CDK5 downregulation enhances synaptic plasticity

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Abstract

CDK5 is a serine/threonine kinase that is involved in the normal function of the adult brain and plays a role in neurotransmission and synaptic plasticity. However, its over-regulation has been associated with Tau hyperphosphorylation and cognitive deficits. Our previous studies have demonstrated that CDK5 targeting using shRNA-miR provides neuroprotection and prevents cognitive deficits. Dendritic spine morphogenesis and forms of long-term synaptic plasticity-such as long-term potentiation (LTP)-have been proposed as essential processes of neuroplasticity. However, whether CDK5 participates in these processes remains controversial and depends on the experimental model. Using wild-type mice that received injections of CDK5 shRNA-miR in CA1 showed an increased LTP and recovered the PPF in deficient LTP of APPswe/PS1ΔE9 transgenic mice. On mature hippocampal neurons CDK5, shRNA-miR for 12 days induced increased dendritic protrusion morphogenesis, which was dependent on Rac activity. In addition, silencing of CDK5 increased BDNF expression, temporarily increased phosphorylation of CaMKII, ERK, and CREB; and facilitated calcium signaling in neurites. Together, our data suggest that CDK5 downregulation induces synaptic plasticity in mature neurons involving Ca2+ signaling and BDNF/CREB activation.

Keywords: BDNF/CREB||CDK5 RNAi||Calcium||Dendritic protrusion morphogenesis||LTP||Synaptic plasticity
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