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

Cellular representation of abstractive space "spatial context cells" - their formation and role in long-term memory

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Purpose and Background of the Research

●Outline of the Research

Once memories are formed, they are gradually transferred to other areas of the brain for long-term storage. This process is called "memory consolidation," but it is not clear what kind of changes occur at the cellular level, when, and in which brain regions. One cellular phenomenon of memory that has become known is long-term potentiation (LTP), in which synaptic responses are potentiated over a long period of time. We have recently shown that LTP during sleep is important for memory consolidation (Goto et al., Science). On the other hand, we also found neurons that may be responsible for abstract spatial memory and named them spatial context cells. Interestingly, spatial context cells share similarities with memory consolidation in their properties and formation (Bota, in preparation for submission). Therefore, based on the hypothesis that "spatial context cells are the identity of long-term spatial memory," this study will investigate how sleep LTP is involved in its formation and what role it plays in memory.

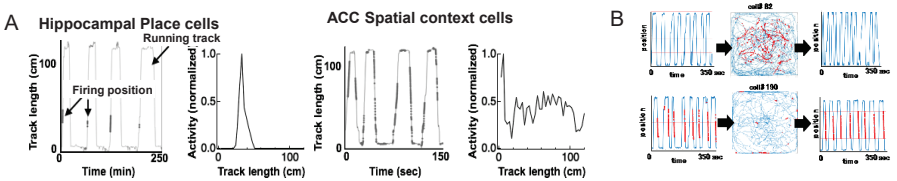

Figure 1: Formation of hippocampal place cells and spatial context cells in the cortex.
A: Place cells (left) fire at specific locations along the travel path, whereas spatial context cells in the anterior cingulate cortex (right) fire throughout space; B: In contrast, spatial context cells are space-specific and do not fire elsewhere; C: Spatial context cells fire in the hippocampus, but not in the cortex; D: Spatial context cells fire in the anterior cingulate cortex, but not in the anterior cingulate cortex.

In this study, the following four specific aims will be established.

SA1 Prove that cells with convergent place cell replay activity during sleep become spatial context cells

We hypothesized that the replay of hippocampal place cells during sleep causes LTP at synapses between cells in the ACC and the hippocampal place cells, which in turn facilitates the firing of ACC cells and makes them spatial context cells. As a first step to prove this hypothesis, we will record neural activity during sleep with EEG by Ca^{2+} imaging and examine whether cells observed to be active in the ACC when replay is observed in the hippocampus subsequently become spatial context cells.

SA2 Investigate the necessity of LTP in ACC cells for the formation of spatial context cells.

To examine whether inhibiting LTP by optogenetically suppressing ACC neuronal activity at the same time as electrophysiologically, we will inhibit REPLAY and test the formation of spatial context cells and memory recall.

SA3 Investigating the Necessity of Spatial Context Cells for Memory Recall

By taking advantage of the fact that spatial context cells express the immediate early gene product c-fos, which is expressed in a neural activity-dependent manner, we will express ArchT, an inhibitory light-driven pump, in spatial context cells. We will examine whether this suppresses memory recall.

SA4: Investigation of the sufficiency of spatial context cells for memory recall

To confirm whether spatial context cells are responsible for memory, we will examine whether optogenetically reactivating only spatial context cells induces memory behavior in that space. For this purpose, we will use an "all-optical approach" to optically detect spatial context cells and stimulate them.

Expected Research Achievements

We will attempt to elucidate the mechanism of memory consolidation at the cellular level. Spatial context cells are downstream of place cells in the hippocampus and grid cells in the olfactory entorhinal cortex. Therefore, our study will be a major breakthrough into the next elucidate of spatial information coding. By clarifying the mechanism of memory consolidation, we expect to be able to more detailed circuit mechanisms in the future. In addition to making a broad contribution to the elucidation of memory, which is one of the great mysteries remaining to mankind, this research will also lead to the understanding of diseases such as PTSD that cause abnormal memories and the development of treatments.

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