UKE Paper of the Month Dezember 2020

Endoplasmic reticulum visits highly active spines and prevents runaway potentiation of synapses

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ABSTRACT:
In hippocampal pyramidal cells, a small subset of dendritic spines contain endoplasmic reticulum (ER). In large spines, ER frequently forms a spine apparatus, while smaller spines contain just a single tubule of smooth ER. Here we show that the ER visits dendritic spines in a non-random manner, targeting spines during periods of high synaptic activity. When we blocked ER motility using a dominant negative approach against myosin V, spine synapses became stronger compared to controls. We were not able to further potentiate these maxed-out synapses, but LTD was readily induced by low-frequency stimulation. We conclude that the brief ER visits to active spines have the important function of preventing runaway potentiation of individual spine synapses, keeping most of them at an intermediate strength level from which both LTP and LTD are possible.

STATEMENT:
This collaboration between two-photon imaging specialists and motor protein experts from two different Institutes of the UKE shows how interdisciplinary projects, here financed by a dedicated DFG Research Unit headed by Matthias Kneussel, can lead to unexpected discoveries. The importance of endoplasmic reticulum for synaptic function has been previously acknowledged, but the extremely dynamic nature of this system and the amazing specificity for highly active synapses only became apparent through advanced imaging approaches combined with targeted genetic manipulations.

BACKGROUND:
This work was performed at the Institute for Synaptic Plasticity in the group of Thomas Oertner who holds a professorship at the UKE since 2011. Alberto Perez-Alvarez, who was supported by the DFG Research Unit FOR 2419 throughout this project, has a strong research interest in the regulation of synaptic plasticity by intracellular organelles. Wolfgang Wagner from the Institute for Molecular Neurogenetics contributed an important myosin V tail domain construct that he originally created in the lab of John Hammer at the NIH.