety of memories. Although accumulating evidence indicates a crucial role of BDNF/TrkB/Akt signaling in the synaptic plasticity of the hippocampus, the mechanism by which Akt, a serine/threonine kinase, controls activity-dependent neuronal plasticity remains unclear. The present study, reported by Professor Kiyofumi Yamada, Associate Professor Taku Nagai, Mr. Tsuyoshi Nakai, and his collaborators Professor Masahide Takahashi, Designated Professor Masahiro Sokabe in Nagoya University Graduate School of Medicine (Dean: Masahide Takahashi, M.D., Ph.D.) identified that Girdin is crucial for memory. Furthermore, activity-dependent Girdin phosphorylation induced by Akt is crucial for NMDA receptor activation associated with synaptic plasticity in the hippocampus underlying memory formation. This study may shed light into the molecular mechanisms underlying neuropsychiatric disorders with cognitive dysfunction. This work was published online in *The Journal of Neuroscience* in November 5, 2014

Research Background

Synaptic plasticity in hippocampal neurons has been thought to represent a variety of memories. Although accumulating evidence indicates a crucial role of BDNF/TrkB/Akt signaling in the synaptic plasticity of the hippocampus, the mechanism by which Akt, a serine/threonine kinase, controls activity-dependent neuronal plasticity remains unclear. Girdin, an actin-binding protein involved both in the remodeling of the actin cytoskeleton and in cell migration, has been identified as a substrate of Akt. Previous studies have demonstrated that deficit of neuronal migration in the hippocampus of Girdin-deficient (Girdin-/-) mice is independent on serine phosphorylation of Girdin by Akt. In the present study, we focused on the role of Girdin phosphorylation in BDNF/TrkB/Akt signaling associated with synaptic

plasticity.

Research Results

We found that Girdin in the hippocampus was phosphorylated in an activity-dependent manner. Phosphorylation-deficient knock-in mice (GirdinSA/SA mice) exhibited shrinkage of spines, deficit of hippocampal long-term potentiation and memory impairment. Furthermore, Girdin interacted with Src kinase and NR2B subunit of NMDA receptor, leading to phosphorylation of the NR2B subunit and NMDA receptor activation.

Research Summary and Future Perspective

Our findings suggest that activity-dependent Girdin phosphorylation induced by Akt is crucial for NMDA receptor activation associated with synaptic plasticity in the hippocampus underlying memory formation (Fig). It is possible that Girdin phosphorylation may contribute to cognitive dysfunction in neuropsychiatric disorders.

The authors and title of the paper

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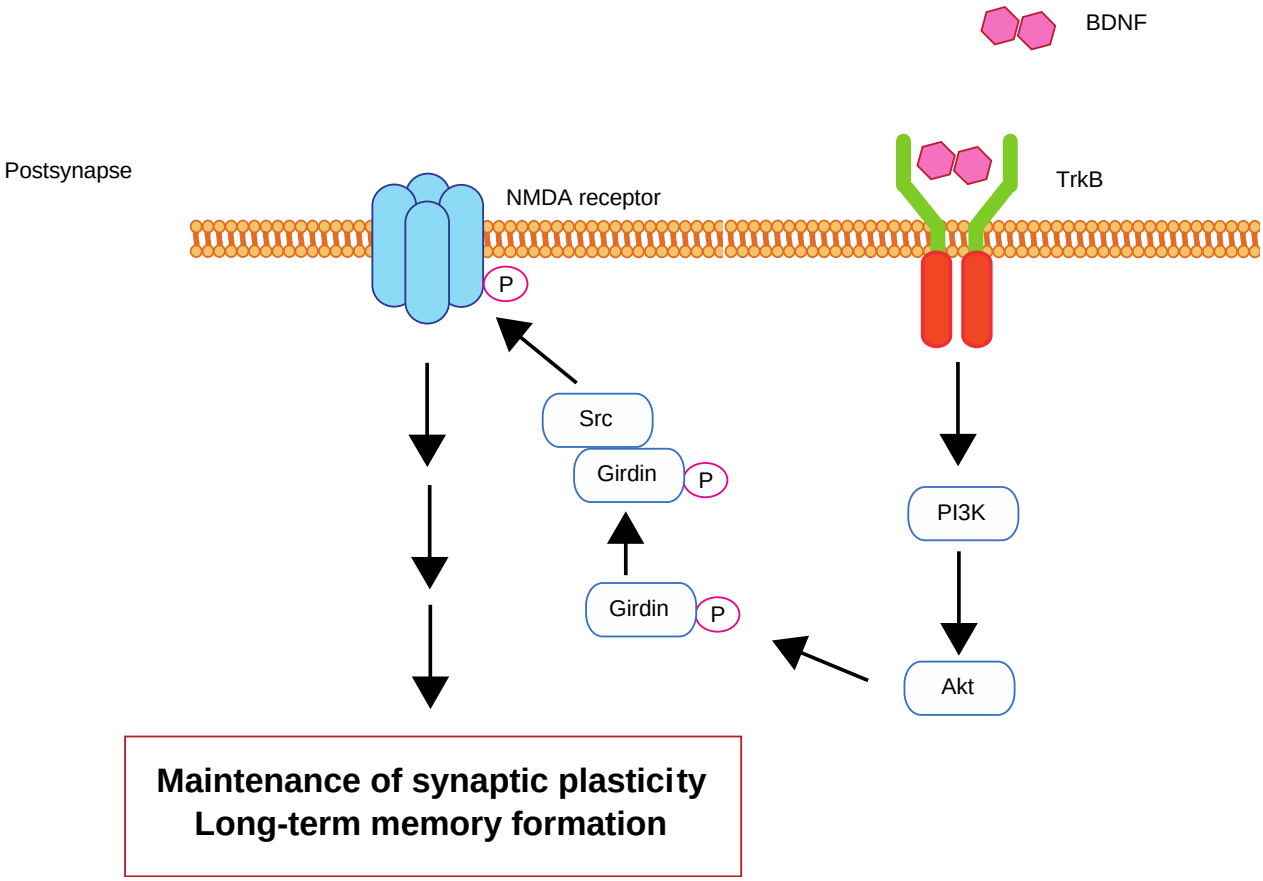
Japanese ver.

http://www.med.nagoya-u.ac.jp/medical/dbps_data/_material_/nu_medical/_res/topix/2014/girdin_20141106jp.pdf


BDNF
Postsynapse
NMDA receptor
TrkB
P
Src
Girdin
P
Girdin
P
PI3K
Akt
Maintenance of synaptic plasticity
Long-term memory formation