

HIPPOPLAST: How rigid and plastic circuits contribute to hippocampal function

Main area: HBP05_The neural bases of spatial navigation and episodic memory

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Abstract

In any given environment, an ensemble of principal excitatory cells in the hippocampus, called place cells, will be active in a specific, usually single, location (their place field). Together, these neurons participate in the formation of a cognitive map, a mental representation of that environment, allowing flexible spatial navigation. For a long time, hippocampal principal cells were thought to form a relatively homogeneous population and the ability of any given hippocampal cell to be active in a new environment was thought to be evenly distributed. Recent data, however, suggest a more complicated scheme. Evidence shows that a small minority of rigid cells are active in most encountered environments and a majority of more plastic cells are active in only one or few encountered environments. However, it remains unknown how rigid and plastic circuits map onto specific cellular/circuit properties, developmental origins and intrinsic/synaptic cellular plasticity already described in the hippocampus. In order to address this specific question this proposal is organized along 3 objectives. Objective#1 is to determine whether plastic vs. rigid circuits are anatomically separate and analyze their stability across conditions and time. Objective #2 is to understand which cellular/circuit properties critically determine whether a neuron is functionally plastic or rigid. We will examine the developmental origin, intrinsic morpho-physiological properties, and synapto-dendritic physiology and plasticity of rigid vs. plastic cells in vivo as well as in vitro. Lastly, objective #3 is to understand the computational benefits for navigational strategies of mixing rigid and plastic neurons into the same network. We will provide a predictive model that combines all the experimental datasets from the two previous objectives. By bringing together leading experts in a wide array of disciplines, ranging from developmental neurobiology, cellular physiology, systems and computational neuroscience, this project will highly contribute to the expected impacts set out in the program of the HBP flagship. It will provide high yield quantitative data, bridging the gap between cellular and circuit analysis of hippocampal function, that will certainly fuel simulations of the hippocampal network, in the framework of the proposal (WP3). It should also benefit society because the ability to flexibly navigate in an environment is vital for human's autonomy and severely disrupted during aging and in various diseases such as Alzheimer's disease and temporal lobe epilepsy. The project will test a new hypothesis concerning the functional organization of the cells responsible for spatial navigation and episodic memory formation. Identifying the fast firing/rigid cell type and understanding their precise functional role within and across networks may therefore allow us to design new therapeutic procedures to restore network, cognitive and behavioral functions in pathological situations.

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