論文の内容の要旨

A Study on Functional Roles and Mathematical Structure of Switching of Hippocampal Local Field Potentials between Distinctive Dynamical States

（海馬局所場電位の異なる動的状態間切り替えの機能的役割と数理構造に関する研究）

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Hippocampus is a brain region of the brain known for its higher cognitive function such as learning, memory, contextual dependency and spatial navigation. It has attracted much attention not only because of its beautiful structural organization and its functional significance, but also because of its clinical importance in some diseases such as dementia, aging, depression and epilepsy. The extensive amount of the knowledge of the anatomical structure and physiological properties of the hippocampus has also attracted theoretical approaches. Elucidating the mechanism of the hippocampal function is one of the most important themes in neuroscience concerning the mammalian brain.

It is believed that the function of the hippocampus is closely related to the dynamics of hippocampal local field potential (LFP). Especially, it is well known that the states of the hippocampal local field potentials are divided distinctively into mutually exclusive states: theta rhythm and non-theta state. The theta rhythm is a highly periodic activity thought to play an important role in storing and retrieving memories. The major non-theta state is referred to as large irregular amplitude activity (LIA), which is a irregular field activity with sharp ripple complex and thought to play an important role in the consolidation process of old memories.

In spite of extensive efforts, the mechanism of generating the distinctive characteristic dynamics of hippocampal LFP and the functional relevance of them have not been understood yet. In order to fully understand the mechanism underlying the neurodynamics and the function of the brain, a combined effort of both experimental and theoretical approach is needed.

In chapter 1, the general introduction for the present studies devoted to the elucidation of the functional role of state transition in the hippocampal LFP and mechanism of the transition is stated.

In chapter 2, an experimental study which examined local field potential of the hippocampus to monitor the brain states during a conditional eyeblink conditioning is described. In this study, five rats underwent a serial feature positive conditional discrimination task in eyeblink conditioning using a preceding light stimulus as a conditional cue. In this task, the light stimulus signaled that the following tone conditioned stimulus (CS) is reinforced with a periorbital electrical shock. The same tone stimulus was not reinforced when the conditional stimulus was not presented. The duration of the conditional cue was 2 seconds and the interval between the end of conditional cue and the onset of the CS averaged 4 s (4 ± 1). The animals successfully acquired differential respondings to the single CS utilizing the preceding light stimulus as the conditional cue. It was found that the presentation of conditional cue elicited hippocampal theta oscillation which showed sustained activity during the interval of conditional cue and the CS. Moreover, the expression of successive conditioned response (CR) correlated with expression of the theta oscillation immediately before the onset of CS. These data support hippocampal involvement in the network underlying conditional discrimination in eyeblink conditioning and also suggest that hippocampal activity determines the information processing for the tone stimulus in cerebellum and its associated circuitries.

In chapter 3, we propose a mathematical model of the state transition of the hippocampal local field potential between the theta rhythm and the large irregular activity. With this model, we propose a possible role of chaotic dynamics in the generation of two distinctive rhythm patterns of the local field potential. In this study, we model hippocampal inhibitory network with electrically coupled class 1 model neurons. Furthermore, we show that periodical external force modelling the oscillatory ascending activity from the medial septum, which is assumed to be the theta rhythm generator experimentally, can entrain the model network and change the network state rapidly to synchronized state.

In chapter 4, we conduct nonlinear time series analysis of the LFP. The Wayland's method is used here to test the determinisity in the time series of the LFP using three types of surrogate data. Significant determinism is discovered in the time series. We also visualize the nonlinear dynamics of the LFP by the mean of recurrence plots.

In chapter 5, the general conclusion and discussion are described.