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Labile glutamate synaptic transmission onto CA1 hippocampal pyramidal neurons: regional, functional and developmental diversity

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i hörsa Arvid Carlsson, Medicinaregatan 3, den 8 Mars 2024, klockan 09:00

av Rong Ma
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Professor Björn Granseth
Linköping Universitet, Sverige

Avhandlingen baseras på följande delarbeten

I. Ma, R., Xiao, M., Gustafsson, B.
Labile glutamate signaling onto CA1 pyramidal cells in the developing hippocampus depends mechanistically on input pathway.
Neuroscience 2016; 337: 27-36.

II. Ma, R., Hanse, E., Gustafsson, B.
Homosynaptic frequency-dependent depression by release site inactivation at neonatal hippocampal synapses in the stratum lacunosum-moleculare.
European Journal of Neuroscience 2021; 54(3):4838-4862

III. Ma, R., Hanse, E., Gustafsson, B.
Labile glutamate synaptic transmission in the adult CA1 stratum-lacunosum-moleculare region.
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Labile glutamate synaptic transmission onto CA1 hippocampal pyramidal neurons: regional, functional and developmental diversity

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Abstract

A single neuron in the brain receives tens of thousands of glutamate synapses from other neurons, and these synapses can differ in their properties depending on their role in the neural circuit, during brain development as well as in the adult brain. In the hippocampus, a cortical region involved in mnemonic functions, CA1 pyramidal cells serve as the output stage for the return of information back to the cortical areas providing input to the hippocampus. On their proximal dendrites in the stratum radiatum (SR) these cells receive learned associations between multimodal sensory events while on their distal dendrites in the stratum-lacunosum-moleculare (SLM) they receive ongoing sensory activity. I studied SLM glutamate synapses using an in vitro slice preparation from neonatal and adult rats. In the CA1 region, the neonatal state is a period of activity dependent organization of synaptic connectivity driven by spontaneous waves of activity. Thereafter, the hippocampus will develop into its adult state through sensory-motor interaction with the environment. For the SR synapses the neonatal period is associated with large changes in the glutamate synapses characterized by labile synaptic transmission, i.e., that even sparse activity removes glutamate receptors of the AMPA-type from the postsynaptic membrane, creating AMPA-silent synapses. For a synapse to survive in this neonatal period, it must be active together with other synapses and participate in evoking postsynaptic activity to remain AMPA stable. Thereafter, this developmental plasticity is replaced by an activity dependent adult plasticity strengthening the synapses associated with a morphological expansion of the SR region. The SLM synapses are much less studied, where previous work has only indicated some quantitative differences compared to SR synapses. However, the SLM region matures morphologically earlier than the SR region, suggesting a faster transition to adult plasticity. I found the neonatal SLM synapses to exhibit much less postsynaptic AMPA labile transmission compatible with this suggestion. The SLM synapses instead showed a presynaptic labile transmission that acted like a habituation-like process at the synaptic level, explained by activity dependent release site inactivation. This lability decreases with age. In contrast, the postsynaptic lability did not disappear but rather enhanced with age and approached that of the neonatal SR synapses. Moreover, only a developmental plasticity was found in the adult SLM synapses and the SLM region did not expand morphologically. These results suggest that adult SLM synapses are adapted to allow the SLM region to serve as a flexible multimodal sensory map for novelty detection and proper backpropagation to neocortical areas.

Keywords: development, hippocampus, short-term plasticity, long-term plasticity

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