



Neural representations in human spatial memory

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Ekstrom *et al.* report the responses of single neurons recorded from the brains of human subjects performing a spatial navigation task in virtual reality. They found cells encoding the subject's current location, view and destination. These data, and related findings in animals, directly reveal some of the representations underlying spatial cognition. They highlight the potential for cognitive psychology and systems neuroscience to combine to provide a neuronal-level understanding of human behaviour.

In a recent paper Ekstrom and colleagues [1] report the first single-unit investigation of the neural representations supporting human navigation. Extra-cellular recordings were made from single neurons in the hippocampus, amygdala, parahippocampal and prefrontal cortices of seven patients with pharmacologically intractable epilepsy. Although the use of intra-cranial EEG depth electrodes for localizing epileptic foci in such patients is widespread, the use of single-unit recording is currently very rare and offers a unique insight into the mechanisms of human cognition. In addition, Ekstrom and colleagues made use of another recent technological advance, virtual reality (VR), to investigate large-scale spatial behaviour in a controlled situation (see also studies reviewed in [2]). The recordings were made while the subjects were playing the part of a taxi driver in a small town who searched for passengers and took them to their destinations. The towns consisted of 9 buildings in a grid, 3 of them shops, each with the same distinctive shop-front on all sides. The shops served as destinations.

Experimental findings

Cellular activity was correlated with the subject's location in the town (their 'place'), what they could see (their 'view') and where they were trying to get to (their 'goal'). A 'place' response was one where the cell fired whenever the subject was in a given location in the town irrespective of his or her orientation i.e. independent of the actual view of the subject. A 'view' response was a response to a particular view e.g. looking at a particular shop-front in the town (note that similar responses were not evoked by shop-front patterns presented alone in 2D). View responses could be location specific or not. A 'goal' response was an increase in firing rate whenever the subject was searching for a specific destination (when delivering a passenger) or, in some cases, whenever the subject was searching for the next passenger.

279 neurons were subjected to analysis of variance in terms of the three factors: 26% showed a main effect of place, 12% of view, and 21% of goal. Sixteen percent of cells showed interaction effects only. More selective criteria revealed that 11% of cells responded purely to spatial location independent of view, i.e. showing no effects of view or place by view interaction. Of these 'pure' place cells, 26% also showed a place by goal interaction. Of the view cells, 73% responded to a single shop-front, and 58% of these were viewpoint independent (i.e. they showed no view by place interaction, firing whenever the shop-front was on the screen from whatever viewing location). Of the goal cells, 22% responded while the subject searched for passengers, 71% responded while searching for a specific store and 7% responded while searching for more than one store. Some significant structure-function relationships exist in these data: place responses clustered in the hippocampus to a greater extent than in the parahippocampus (24% of hippocampal cells being 'pure' place cells versus 8.5% in the parahippocampus), and 'pure' location-independent view cells clustering in the parahippocampus (17% versus 5% in the hippocampus).

Relation to previous work in rats, monkeys and humans

These data are consistent with previous single-unit recording work in animals, including the finding of place cells in the hippocampus of rats [3–5] and monkeys [6] and the finding of viewpoint-independent spatial view cells in the vicinity of the hippocampus in monkeys [7]. On the other hand, the demonstration of goal-responsive cells is a distinct advance on the previous animal research. Previous findings in rats showed modulation of the pattern of place cell firing according to whether or not a goal was being approached, or which of two well-learned trajectories the rat is running along [8,9]. However, similar modulation according to the rat's destination was not found in experiments in which the rat's trajectory was less stereotyped [10,11], leaving open the question of whether the goal responses were more related to past behaviour than to future intentions. The present results unambiguously demonstrate the existence of goal-related cells in the human hippocampus and related regions.

Ekstrom *et al.*'s results support a functional division within the medial temporal lobe such that the hippocampus is involved in spatial navigation whereas the parahippocampus is involved in the identification of landmarks and spatial scenes. Previous functional neuroimaging studies of human navigation, many using VR, have shown involvement of the hippocampus (reviewed in [2]) consistent with the higher density of place cells found

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there in the present study. Similarly, electrophysiological studies in rats have demonstrated the link between the place-cell representation and the behavioural response in spatial memory tasks [12–14], and lesion studies in rats (e.g. [15]) and human neuropsychology (reviewed in [2]) have demonstrated the importance of the hippocampus in spatial navigation and related tasks. By contrast, activation of the parahippocampus has been found when the subject views spatial scenes [16], and damage there can produce landmark agnosia (reviewed in [17]) as well as consequent impairments in navigation, consistent with the higher density of viewpoint-independent view cells found there. This area might thus be best described as the Parahippocampal Spatial Scene Area (rather than ‘Place Area’ [16]). The pattern of functional activations, lesion deficits and the current single-unit results would be consistent with a parahippocampal representation of environmental boundaries being used to drive the hippocampal place response [2,18,19].

Theoretical implications

A central problem within cognitive psychology illuminated by the Ekstrom paper is whether allocentric mental representations are required for spatial memory and navigation, or whether purely egocentric ones suffice. Some models assume the latter [20,21], whereas others suggest that both allocentric and egocentric representations are required ([22,23] and Burgess, N. *et al.*, submitted). One of the problems here is that a given behavioural result might theoretically be achieved in several different ways. The ability to directly observe the neural code in structures known to support a given behaviour radically changes the nature of this problem. Thus, the proposal of an allocentric representation of space, or ‘cognitive map’, by O’Keefe and Nadel [4] was primarily driven by the discovery of place cells in the rat hippocampus. Their discovery in the human hippocampus similarly supports the existence of representations of a subject’s environmental location independent of their orientation, and their use in hippocampal-dependent tasks such as navigation.

Data of the type reported by Ekstrom and colleagues raise the challenge to integrate neuronal-level with process-level models to produce complete models of the neural mechanisms of spatial cognition going from sensory input to behaviour. This would enable prediction of human behaviour in spatial tasks, and of the effects on behaviour of differences in the brain due to pharmacological intervention, or population differences due to disease, age or gender. Computational modeling will clearly be important for quantifying the implications of information at one level on processing at another level, if only because of the complexity of the system. In this regard, the similarities between the responses found in humans and those found in rats make it tempting to try to predict human spatial behaviour based on our detailed knowledge of the firing of place cells in rats (Hartley, T. *et al.*, submitted). In turn, the details of Ekstrom *et al.*’s findings imply further modification of such models. For example, the cell that fires whenever one specific store is viewed while the subject is searching for a second specific store (see Ekstrom *et al.*,

supplementary Fig. 2) is suggestive of the use of a representation of the relative locations of stores, but how such a mechanism might actually work requires further computational analysis.

In conclusion, the study reported by Ekstrom *et al.* highlights the exciting window of opportunity that is opening up for interaction between the fields of cognitive psychology and systems neuroscience, possibly mediated by computational modeling. We would expect the meeting of these two fields to have far-reaching implications for our understanding of spatial cognition in humans. It is also possible that insights gained from understanding the neural mechanisms underpinning spatial memory will provide a starting point for understanding the neural bases of other functions, such as the long-established role of the human hippocampus in context-dependent episodic memory (e.g. see [4], Chapter 14).

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