Sensory Integration in Memory-driven Choice Behaviors

Miguel Remondes
Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa

Cognitive deficits such as Alzheimer's Disease, Anhedonia, Depression, and Schizophrenia, have been mapped to neuropathological changes in medial mesocortical (MMC) structures, such as the anterior cingulate cortex (ACC), necessary for appropriate decision-making, the retrosplenial cortex (RSC), critically involved in visual-spatial processing, and the hippocampal formation, (entorhinal cortex (EC), subiculum (SUB), and hippocampus (HIPP)), critical for episodic memory and any mental function therein dependent. To understand, and ultimately ameliorate or cure, such disorders, it is imperative that we identify the structures and mechanisms underlying the behaviors they affect. We model such behaviors as the reward-seeking trajectory choices present when rodents learn to negotiate goal-directed tasks of variable complexity. In such tasks, we create a contingency regulating the delivery of a reward after rodents chose a given spatial trajectory, from 2+ available, at a defined point (the choice point, or CP).

Current evidence shows that hippocampus (HIPP) and adjacent entorhinal cortex (EC) form a complex circuit whose neurons store a spatial memory engram. Reactivation of such memory engram would allow its use by the "executive" cingulate (ACC) and retrosplenial (RSC) regions (medial mesocortex, MMC), whenever such information is needed for decision-making. Evidence for this model is largely correlative. We do not know the mechanisms converting sensory information to EC- HIPP spatial-maps, neither how MC retrieves and uses memory engrams to support behavior. The findings we now present are the result of joint cutting-edge techniques from multiple disciplines: a) Anatomical tracings in rodent models b) in vivo and in vitro electrophysiology, c) Fine manipulation of neural activity using genetically-encoded neural actuators, and d) Place-dependent, decision-making protocols. We have identified the neural circuitry connecting sensory areas, HIPP and MMC, successfully manipulated neural activity in said circuitry, and begun to dissect the mechanisms linking primary sensory input, spatial memory, and decision-making. Ultimately we want to understand how we go from receiving primary sensory inputs, to building an enduring mental map of context, and to decide on the appropriate actions in a changing world.