Neural Correlates of a Spatial Learning Task in Parietal Cortex, Prefrontal Cortex and Hippocampus

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Learning and execution of complex behaviours require interactions between networks of neurons that encode, store and share information across numerous brain regions. Systems level analyses of how the brain processes information are therefore central to understanding how behaviour is generated. Spatial learning in rodents constitutes a useful model in which to correlate neurophysiology with cognitive behaviours. We studied neuronal activity recording multiple individual neurons and local field potentials from chronically implanted tetrode arrays in the posterior parietal cortex (PPC), the medial prefrontal cortex (mPFC) and the hippocampus (HPC) of rats while they were trained in a maze task that involved decision making, working memory and rule learning based on spatial navigation. To date, recording single neuron firing from multiple brain areas in behaving animals is an unparalleled approach to shed light on the neuronal mechanisms underlying behaviour with millisecond resolution [1].

A key feature of hippocampal activity is the firing of place cells, HPC principal neurons encoding the spatial location of an animal. Like the HPC, the PPC is involved in spatial processing, with PPC neurons selectively responding to navigational features that are also represented in the HPC, such as directed body movements and spatial novelty [2]. Interestingly, there is no direct anatomical connection between PPC and HPC, yet the simultaneous processing of spatial information renders their coordination highly likely. In recent years, evidence accumulated that PPC neurons are concurrently controlled by a range of spatial and non-spatial features, involving temporal sequence and intention [3, 4, 5]. Like the mPFC, the PPC is part of the association cortex, which is thought to be the key site for integrating sensory and internal information to form decisions. PPC and mPFC receive a wide range of sensory afferents [6] and neurons in both structures have been found to adaptively respond to current cognitive demands [7, 8]. In addition, lesions of either brain region lead to impaired spatial learning [9, 10]. We hence expect spatial information to be coordinated between PPC, mPFC and HPC. A mechanism of how neuronal activity can be coordinated within and across brain regions has been linked to the second hippocampal hallmark, the theta rhythm, a 4-12 Hz oscillation arising during spatial exploration and other complex behaviours requiring working memory and decision making. Recent studies suggest that phase-locking of neuronal firing to hippocampal theta frequency underlies the functional connectivity between brain regions involved in solving complex spatial tasks [11, 12]. Furthermore, LFP coherence across distant brain regions has been suggested as a measure of synchronised neuronal activity, indicating transient coordination [11, 13]. We set out to assess how spatial information is differentially encoded in PPC, mPFC and HPC and how information processing is coordinated between these brain regions.

To this end, we chronically implanted rats with microelectrode arrays consisting of 20 individually adjustable tetrodes distributed over PPC, mPFC and HPC. In each brain region, we simultaneously recorded spiking activity of multiple individual neurons and local field potentials (LFP) as a measure of neuronal population activity. Recordings were made over up to seven weeks from each rat while they were trained on two subsequent sets of rules on an end-to-end T-maze. For each set of rules, rats were trained to perform 85% correct trials per day. The maze tasks involve distinct working memory and decision-making (choice) episodes and control (guided) episodes, which are spatially segregated. Same clock time-stamping was used for the neurophysiological recordings at a rate of 2 kHz for LFP and 32 kHz for action potential recordings and video-tracking of the animal's position via head-mounted diodes at a frame rate of 25 Hz. This experimental approach enabled us to assess coordination of neuronal activity on the single cell and population level within and across brain regions in relation to distinct task episodes, spatial location and training stages. Specifically, we analysed the firing patterns of each neuron using linearised firing rate maps with a spatial bin size of 11 cm, shuffle-corrected cross-correlations of spike trains of ± 0.5 seconds and 5 ms bins, and multi-taper Fourier analysis with a frequency resolution of 3 Hz and a temporal resolution of 0.5 seconds to calculate LFP coherence. We compared these parameters in choice versus guided trials to assess the impact of cognitive load and decision. Correct versus error trials were compared to determine the neurophysiological and temporal origin of error. For all trial types, left hand and right hand trials were analysed separately to examine the spatial component of solving the task. Finally, all analyses were performed at different training stages to check for neurophysiological correlates of learning.

As shown previously, HPC and PPC are required for spatial navigation, while HPC and mPFC are critically involved in working memory and are coherently active during decision making. Accordingly, we expected all three brain regions to be activated differentially during task episodes and learning stages that selectively recruit working memory, decision-making and rule acquisition. We demonstrate that spatial features were crucially involved in determining firing patterns in all three areas, but trajectory encoding was highly complex and not limited to spatial features in the cortical areas. While hippocampal firing was almost entirely controlled by location and running direction, the neuronal code in the cortical areas was determined by a combination of factors such as location, start-to-goal sequence, turn sequence and correct versus error trials. PPC and mPFC neurons hence exhibited much more complex firing patterns than place cells, nevertheless the patterns were highly reproducible on a trial-by-trial basis. Analysis of LFP coherence and single neuron activity across brain regions revealed task episode-specific coordination of neuronal activity in a training-dependent manner. In summary, we present an experimental approach that is able to shed light on the fundamental nature of information coding, sharing and integration in the brain.

All procedures were conducted in accordance with the UK Animals (Scientific Procedures) Act, 1986 and with the approval of the University of Bristol Ethics Committee.

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