【Grant-in-Aid for Scientific Research (S)】

# Elucidating the mechanisms of fast learning

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| Project Information | Project Number : 23H05478<br>Keywords : Memory, Knowledge, Schema, Learning Speed | Project Period (FY) : 2023-2027 |

## Purpose and Background of the Research

**●Outline of the Research**

Over the last decade experimental neuroscience has made tremendous progress defining the circuits in the mammalian brain required for memory, including the canonical circuits of the hippocampus responsible for episodic memory, as well as non-canonical circuits impinging on, and radiating from, the hippocampus which modulate these processes. However, although it is well established that pre-existing knowledge impacts the speed and efficacy of new learning, most animal experiments have examined learning in isolation from previous experience, precluding our understanding of the circuits and mechanisms underlying the interplay between slow learning in the past and fast learning in the present. Here we will employ emerging genetic, in vivo functional recoding, behavior and computational and analytical modeling approaches to examine how non-canonical memory circuits permit the brain to integrate experiences across time and quickly extract regularities. Specifically, we will focus on four topics, the formation of memory schemas, the integration of related experiences to support inferential learning, the coordination of circuits for long-term memory storage and how oscillations permit fast learning (Figure 1). By characterizing the circuits and mechanism which underlie these abstract functions we will advance the understanding of how our brains acquire and use knowledge, and crucially, how this can be improved.

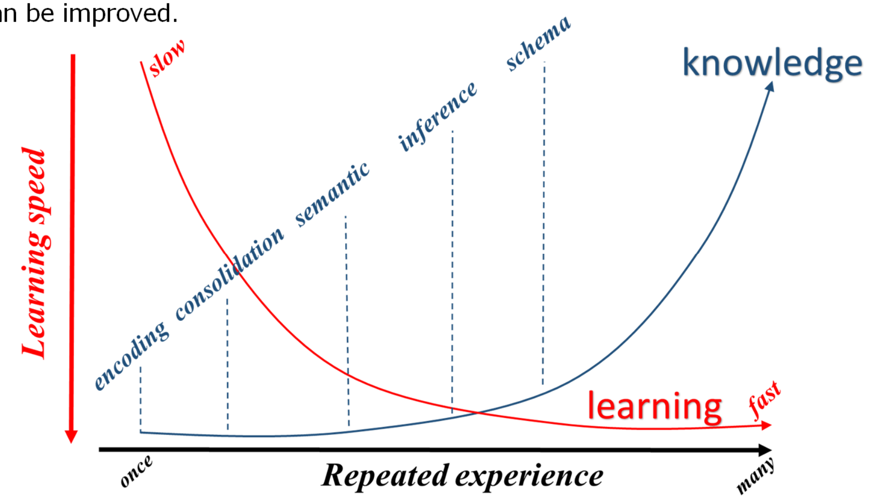


Figure 1. Across repeated experiences our brains can construct more abstract knowledge, using prior episodes to speed later learning. The circuitry and mechanisms underlying these processes are poorly understood. In this project we will reveal novel circuits and processes that impact learning speed, stretching from the initial encoding of experience, through its consolidation, the ability to infer outcome based on related experience and the construction of memory schema which underlie rapid learning.

Technical advances in every domain we employ in our work now permit us to identify and characterize novel circuits in the brain that underlie complex and abstract mnemonic processes. Building on our previous work we will now retool and refocus our efforts to remain on the cutting-edge of the research field. This project will allow us to move beyond the interrogation of the learning of single events and study for the first-time novel circuitries and cells responsible for learning across experiences and how the brain uses previous knowledge to speed new information storage; processes that underlie how our own brains operate. This include connections between the hippocampus and both subcortical (Figure 2) and cortical structures (Figure 3) that modulate learning speed.

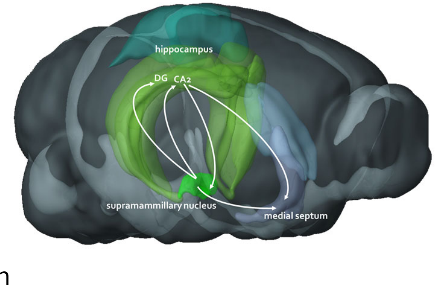


Figure 2. The medial septum is bi-directionally connected with both the hippocampus and hypothalamus, but a detailed understanding of how these circuits impact the speed of learning if unknown.

## Expected Research Achievements

The last five years has seen the pace of technological advances in the field of systems neuroscience continue to accelerate, facilitating the design and execution of experimental paradigms that hitherto seemed impossible. This progress has been evident in every domain we employ in our work, viral and genetic approaches, high-density activity monitoring using physiology and imaging, the analysis of behavioral and physiological data via machine-learning and novel analytical and computational approaches to decipher these high-dimensional data. Here we will harness these advancements us to identify and characterize novel circuits in the brain that underlie complex and abstract mnemonic processes. While these abstract representations have been observed in multiple species, ranging from mice to humans, the circuit and cellular mechanisms underlying their formation and, most importantly, how they serve to facilitate faster and more efficient learning of new information, remain unexplored. In this project we will build on our success characterizing the canonical hippocampal memory circuits and expand our interests to novel and less understood circuit interactions that underlie the creation of not just memory, but knowledge.

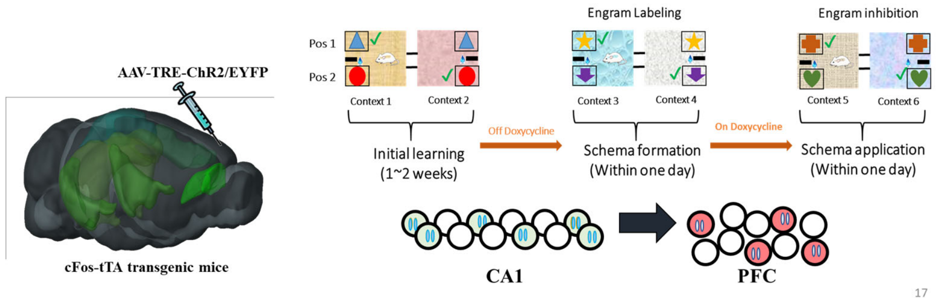


Figure 3. This project will combine genetic. physiological and behavioral approaches to tag, manipulate and record neurons encoding memory schemas in behaving mice, focusing on the frontal cortex where schema-related neuronal activity has been reported. A context-cue association task designed to study memory scheme. Initial training (left) is a slow process, but subsequent learning of similar tasks (center) is rapid due to schema formation. Genetic approaches to engram labeling and manipulation can test the underlying mechanisms that allow rapid learning of related information.

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