



# Circuit mechanisms of item memory and its disruption in Alzheimer's disease

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2025年12月19日(金) 9:30~11:00

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Memory has multiple components: “what” memory (item/object), “when” memory (time) and “where” memory (space). Research in the past decades revealed neurons involved in spatial memory, including place cells in the hippocampus and grid cells in the medial entorhinal cortex (MEC). However, circuit mechanisms of memory about item and time remain largely unclear. Our lab focuses on identifying neural circuits for item memory, and how these circuits become impaired in the disease of memory – Alzheimer's disease. We previously reported the encoding of item-outcome associative memory in the lateral entorhinal cortex (LEC) (Igarashi et al., Nature, 2014), and this encoding is controlled by dopamine signals from the ventral tegmental area (Lee et al., Nature, 2021). We recently found that neuronal populations of both the LEC (layer 5/6) and their major target, the medial prefrontal cortex, formed an internal map of pre-learned and novel items, classified into dichotomic rewarded vs. punished groups (Jun et al., Nature 2024). The formation of this internal map was mutually dependent. Our result suggests that the LEC and mPFC encodes a cognitive map of item-outcome rules.

In the second part of the talk, I will share our recent finding of dysfunctional dopamine in the LEC of Alzheimer's disease mouse models (Nakagawa et al., Nat Neurosci 2025), which further suggests the critical role of dopamine in Alzheimer's disease.

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