UKE Paper of the Month December 2013

Proceedings of the National Academy of Sciences, November 2013, epub ahead of print, PMID: 24191047

Long-term depression triggers the selective elimination of weakly integrated synapses

J. Simon Wiegert, Thomas G. Oertner

ABSTRACT: Long-term depression (LTD) weakens synaptic transmission in an activity-dependent manner. It is not clear, however, whether individual synapses are able to maintain a depressed state indefinitely, as intracellular recordings rarely exceed one hour. Here, we combine optogenetic stimulation of identified Schaffer collateral axons with two-photon imaging of postsynaptic calcium signals and follow the fate of individual synapses for seven days after LTD induction. Optogenetic stimulation of CA3 pyramidal cells at 1 Hz led to strong and reliable depression of postsynaptic calcium transients in CA1. NMDA receptor activation was necessary for successful induction of LTD. We found that in the days following LTD, many depressed synapses and their neighbors were eliminated from the hippocampal circuit. The average lifetime of synapses on non-stimulated dendritic branches of the same neurons remained unaffected. Persistence of individual depressed synapses was highly correlated with reliability of synaptic transmission, but not with spine size or the amplitude of spine calcium transients. Our data suggest that LTD initially leads to homogeneous depression of synaptic function, followed by selective removal of unreliable synapses and recovery of function in the persistent fraction.

STATEMENT: *“This is the first time that the function and stability of individual synapses could be measured over one week in intact tissue. The surprising results question the idea that memory is permanently stored in the strength of synapses. Instead, activity-induced changes in synaptic strength control the lifetime a synapse, so that unreliable synapses get eliminated from the circuit and only the strongest survive. This process of 'synaptic Darwinism' leads to constant rewiring and optimization of the brain.”*

BACKGROUND: This work was performed by Dr. Simon Wiegert who received a Marie Curie Intra-European Fellowship to pursue this project in 2010. Dr. Wiegert works at the ZMNH's Institute of Synaptic Physiology, headed by Thomas Oertner who holds a professorship at the UKE since 2011. Both authors have strong research interests in the field of synaptic plasticity with a special focus on the mechanisms of memory.