Research Focus

Complementary memory systems: competition, cooperation and compensation

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Spatial navigation depends on dissociable memory systems that have distinct neural bases and employ different forms of representation. One system gradually acquires reliable sequences of responses to given situations (e.g. repeatedly following a fixed route), and depends on the striatum. The other develops flexible representations permitting novel responses (e.g. finding new shortcuts), and depends on the hippocampus. Voermans and colleagues explore the interaction between these two systems using functional neuroimaging and behavioural measures in a clinical population.

Introduction

Voermans and colleagues [1] used fMRI to investigate the neural bases of memory for routes in patients with Huntington's disease (HD) – a heritable neurodegenerative disorder characterized by progressive atrophy of the corpus striatum (caudate nucleus, putamen and globus pallidus). They examined the relationship between disease severity (as measured by standardized behavioural indices [2]) and task-related activation in the caudate nucleus and hippocampus. Their results are interesting in themselves, and also link together several intriguing historical and recent strands of investigation into the neural bases of memory.

Memory for routes was tested by viewing first-person-perspective video sequences of a path around a virtual house. During the encoding phase the video paused at five decision points for arrows to indicate the possible turn directions. At each point participants had to remember the direction to be taken (indicated by highlighting one arrow). During the navigation phase subjects saw the same sequence and indicated the direction taken at each decision point (none of the arrows being highlighted). Interspersed between these conditions were a visuomotor control condition and a rest period. Subjects completed 14 cycles of this procedure, each cycle using a distinct but topologically similar virtual environment. The main finding was a link between behavioural indices of disease progression and the relative involvement of the caudate and hippocampus in the navigation task. Patients with less severe symptoms showed greater activation of the caudate, whereas patients with more severe symptoms showed increased hippocampal activation. This suggests that the hippocampus could compensate for caudate dysfunction in more advanced HD.

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Dissociations in learning and memory

Voermans and colleagues' finding is consistent with animal studies suggesting that the hippocampus and dorsal striatum have distinct but complementary functions (reviewed in Ref. [3]). The caudate is crucial for the acquisition of 'habits' – stereotypical responses to repeatedly reinforced situations, such as learning to turn right at a particular point in a route [4] or to approach one cue rather than another [5]. Behaviours involving more flexible responses contingent on multiple cues depend on the hippocampus. These include finding a direct path to a hidden goal location from an arbitrary starting location [6], or learning to avoid previously visited locations in an efficient search [7]. Single-unit recording suggests that these behaviours are supported by a specialized representation of location in the hippocampus: 'place cells' seen in rodents [8] and humans [9] whose firing rates vary with the location of the animal, independent of other factors such as orientation.

Behavioural differences relating to hippocampal or caudate involvement have also been found in humans. After free exploration in a virtual town, greater hippocampal activation is associated with more accurate navigation [10,11]. This effect is largely driven by individual differences: more accurate navigators show greater hippocampal activation when finding new routes. Interestingly, the same individuals show greater activation of the caudate when following a well-learned route than when finding new routes [11], whereas poor navigators show the reverse pattern. In a related study, Iaria and colleagues [12] showed that solving a virtual eight-arm-maze task by remembering the relationship of target locations to distant visual cues was associated with greater hippocampal activation, whereas solving it using a rote-counting strategy was associated with greater caudate activation.

Complementary representations: competition and cooperation

The spatial studies reviewed here are consistent with the hippocampus providing a flexibly applicable or map-like representation of the environment, with more inflexible route-following or cue-approach behaviours provided by the striatum [13]. This distinction extends to non-spatial tasks, with the hippocampus more generally associated with 'flexible relational' [14] or 'declarative' [15] memory. For instance, the hippocampus is involved in learning novel paired associates, whereas the caudate is involved in

the gradual learning of similar material through reinforcement [16,17].

The presence of distinct systems operating in parallel raises the question of how one or other comes to drive behaviour. Voermans and colleagues describe the interaction between the systems in terms of cooperation, although other authors refer to competition [18]. Both positions have some truth: in some tasks, cooperation is possible because the parallel systems support compatible behaviours, whereas in other tasks they drive conflicting responses and must therefore compete to control behaviour [19]. In the case of the striatal and hippocampal systems, there are some in-built asymmetries. The hippocampus is well adapted to rapid learning. It tends to control behaviour early in learning, with control passing to the caudate only after many repeated trials [4,12,16]. The greater flexibility of hippocampal processing causes an asymmetry in the ability of one system to compensate for damage in the other. By providing a complementary representation, the hippocampus can compensate for caudate dysfunction in the route memory task [1], but the caudate could only be expected to compensate for hippocampal dysfunction in very constrained circumstances (e.g. where a well-learned route is available). Thus, although HD patients showed preserved route recognition, hippocampal damage severely impairs allocentric spatial memory [20].

Revealing functional interactions through pathology and genetics

Voermans and colleagues' demonstration of a remote effect of dysfunction in one region (caudate) upon activation in a distant region (hippocampus) is a powerful method for revealing functional interactions between regions. A similar approach recently showed that amygdala pathology modulates both hippocampal involvement in encoding emotional memories [21] and the response of the fusiform gyrus to fearful faces [22]. Indeed, the amygdala is thought to constitute a third complementary memory system [3], mediating learned associations between neutral stimuli and reinforcers.

Finally, because the genetic basis of HD is well understood [23], Voermans and colleagues' study begins to expose the neurogenetic bases of spatial memory in humans. Future work in this field is also likely to include the role of normal genetic variation in human spatial memory and in interactions among the hippocampus, caudate and amygdala. A recent example of this approach [24] showed that a common polymorphism of the brain-derived neurotrophic factor (BDNF) genotype accounts for a substantial proportion of variance in performance-related activation of the hippocampus during a spatial memory task.

Concluding remarks

Decades of research in animals and humans have produced a compelling picture of multiple complementary memory systems in the brain. Voermans and colleagues' study adds to the developing understanding of the way these systems interact to control behaviour. It also highlights some of the exciting possibilities that are emerging as behavioural and neuropsychological methods are increasingly combined with recent advances in neuroimaging and genetic techniques.

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