



## Group differences in anterior hippocampal volume and in the retrieval of spatial and temporal context memory in healthy young versus older adults

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### ABSTRACT

The ability to retrieve temporal and spatial context information from memory declines with healthy aging. The hippocampus (HC) has been shown to be associated with successful encoding and retrieval of spatio-temporal context, versus item recognition information (Davachi, Mitchell, & Wagner, 2003; Nadel, Samsonovich, Ryan, & Moscovitch, 2000; Ross & Slotnick, 2008). Aging has been linked to volume reduction in the HC (Bouchard, Malykhin, Martin, Hanstock, Emery, Fisher, & Camicioli, 2008; Malykhin, Bouchard, Camicioli, & Coupland, 2008; Raz et al., 2005). As such, age-associated reductions in anterior HC volume may contribute to the context memory deficits observed in older adults. In the current MRI study we investigated whether item recognition, spatial context and temporal context memory performance would be predicted by regional volumes in HC head (HH), body (HB) and tail (HT) volumes, using within group multiple regression analyses in a sample of 19 healthy young (mean age 24.3) and 20 older adults (mean age 67.7). We further examined between age-group differences in the volumes of the same HC sub-regions. Multiple regression analyses revealed that in younger adults both spatial and temporal context retrieval performance was predicted by anterior HC volume. Older age was associated with significant volume reductions in HH and HB, but not HT; and with reduced ability to retrieve spatial and temporal contextual details from episodic memory. However, HC volumes did not predict context retrieval performance in older adults. We conclude that individual differences in anterior, not posterior, HC volumes predict context memory performance in young adults. With age there may be a posterior-to-anterior shift from using HC-related processes, due to HC volume loss, to employing the prefrontal cortex to aid in the performance of cognitively demanding context memory tasks. However, due to concomitant changes in the prefrontal system with age, there are limits to compensation in the aging brain.

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### 1. Introduction

Healthy aging is generally linked to reductions in the ability to encode and retrieve past personal memories (episodic memories; EM) in rich spatio-temporal contextual detail ( Craik & Salthouse, 2000). In general, an episodic event can be broken down into the salient focal element or elements of attention (content memory) and the temporal-spatial setting in which an episode occurred (context memory) (Tulving, 1972, 1984). Content memory has been assessed using forced-choice item recognition memory tasks, and spatial and temporal context memory has been assessed using forced choice 'left/right' discrimination tasks (spa-

tial context memory task) and forced choice recency memory tasks (temporal context memory task) (Cabeza, Anderson, Houle, Mangels, Nyberg, 2000; Cabeza, Anderson, Locantore, & McIntosh, 2002; Dobbins, Rice, Wagner, & Schacter, 2003; Duarte, Henson, & Graham, 2008; Glisky, Polster, & Routhieaux, 1995; Rajah, Ames, & D'Esposito, 2008; Rajah & McIntosh, 2008). Compared to young adults, older adults perform equivalently on simple two-alternative forced-choice item recognition tasks that are believed to assess one's ability to retrieve item or content information from EM; but, older adults exhibit poorer performance on context memory tasks, which require one to retrieve either the spatial and/or temporal context about a previously encoded event (Cabeza et al., 2000; Cabeza et al., 2002; Duarte et al., 2008; Kukolja, Thiel, Wilms, Mirzazade, & Fink, 2009; Rajah, Languay, Valiquette, 2010). This suggests that with healthy aging there is a specific decline in performance on context memory tasks versus item recognition tasks, suggesting that brain regions that are associated with successful context retrieval are impacted with age (Spencer & Raz, 1995).

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Neuropsychological studies of patients with brain lesions and neuroimaging studies of healthy young adults indicate that the hippocampus and lateral prefrontal cortex, and the cognitive processes they help mediate, are more important for performing context memory tasks versus simpler forced-choice item recognition tasks (Cabeza et al., 2000; Daselaar, Fleck, Dobbins, Madden, & Cabeza, 2006; Duarte et al., 2008; McAndrews & Milner, 1991; Mitchell, Raye, Johnson, & Greene, 2006; Spencer & Raz, 1994; Stuss, Craik, Sayer, Franchi, & Alexander, 1996; Yonelinas et al., 2007). In this manuscript we focus on how age-related changes in the ability to retrieve spatial and temporal contextual details may be related to changes in hippocampal volumes, and in-turn its function. The hippocampus (HC) has been shown to be important for both encoding and retrieving episodic memories in rich contextual detail (Eichenbaum, Otto, & Cohen, 1992; Moscovitch & Nadel, 1998; Scoville & Milner, 1957; Squire, 1992). Some researchers have suggested that the HC is important for memory recollection via its role in relational binding of stimulus-stimulus and stimulus-response associations during encoding and retrieval, a process critical for successful context memory (Brasted, Bussey, Murray, & Wise, 2003; Cohen & Eichenbaum, 1993). Consistent with this hypothesis, functional magnetic resonance imaging (fMRI) studies of young adults have shown that the HC exhibits greater activity during encoding and retrieval phases of memory tasks that require greater relational binding, such as spatial and/or temporal context memory tasks versus item recognition tasks (Davachi, 2006; Davachi, Mitchell, & Wagner, 2003; Dougal, Phelps, & Davachi, 2007; Giovanello, Schnyer, & Verfaellie, 2009; Hayes, Nadel, & Ryan, 2007; Ross & Slotnick, 2008; Smith & Mizumori, 2006). Recent fMRI findings have further shown that the anterior HC may be especially important for mediating flexible relational binding processes at encoding and retrieval during the performance of associative tasks (Giovanello et al., 2009; Giovanello, Schnyer, & Verfaellie, 2004). However, Awipi and Davachi (2008) reported increased anterior HC activity during successful versus unsuccessful encoding of both scene/item information alone, and scene-object source information. Indicating that the anterior HC may be important for mediating domain-general relational binding processes which may be engaged to varying degrees in either recognition or context memory tasks, depending on task demands (Awipi & Davachi, 2008; Davachi, 2006).

Therefore, age-associated decrements in EM may be attributable to changes in anterior HC function and reductions in relational binding/associative processes engaged during EM encoding and retrieval. As such, performance on memory tasks that engage the HC and its associative memory processes to a greater extent, such as spatial and temporal context memory tasks, may be especially impacted following changes in the structural and/or functional integrity of the anterior HC (Naveh-Benjamin, 2000; Naveh-Benjamin, Brav, & Levy, 2007). Consistent with this idea, Kukulja et al. (2009) have recently reported age-associated differences in anterior hippocampal activity during the retrieval of spatial context information for previously encoded objects. Specifically, increased left anterior HC activity was associated with successful spatial context retrieval in young, but not older adults (Kukulja et al., 2009). Dennis and colleagues also conducted an fMRI study to examine the neural correlates of source/context memory encoding in young and older adults (Dennis et al., 2008). They reported that greater HC activity during source encoding was predictive of subsequent successful recollection only in young adults. These findings support the hypothesis that older adults' context retrieval deficits are likely related to reductions in HC activation during both encoding (Dennis et al., 2008) and retrieval (Daselaar et al., 2006; Kukulja et al., 2009).

The aforementioned fMRI studies provide evidence that age-associated differences in context memory may result from changes in HC function. However, our understanding of the relationship

between individual differences in HC structure and the ability to retrieve spatial and temporal contextual detail from memory, and the impact of healthy aging on this relationship, is weaker. For example, MRI studies of HC volumetry in young adults often report negative correlations between HC volume and EM performance (see (Van Petten, 2004) for review). However, the majority of these previous studies examined verbal item recognition memory. As such, this negative association is not surprising, given the evidence presented above that the main contribution of the HC may be to support associative processes more important for successfully performing context memory tasks versus item recognition tasks (Davachi et al., 2003). Therefore, one can speculate whether HC volume in young adults may be more associated with context memory performance, but to date no study has investigated this.

Similarly, there is significant evidence that healthy aging is associated with HC volumetric reductions, which in turn have been linked with general age-associated EM reductions, such as free recall (de Leon et al., 1996; Lupien et al., 2005; Persson et al., 2006; Pruessner, Collins, Pruessner, & Evans, 2001; Raz et al., 2004; Raz, Gunning-Dixon, Head, Dupuis, & Acker, 1998; Raz et al., 2005). In addition, there are few studies that have examined whether healthy aging is associated with region-specific volumetric reductions in anterior versus posterior portions of the HC. Given the fMRI findings reviewed above, one may predict that healthy aging may be associated with volume reduction in anterior, more than posterior, HC. However, to date there have been differing reports regarding region-specific changes in HC volume in healthy elders (Malykhin, Bouchard, Camicioli, & Coupland, 2008; Martin, Smith, Collins, Schmitt, & Gold, 2010; Wang et al., 2003). Using a cross-sectional design, Malykhin et al. (2008) have reported greater posterior versus anterior HC volume loss in healthy older versus younger adults. However, in a two-year follow-up study of older adults with dementia of the Alzheimer's type (DAT) versus healthy older adult controls, Wang et al. (2003) reported changes in the shape of the hippocampal head in the healthy older adult cohort at two-year follow-up, whereas the DAT group exhibited HC shape change in hippocampal head, body and subiculum; both groups of elders exhibited total HC volumetric reductions over the course of 2 yrs. Martin et al. (2010) reported anterior HC volume loss in healthy elders who later converted to mild cognitive impairment, compared to healthy elderly who remained cognitively intact; however, there was no healthy young control group in this study to determine if healthy aging was also associated with milder volume reductions in distinct regions of HC, relative to young controls. Therefore, to date it remains unclear if healthy aging has a region-specific effect on HC volumes compared to young adults. Moreover, to our knowledge, no study to date has investigated the relationship between spatial context memory, temporal context memory, item recognition performance and the integrity of HC volumes in a region-specific manner, in either healthy young or older adult populations, in a single experiment.

Thus, in the current study we used MRI to examine how regional grey matter volumetric measures of hippocampal head, body and tail predict performance on item recognition, temporal context retrieval and spatial context retrieval tasks. We tested young and older adults, to be able to further investigate how older age impacts HC regional volumes and memory performance, respectively. To our knowledge, this is the first study to investigate how regional HC grey matter volumes relate to context memory performance in young and older adults. Given previous fMRI results (Awipi & Davachi, 2008; Davachi, 2006; Giovanello et al., 2009; Giovanello et al., 2004) we hypothesized that context memory performance could be significantly predicted by anterior, but not posterior, HC volumes in young adults and that age-associated reductions in context memory performance may be related to volume reductions in anterior HC volume.

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