Chapter 50
Neural Ensembles and Local Field Potentials in the Hippocampal-Prefrontal Cortex System During Spatial Learning and Strategy Shifts in Rats

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Abstract To better understand the mechanisms of hippocampal-cortical signalling for mnemonic function and behavior, we recorded ventral hippocampal local field potentials (LFPs) simultaneously with ensemble neural activity and LFPs in the prefrontal cortex in rats learning and switching strategies in a Y-maze variant of the Wisconsin Card Sorting Task. Behaviorally correlated activity of individual neurons changed after task contingency changes or as the animal adopted different strategies. Curiously, within ensembles of simultaneously recorded neurons, individual neurons showed different responses to contingency or strategy while others did not change at all. Furthermore some prefrontal neurons are significantly modulated by hippocampal theta activity and also by hippocampal sharp waves (with 150 Hz ripples). Finally we present data showing that coherence between the hippocampus and prefrontal cortex in the theta band is behaviorally modulated. These observations provide evidence for engagement of hippocampal signals by prefrontal neurons as a mechanism underlying learning this task.

Keywords Memory · EEG · unit recordings · theta · coherence · prelimbic area

Introduction

The hippocampus and prefrontal cortex are sometimes attributed complementary functions for memory processing (memory consolidation and working memory respectively), which must be reconciliated with the fact that there is a direct hippocampal-prefrontal pathway in the rat. The problem may however be a problem of interpretation, since experimental interventions inducing local inactivation in one

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structure or the other often lead to the assignment of distinct functions to individual structures. Thus neuropsychological studies employing inactivation protocols must be complemented by other approaches such as unit activity recordings. However interpretation of many recording studies of this system is hampered by experiments being carried out on overtrained animals. Thus the experiments described here concern cell activity in animals still learning.

While recordings of single neurons, of evoked potentials and of images of brain activation shed light on fundamental processes, it is our belief that it is also important to focus on recordings of ensemble activity and its relations with local field potentials in order to integrate findings at these three orders of magnitude and hence elucidate dynamic functional mechanisms for cognitive functions. Of particular interest is synchronous oscillatory activity which has received much recent attention as a reference for phase coding of neuronal discharges, and may also underlie mechanisms of synchronization and privileging communication among select distant brain areas, as in 'binding'.

Thus we developed a variant of the Wisconsin Card Sorting Task for rats. Performance in this task is known to be impaired in neurological patients suffering from damage to the prefrontal cortex. Once the rats had been familiarized with the maze, tetrode recordings were made of local field potentials in ventral hippocampal CA1 and prefrontal (prelimbic area) as well as ensemble activity of prelimbic neurons.

Methods

Prefrontal neurons as well as prefrontal and hippocampal LFPs were recorded from multiple tetrodes in rats successively learning four reward contingency strategies on a Y maze: go right, go to the lit arm, go left, then go to the dark arm (the lit arm was selected randomly). Rats were required to return to the start arm after consuming the chocolate milk reward. A delay of 5 s was imposed between trials.

In analyses, modulation by theta was defined as the amplitude of the sine-wave fitting the phase histograms of one cell spikes' phases relative to theta. Modulation by sharp waves is taken as the logarithm of the ratio between mean firing rate of a cell in a 100 ms window surrounding (± 25 ms) ripples' amplitude peak and the mean firing rate of the cell in a window lasting from 1 s to 50 ms before ripple peaks.

Results

Hippocampal LFP and medial prefrontal neurons and LFP were recorded in five freely moving rats during 98 recording sessions in a Y maze and in previous and subsequent sessions of quiet repose.

Task-Related Shifts in Behavioral Correlates

In 238 of the 1894 neurons analysed, there were abrupt changes in firing correlates following changes in the task rule ($n = 99$) or in the rat's strategy ($n = 139$). These changes included appearance of a new behavioral correlate or reduction in behaviorally correlated activity. Other neurons discriminated from the same tetrode showed no such changes reducing the risk that this corresponds recording instability. Within groups of simultaneously recorded neurons, the reaction to the task or strategy shift varied.

Hippocampal Theta Modulation and Sharp Wave ('Ripple') of Prefrontal Neurons

In 35% of the 2230 cells analysed, action potentials were significantly phase modulated by hippocampal theta during task performance (Rayleigh test, $p < 0.05$) as shown previously. Furthermore, in 21%, firing rates increased (11%) or decreased (10%) during hippocampal ripples occurring during previous or subsequent resting periods (t-test, $p < 0.05$). (Modulation by sharp waves is taken as the logarithm of the ratio between mean firing rate of a cell in a window surrounding (± 25 ms) ripples' peak and the mean firing rate of the cell in a window lasting from 1 s to 50 ms before ripples' peak.) In 10% of the cells there was significant modulation by both theta and ripples, and the amplitude of these respective modulations was significantly correlated (Pearson's correlation test, $p < 0.05$). This correlation may correspond to the strength of hippocampal afferences to the respective neurons and their local circuits, suggesting that the hippocampal/prefrontal interaction is mediated by the same population of prefrontal cells both during sleep and active behavior.

LFP Coherence Between Hippocampus and Prefrontal Cortex in the Theta Band

A robust theta rhythm at 6–8 Hz was observed in the prefrontal LFP. During learning, high hippocampal-PFC coherence (values > 0.7) in the theta band (5–10 Hz) was observed. This occurred principally at the decision point in the maze, suggesting heightened communication between hippocampus and PFC at the moment of behavioural choice.

Discussion

These results demonstrate that the hippocampal-prefrontal system was engaged by this variation of a set-shifting task that is used to diagnose prefrontal dysfunction in human patients. The transitions in cell activity corresponded to the rat's strategy shifts may reveal an underlying mechanism of prefrontal action in this task. In previous recordings of rats switching strategies (albeit with triggering cues) [1] we observed comparable changes in responses in prefrontal afferent zones of the nucleus accumbens, but not hippocampal place cells which also project to accumbens [2].

This is consistent with the hypothesis that this 'set-shifting' activity is mediated by the prefrontal cortex.

The observation of prefrontal neurons modulated by hippocampal theta oscillatory activity and by hippocampal sharp waves demo nstrates nevertheless that there is a powerful hippocampal influence on a subset of prefrontal neurons. This is hypothesized to correspond to a pathway transmitting signals for executing strategies requiring contextual information such as spatial position.

The behaviorally modulated coherence of simultaneously recorded hippocampal and prefrontal LFPs reinforces the latter evidence for hippocampal influences on the prefrontal cortex. Conversely, the reduced modulation during behaviors other than the decision period suggests that perhaps other brain areas are oscillating coherently with the prefrontal cortex then. This is reminiscent of the observations of greater incidence of cross-correlations between neurons of the hippocampus and the nucleus accumbens during approaches to a goal site, but not during return visits [3]. This suggests that certain circuits can be selectively gated in a behaviorally relevant manner.

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References

1. Shibata, R., Mulder, A.B., Trullier, O., Wiener, S.I.: Position sensitivity in phasically discharging nucleus accumbens neurons of rats alternating between tasks requiring complementary types of spatial cues. Neuroscience 108 (2001) 391–411.
2. Trullier, O., Shibata, R., Mulder, A.B., Wiener, S.I.: Hippocampal neuronal position selectivity remains fixed to room cue in rats alternating between place navigation and beacon approach tasks. Eur. J. Neurosci. 11(12) (1999) 4381–4388.
3. Tabuchi, E., Mulder, A.B., Wiener, S.I.: Position and behavioral modulation of synchronization of hippocampal and accumbens neuronal discharges in freely moving rats. Hippocampus 10 (2000) 717–728.