PLASTICITY OF THE DEVELOPING GLUTAMATE SYNAPSE IN THE HIPPOCAMPUS

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien vid Göteborgs universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Medicinaregatan 3, Göteborg, fredagen den 7 september 2007 kl. 09.00

av
Therése Abrahamsson

Fakultetsopponent:
Professor Tomi Taira
Neuroscience Center and Department of Biosciences
University of Helsinki, Finland

Avhandlingen baseras på följande delarbeten:

I. Abrahamsson T., Gustafsson B. and Hanse E.
Synaptic fatigue at the naïve perforant path-dentate granule cell synapse in the rat.
Journal of Physiology (2005) 569.3 pp 737-750

II. Abrahamsson T., Gustafsson B. and Hanse E.
A reversible synaptic depression in developing rat CA3-CA1 synapses explained by a novel cycle of AMPA silencing-unsilencing.
Submitted

III: Abrahamsson T., Gustafsson B. and Hanse E.
AMPA silencing: a prerequisite for LTP at developing CA3-CA1 synapses.
In manuscript

IV. Abrahamsson T., Gustafsson B. and Hanse E.
Hebbian induction adds an AMPA labile signaling module to developing AMPA signaling CA3-CA1 synapses.
In manuscript

Göteborg 2007

PLASTICITY OF THE DEVELOPING GLUTAMATE SYNAPSE IN THE HIPPOCAMPUS

Therése Abrahamsson
Department of Physiology, Institute of Neuroscience and Physiology, Göteborg University, Göteborg, Sweden, 2007

Abstract
Synapses are highly plastic, i.e. they have the ability to change their signaling strength both in the short- and long-term (e.g. long-term potentiation - LTP) in response to specific patterns of activity. In the developing brain synaptic plasticity promotes activity-dependent development, whereas in the mature brain synaptic plasticity forms the basis for learning and memory. Although both development and learning involve organization and reorganization of synaptic circuits, the extent to which the plasticity behind these two phenomena uses the same mechanisms is unknown. The glutamate synapse which represents > 90 % of the brain synapses signals mainly via postsynaptic AMPA and NMDA receptors. In the developing brain, sparse synaptic activation can make the synapse lose its AMPA signaling capacity, i.e. make it AMPA silent, while LTP can reinstall the AMPA signaling (unsilencing). The aim of this study was to investigate the possible role of the AMPA silent synapse, and its unsilencing, in developmental and mature synaptic plasticity. Electrophysiological recordings of synaptic transmission in the CA1 region and in the dentate gyrus of acute hippocampal slices were used for these studies.

A new and unexpected finding was that AMPA unsilencing can also be induced by not activating the AMPA silent synapse for tens of minutes. Together with previous findings this suggests a model in which the glutamate synapse is born with a single AMPA labile module, i.e. the synapse cycles between an AMPA silent state, induced by sparse synaptic activity, and an AMPA signaling state, induced by the absence of synaptic activity. The results further suggest that AMPA silencing is a prerequisite for developmental LTP to occur. In other words, developmental LTP does not potentiate synaptic transmission but rather stabilizes the AMPA labile module. It can, however, transiently potentiate the synapse by the addition of a labile AMPA module to an existing synapse with a single stable AMPA module. After this initial period of synaptic stabilization there is an increase in synaptic connectivity between pre- and postsynaptic neurons. It is proposed that this increased connectivity can be explained, at least partly, by the addition of stable AMPA modules to existing synapses promoted by mature LTP. This thesis thus proposes that, using the same principle mechanism, namely the addition of stable AMPA modules, developmental LTP promotes initial synaptic stabilization while mature LTP promotes synaptic growth.

Keywords: synaptic plasticity, long-term potentiation, short-term potentiation, silent synapse, development, glutamate, hippocampus

ISBN 978-91-628-7255-7