Stony Brook University
The Graduate School

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Abstract

Plasticity of the Dentate Gyrus

By

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The hippocampus holds a variety of dimensions of plasticity. The long-term potentiation in the hippocampal synapse is suggested to play a fundamental role in Hebbian learning. The dentate gyrus (DG), a subregion of the hippocampus, holds the capacity to generate new neurons throughout the adulthood. In addition, the hippocampus is believed to construct new episodic memories. And this memory encoding neural representation is flexible, and can be modulated by both internal networks as well as external stimuli. However, how the DG network ensures the proper number of granule cells and encodes learning and memory is largely unknown. This dissertation work aims to address this question in two aspects: 1) how the adult brain regulates newborn neuron survival in the DG. Using a novel *in vivo* optical imaging method in freely moving mice, we found that hippocampus-engaged behaviors, such as exploration in a novel environment, rapidly increased microvascular blood flow velocity in the DG. Importantly, blocking this exploration-elevated blood flow dampened experience-induced hippocampal neurogenesis. By imaging the neurovascular niche in combination with chemogenetic manipulation, we revealed that pre-existing dentate granule cells (DGCs) and parvalbumin-expressing interneurons actively regulated microvascular blood flow, primarily through nitric oxide signaling. Together, our findings revealed a neurovascular coupling network that regulates experience-induced neurogenesis in the adult brain. 2) how the DGC is modulated by learning to encode decision-making. We developed an auditory frequency discrimination task in which rats learn to navigate to the goal locations based on the frequencies of auditory stimuli. Using *in vivo* calcium imaging and chemogenetic approach in freely behaving rates, we found that along the task learning, DGCs become more active and spatially tuned, and more DGCs express task even-related activities. We further found that in well-trained rats DGC ensembles express the navigation path and encode auditory decisions as early as the rats began to approach goals. Together, our results demonstrate that DGCs gain task-relevant firing pattern through learning and suggesting a potential locus for sensor decision linked to spatial navigation.

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