Stability and Plasticity of Hippocampal Circuits: From Physiology to Alzheimer’s Pathology

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Abstract

How neuronal circuits maintain the balance between stability and plasticity in a constantly changing environment remains a fundamental question in neuroscience. Empirical and theoretical studies suggest that homeostatic negative feedback mechanisms operate to stabilize the function of a system at a set point level of activity. While extensive research uncovered diverse homeostatic mechanisms that maintain activity of neural circuits at extended timescales, several key questions remain open. First, what are the basic principles and the molecular machinery underlying invariant population dynamics of neural circuits, composed from intrinsically unstable activity patterns of individual neurons? Second, how are activity set-points regulated? Third, does homeostatic regulation fail in neurodegenerative disorders such as Alzheimer’s disease, driving aberrant brain activity and memory loss? To target these questions, we have developed an integrative approach to study the relationships between ongoing spiking activity of individual neurons and neuronal populations, inhibition-excitation balance, intrinsic excitability of neurons and signaling processes at the level of individual hippocampal synapses. I will describe the basic relationships between ongoing spiking properties of individual neurons, population dynamics and neuronal adaptive mechanisms. Moreover, I will discuss how failure in the core homeostatic machinery may contribute to hippocampal hyperactivity associated with Alzheimer's disease.