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Arg3.1/Arc is required for long-lasting plasticity and memory consolidation

Enduring forms of synaptic plasticity like long-term potentiation (LTP) and long-term memory require alterations in the molecular composition and structure of neurons and are dependent on RNA and protein synthesis. Plasticity might therefore be achieved by activity-dependent changes in the expression of specific genes. Arg3.1 is robustly induced by LTP stimulation. Moreover, following induction Arg3.1 is rapidly distributed throughout the dendritic arbor and is specifically targeted to stimulated synapses. Arg3.1 protein is embedded into the postsynaptic density that coordinates activity-dependent changes on the postsynaptic side. In the PSD Arg3.1 is associated dynamically with a protein network that consists of the NMDAR, PSD-95, synGAP and Shank. Here, Arg3.1 lies downstream of PSD-95 which in turn is directly linked to the NMDAR. Electrophysiological analyses of Arg3.1 ko mice exhibit a remarkable biphasic alteration of hippocampal LTP. Whereas baseline synaptic transmission is normal the initial, early phase of LTP is enlarged in Arg3.1 deficient animals. However, elevated potentials completely decay to baseline and no late phase LTP can be observed. This cellular phenotype corresponds to severe deficits in numerous behavioral learning and memory tasks. Whereas working and short-term memories were unaffected Arg3.1 ko mice are strongly impaired in the formation of a stable long-lasting memory. Thus, Arg3.1 may act to maintain the structural or functional integrity of the NMDAR complex and thereby control the signaling pathways that coordinate activity-dependent changes underlying long-lasting synaptic plasticity and memory storage.
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