Universität Basel

Research Project

Synaptic recruitement of adult-born hippocampal granule cells

Third-party funded project

Project title Synaptic recruitement of adult-born hippocampal granule cells
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Background. In the mammalian hippocampus new neurons are continuously generated throughout life. The adult-born hippocampal granule cells are well known to improve learning and memory, by enhancing the brains capability to discriminate similar memory items. Disturbed adult neurogenesis may contribute to many pathophysiological conditions, including anxiety disorders and major depression. On a cellular level, distinct functional properties of the young neurons have been described, including enhanced excitability, reduced GABAergic inhibition and enhanced synaptic plasticity. However, so far, it is absolutely unclear how these cellular properties might contribute to hippocampal information processing on a network level to finally generate the behaviorally determined memory improvements. Specific Aims. In the new project, we will analyze population activity in young granule cells, to investigate how the new neurons might contribute to encoding and discrimination of different neuronal input patterns on a network level. Specifically, we will test the hypothesis that sparse glutamatergic connectivity together with dynamically regulated GABAergic interneuron activity might tune sparse coding within the newborn young population. Therefore, we will systematically investigate synaptic activation of newborn granule cells at different time points after cell division in vitro and in vivo. Young neurons will be identified by different means including retrovirus-mediated birth dating and Mash1-CreERT-dependent tdTomato expression, which allows to label a cohort of newborn 2-, 3-, 4- or 8-week-old neurons. By making use of various optogenetic tools, we will first map synaptic responses of neighboring young neurons to cortical and subcortical afferent synaptic inputs using paired patch-clamp recordings in hippocampal brain slices from adult mice. Second, we will make use of Cre-dependent genetically encoded calcium indicators (GECIs) to characterize population activity in response to different afferent spatio-temporal activity patterns. Third, we will characterize the contribution of different types of local GABAergic interneurons to the spiking activity of young granule cells. It will be of particular interest to study the potentially different excitatory and inhibitory effects of different interneuron subtypes onto young cells. Finally, we will establish in vivo calcium imaging with the new Inscopix nVoke endoscopic imaging system, which not only enables recording from GCaMP6-labeled young neurons in freely moving animals, but also allows for temporally controlled optogenetic silencing of young neurons. The animals will be exposed to different behavioral conditions including novel objects and environments. Young neurons will be recorded across subsequent recording sessions to finally see how their activity adapts during conditions of novelty learning and memory recall. Temporally controlled silencing or activation of the young neurons during learning and recall will further allow to correlate network activity with behavioral outcome.

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