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

Broad Section G

Title of Project： Elucidating the Dynamics of Memory

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Research Project Number：19H05646　Researcher Number：50553731
Keyword：hippocampus, cortex, memory, oscillations

【Purpose and Background of the Research】

Information in the brain is conveyed by the spiking of neurons and the computations underlying memory require these spikes be organized, both spatially and temporally. This is achieved through rhythmic oscillations, a fundamental mechanism of communication and organization throughout the brain. Here we will build on our work in the control and decoding of the physiology of memory to investigate how oscillations in hippocampal/cortical circuits organize the information required for memory and how temporally organized information is altered by dysfunction and disease. Combining novel optogenetic techniques with *in vivo* physiology and computational and analytical approaches we will address several fundamental questions:

•What determines which of a brain's millions of neurons contribute to a given memory trace?
•How are those neurons interconnected, and how does that trace evolve with time and experience?
•How are those neurons engaged during memory consolidation and recall?
•Can memory loss due to aging and disease be treated by intervention to improve synchronous activity?

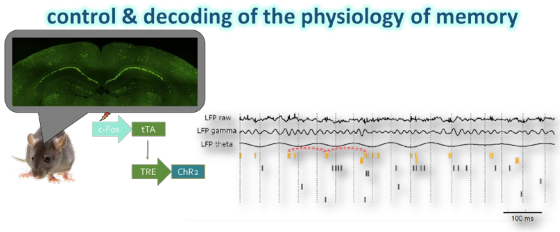

Fig. 1

【Research Methods】

We have recently combined our expertise in physiology with the emerging technology of memory engram labeling, based on the combination of immediate early gene expression and optogenetics, to functionally tag, identify & manipulate neurons involved in the encoding of a specific memory (Fig. 1). Building on this we will collect and analyze high-density recording of neuronal activity in the other regions of the hippocampus and cortex, allowing us to examine the interactions of neurons across brain regions during memory consolidation and recall. Further, the identification of a general signature of neurons engaged by memory will allow us to train algorithms with data from the high density recording to permit the identification of engram neurons based on physiology alone, without the need for optogenetic identification. These efforts will allow us to create models to classify memory age and quality based on physiology (Fig. 2) and better understand how temporal and spatial organization of activity can improve memory and brain health in cases of disease.

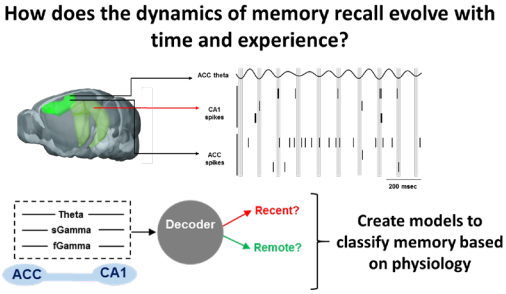

Fig. 2

【Expected Research Achievements and Scientific Significance】

This research will build on our ability to disambiguate information (spiking) and oscillations in the encoding, consolidation and recall of a specific memory. These advances leave us in a unique positon to investigate the mechanisms of integration of information and oscillations across regions of the brain and reveal their individual roles in memory, as well as yield insight to treatments of disorders involving aberrant neural dynamics.

【Publications Relevant to the Project】

Tanaka et al (2018) The hippocampal engram maps experience but not place. Science, 361(6400):392-397.
Middleton et al (2018) Altered hippocampal replay is associated with memory impairment in mice heterozygous for the SCN2A gene. Nature Neuroscience, 21(7):996-1003.
Middleton and McHugh (2016) Silencing CA3 disrupts temporal coding in the CA1 Ensemble. Nature Neuroscience, 19(7): 945-951.

【Term of Project】

FY2019-2023

【Budget Allocation】

127,900 Thousand Yen

【Homepage Address and Other Contact Information】

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