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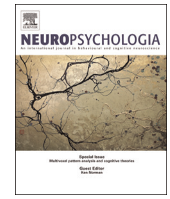

Memory integration in amnesia: Prior knowledge supports verbal short-term memory

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ABSTRACT

Short-term memory (STM) and long-term memory (LTM) have traditionally been considered cognitively distinct. However, it is known that STM can improve when to-be-remembered information appears in contexts that make contact with prior knowledge, suggesting a more interactive relationship between STM and LTM. The current study investigated whether the ability to leverage LTM in support of STM critically depends on the integrity of the hippocampus. Specifically, we investigated whether the hippocampus differentially supports between-domain versus within-domain STM–LTM integration given prior evidence that the representational domain of the elements being integrated in memory is a critical determinant of whether memory performance depends on the hippocampus. In Experiment 1, we investigated hippocampal contributions to within-domain STM–LTM integration by testing whether immediate verbal recall of words improves in MTL amnesic patients when words are presented in familiar verbal contexts (meaningful sentences) compared to unfamiliar verbal contexts (random word lists). Patients demonstrated a robust sentence superiority effect, whereby verbal STM performance improved in familiar compared to unfamiliar verbal contexts, and the magnitude of this effect did not differ from that in controls. In Experiment 2, we investigated hippocampal contributions to between-domain STM–LTM integration by testing whether immediate verbal recall of digits improves in MTL amnesic patients when digits are presented in a familiar visuospatial context (a typical keypad layout) compared to an unfamiliar visuospatial context (a random keypad layout). Immediate verbal recall improved in both patients and controls when digits were presented in the familiar compared to the unfamiliar keypad array, indicating a preserved ability to integrate activated verbal information with stored visuospatial knowledge. Together, these results demonstrate that immediate verbal recall in amnesia can benefit from two distinct types of semantic support, verbal and visuospatial, and that the hippocampus is not critical for leveraging stored semantic knowledge to improve memory performance.

1. Introduction

In everyday life, we frequently have to maintain information in mind over brief delays. Common examples include remembering a friend's telephone number between the time of hearing it and dialing it, or keeping a colleague's message in mind so that it can be conveyed to another colleague. It is well established that the ability to temporarily maintain information in mind is greatly improved when that information makes contact with pre-existing semantic knowledge. For example, a friend's telephone number is much easier to remember if it contains an ordered sequence of numbers (543–6789) compared to a random sequence of numbers (473–9586). Indeed, experimental studies have demonstrated that stored semantic knowledge can strongly impact immediate memory performance. Short-term serial recall of digits improves when digits appear in structured versus unstructured sequences (Bor et al., 2004) and short-term serial recall of words improves when words are presented within familiar verbal contexts (sentences) compared to unfamiliar verbal contexts (lists), a phenomenon that has been labeled the 'sentence superiority effect' (Baddeley et al., 2009; Brener, 1940; Miller and Selfridge, 1950).

Recently, a series of studies has demonstrated that immediate verbal recall also improves when to-be-remembered items are presented within familiar visuospatial contexts, even when those visuospatial contexts are incidental to the memory task at hand. Specifically, when subjects are presented with sequences of digits in a spatial array, immediate verbal recall of these digits (akin to a digit span test) improves when digits are presented in a familiar visuospatial context (a typical keypad display) compared to an unfamiliar visuospatial context (an atypical keypad display; Allen

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et al., In press; Darling et al., 2012, 2014; Darling and Havelka, 2010). This 'visuospatial bootstrapping effect' is thought to reflect facilitated recall when verbal digit information can be linked to pre-existing visuospatial representations. Together, these examples demonstrate the importance of interactions between short-term memory (STM) and long-term memory (LTM), and reveal how both verbal and visuospatial knowledge can be leveraged to support immediate verbal recall.

Although traditional models of human memory make clear distinctions between STM and LTM (Atkinson and Shiffrin, 1968; Baddeley and Hitch, 1974; James, 1890), more recent models of STM emphasize the importance of interactions between these two forms of memory (Baddeley, 2000; Cowan, 1988; Ranganath and Blumenfeld, 2005; Zhou et al., 2007). Baddeley (2000) has proposed that an episodic buffer serves as an interface between STM and LTM in which activated information held in STM can be integrated with stored long-term knowledge (Baddeley, 2000). An alternative, but complementary view, is that stored long-term knowledge influences immediate memory as a byproduct of an overlapping representational system in which STM reflects an activated subset of LTM representations (Cowan, 1999; Ericsson and Kintsch, 1995; Postle, 2006; Ranganath and Blumenfeld, 2005; Zhou et al., 2007). While the influence of pre-existing knowledge on STM is now widely recognized both theoretically and behaviorally, an important outstanding question is how interactions between STM and LTM are supported in the brain.

The current study investigates whether the contribution of pre-existing semantic representations to STM critically depends on associative processes supported by the medial temporal lobe (MTL), and the hippocampus in particular. The hippocampus is widely recognized as a key neural region that links individual elements within LTM, and recent evidence suggests that the hippocampus may play a similar role when linking elements within STM (Cashdollar et al., 2009; Finke et al., 2008; Hannula et al., 2006; Jonides et al., 2008; Olsen et al., 2012; Olson et al., 2006a, 2006b; Rose et al., 2012). However, it is currently unknown whether the hippocampus also supports interactions *across* STM and LTM. Consistent with this possibility, several recent neuroimaging studies have reported increased hippocampal activity associated with facilitated immediate verbal recall in familiar versus unfamiliar encoding contexts (Bonhage et al., 2014; Bor et al., 2004; Bor and Owen, 2007). Bor et al. (2004) found greater hippocampal activity when participants memorized mathematically structured digit sequences (2, 4, 6, 8, 9, 7, 5, 3) compared to unstructured digit sequences (9, 2, 7, 1, 4, 6, 5, 8) and Bonhage et al. (2014) found greater hippocampal activity when participants memorized lists of words appearing in the context of sentences versus lists. Interestingly, Bonhage et al. found that increased hippocampal activity during sentence encoding was accompanied by decreased frontal activity in classic language-related areas during sentence maintenance. They proposed that hippocampal activity during encoding may reflect relational binding processes that combine individual items (words) into larger units (chunks) based on syntactic or semantic information stored in LTM, and that this hippocampally-mediated chunking at encoding may unburden the neural systems supporting maintenance and rehearsal.

Although recent neuroimaging evidence is consistent with the notion that the hippocampus links activated verbal representations in STM to stored knowledge in LTM (see also Rudner et al., 2007; Rudner and Ronnberg, 2008), it is currently unclear whether hippocampal activity observed in these neuroimaging studies is directly related to memory integration. Arguments against this notion come from a recent neuropsychological report that the sentence superiority effect is intact in a patient with developmental amnesia, who has extensive hippocampal damage acquired in childhood (Baddeley et al., 2010). This finding suggests that the ability to leverage stored linguistic knowledge in support of immediate verbal recall may not critically depend on the hippocampus. However, it is also important to note that the case of developmental amnesia may not be typical of adult-onset hippocampal damage, and that intact performance in this patient may reflect compensatory recruitment of brain regions outside the hippocampus (Baddeley et al., 2010).

Another intriguing possibility is that hippocampal involvement in the semantic facilitation of STM depends on the nature of the features being integrated in memory. Specifically, the hippocampus may not be necessary for linking activated representations with semantic knowledge from the same representational domain (e.g., integrating verbal representations held in STM with pre-existing verbal knowledge), but may instead be critical for integrating activated representations with semantic knowledge from a different domain (e.g., integrating verbal representations held in STM with pre-existing visuospatial knowledge). This hypothesis is informed by prior evidence from both the STM and LTM literature suggesting that the representational domain of the elements being integrated in memory is a critical determinant of whether memory performance depends on the hippocampus, with the hippocampus primarily involved in memory for cross-domain associations (Mayes et al., 2007; Mayes et al., 2004; Piekema et al., 2006, 2009; Race et al., 2013; Vargha-Khadem et al., 1997). However, there is also evidence that the hippocampus supports memory for all types of associations, both within-domain and cross-domain (Holdstock et al., 2010; Park and Rugg, 2011; Stark and Squire, 2003; Turriziani et al., 2004). Thus, important questions remain about hippocampal contributions to facilitated STM when to-be-remembered information is congruent with stored knowledge from (a) the same domain and (b) a different domain.

The current study uses a lesion-deficit approach to investigate the nature and necessity of hippocampal contributions to STM–LTM integration. Specifically, we investigate whether the hippocampus differentially supports cross-domain versus within-domain STM–LTM integration. Immediate verbal recall was measured in amnesic patients with adult-onset MTL damage in (1) verbal contexts (Experiment 1) and (2) visuospatial contexts (Experiment 2). If the hippocampus is only critical for integrating activated verbal material with semantic knowledge from a different domain, then amnesic patients should demonstrate a preserved immediate memory benefit when verbal items are encoded within familiar verbal contexts (Experiment 1) but should not demonstrate an immediate memory benefit when verbal items are presented in familiar visuospatial contexts (Experiment 2). In contrast, if the hippocampus plays a critical role in all types of STM–LTM integration, regardless of the representational domain of the features being integrated, amnesic patients should demonstrate a reduced immediate recall benefit in both familiar verbal and familiar visuospatial contexts. Finally, a third possibility is that the hippocampus does not play a critical role in *any* type of STM–LTM integration. If this is the case, then amnesic patients, like controls, should demonstrate immediate recall benefits in *both* familiar verbal and familiar visuospatial contexts.

2. Experiment 1: sentence superiority effect

2.1. Materials and methods

2.1.1. Participants

Participants included eight amnesic patients with MTL lesions (P01–P08; Table 1). Patients' neuropsychological profiles indicate impairments isolated to the domain of memory with profound impairments in new learning. Three patients (P03, P04, and P08) had lesions restricted to the hippocampus (confirmed with