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Impairments in precision, rather than spatial strategy, characterize performance on the virtual Morris Water Maze: A case study

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ABSTRACT

Damage to the medial temporal lobes produces profound amnesia, greatly impairing the ability of patients to learn about new associations and events. While studies in rodents suggest a strong link between damage to the hippocampus and the ability to navigate using distal landmarks in a spatial environment, the connection between navigation and memory in humans remains less clear. Past studies on human navigation have provided mixed findings about whether patients with damage to the medial temporal lobes can successfully acquire and navigate new spatial environments, possibly due, in part, to issues related to patient demographics and characterization of medial temporal lobe damage. Here, we report findings from a young, high functioning patient who suffered severe medial temporal lobe damage. Although the patient is densely amnestic, her ability to acquire and utilize new, but coarse, spatial "maps" appears largely intact. Specifically, a novel computational analysis focused on the precision of her spatial search revealed a significant deficit in spatial precision rather than spatial search strategy. These findings argue that an intact hippocampus in humans is not necessary for representing multiple external landmarks during spatial navigation of new environments. We suggest instead that the human hippocampus may store and represent complex high-resolution bindings of features in the environment as part of a larger role in perception, memory, and navigation.

1. Introduction

The ability to navigate is a vital skill for both animals and humans alike. One prominent idea proposed by Tolman (1948) is that the brain forms a cognitive map that represents a spatial environment in a metric, map-like format. Cognitive Map Theory (CMT) further posits that the hippocampus, a bilateral medial temporal lobe (MTL) structure, is both responsible and necessary for forming map-like representations of the environment (O'Keefe and Nadel, 1978). In particular, CMT argues that navigation combining multiple distal cues to derive locations in space ("allocentric navigation") depends on the hippocampus. In contrast, navigation involving egocentric cues, or locations referenced to one's current position, does not depend on the hippocampus. Support for this idea comes from computational theories based on the neural architecture of the hippocampal formation and the fact that "place cells," neurons that code an animals location, are present in the hippocampus (O'Keefe and Dostrovsky, 1971; Samsonovich and McNaughton, 1997), and alter their firing depending on changes in the location of distal cues (Muller and Kubie, 1987; O'Keefe and Speakman, 1987). Another critical line of support involves the detrimental effect of hippocampal lesions on spatial memory, or more specifically, gross impairments in the ability to find a hidden location via reference to distal landmarks in the environment. (Eichenbaum et al., 1999; Morris et al., 1982; White and Wallet, 2000). Thus, two critical lines of research provide support for CMT, the "map-like" nature of place cells and the fact that hippocampal lesions abolish the ability of rodents to find a location based on external landmarks in the environment.

One paradigm extensively used to demonstrate the necessity of the hippocampus to spatial memory is the Morris Water Maze (Morris, 1984; Morris et al., 1982). A basic finding, replicated across numerous studies in rodents, is that lesions to the hippocampus abolish the ability of a rat to find a hidden platform using cues outside of a pool of water (termed allocentric cues). These same lesions, however, do not affect the ability of the rat to find a

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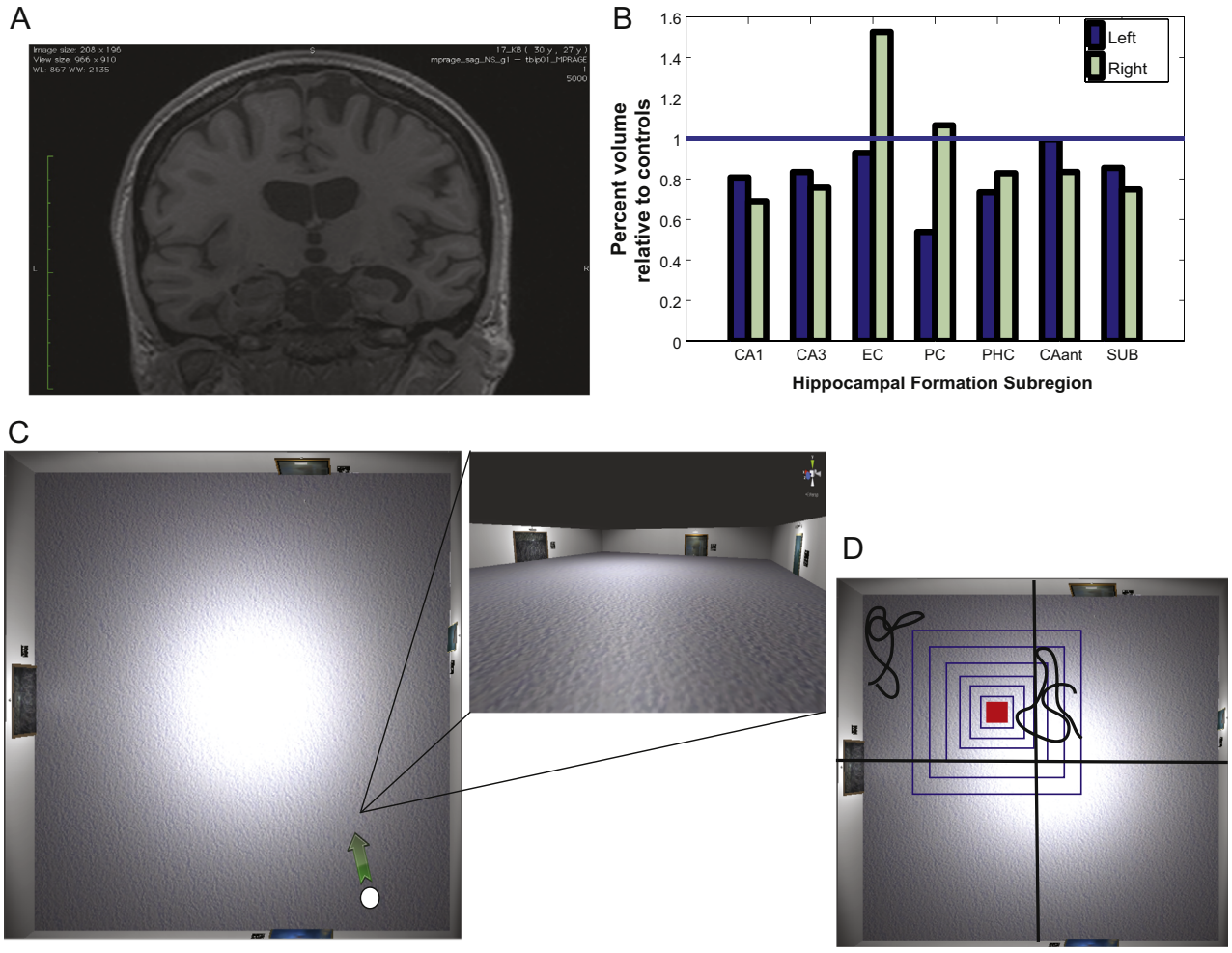

Fig. 1. Patient characteristics and experimental design. (A) T1-weighted structural MRI of patient RT highlighting significant volume loss in the medial temporal lobes including the hippocampus. (B) Relative normalized hippocampal subfield volumes of patient RT compared to 14 controls subjects. (C) Virtual room schematic with first-person perspective. (D) Illustration of standard quadrant analysis procedure and the precision window analysis used in the current study.

hidden location using a brightly colored cue card or a familiar trajectory (D'Hooge and De Deyn, 2001; de Hoz et al., 2003; Morris, 1984; Morris et al., 1982; Moser et al., 1995; Vorhees and Williams, 2006; Eichenbaum et al., 1990 but see Day et al., 1999). These findings suggest that damage to the rodent hippocampus impairs its ability to use allocentric cues to navigate, while leaving egocentric search strategies intact. Partial lesions to the hippocampus, in particular, to the dorsal/posterior hippocampus, similarly significantly impair the ability of the rat to employ an allocentric search strategy based on distal cues outside of the Water Maze (Moser et al., 1993, 1995). These findings provide support for CMT and suggest that an intact hippocampus is necessary for allocentric spatial navigation.

Extending these findings to humans, though, has been more challenging. Studies in humans using virtual and real analogs of the Morris Water Maze task have shown mixed results, as reviewed in a recent paper (Ekstrom et al., 2014). In one study, consistent with rodent findings, a desktop virtual reality version of the Morris Water Maze was employed in which unilaterally damaged MTL patients and controls navigated a virtual pool to find a hidden goal location. The authors found that MTL patients performed at chance levels on "probe trials" (in which the hidden platform was removed to allow for a more complete assay of spatial knowledge) (Astur et al., 2002; Bartsch et al., 2010). Additionally, a second study, using a similar paradigm but with patients with lesions more circumscribed to the hippocampus, found above chance yet impaired performance on the virtual Morris Water Maze (Goodrich-Hunsaker et al., 2010). In a real world analog of the Morris Water Maze, a recent study again demonstrated impaired, but again, above chance allocentric navigation in a single hippocampally lesioned patient (Banta-Lavenex et al., 2014). Another study that used a real-world analog of the Morris Water Maze, however, reported no allocentric navigation impairments for patients with damage limited to the hippocampus, although impairments did appear when lesions extended into the parahippocampal cortex (PHC) (Bohbot et al., 1998). Finally, the patient HM, who had some damage to the hippocampus and surrounding cortex, showed no impairment on finding a single hidden target but severely impaired performance on a second location (Bohbot and Corkin, 2007).

There are several potential considerations with previous work in humans, however, warranting further investigation. One issue, which we explore in detail here, is that the analyses used in previous studies of the human Morris Water Maze analogs do not provide a continuous measure of navigation, but rather coarse assessments of spatial memory based on dividing the arena into discrete quadrants. Recent findings, though, suggest that the hippocampus is involved in perceptual precision (Olson et al., 2006; see also Erez et al., 2013; Ryan et al., 2013; Warren et al., 2012) and a recently proposed alternative theory (which we refer to here as the Precision and Binding Model [PBM]) argues for a role of the hippocampus in spatial precision rather than spatial strategy