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Age-related changes in prefrontal cortex activity are associated with behavioural deficits in both temporal and spatial context memory retrieval in older adults

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ABSTRACT

Aging is associated with decrements in both spatial and temporal context retrieval. Functional neuroimaging studies of young adults suggest that there are differences in left versus right lateral prefrontal cortex (PFC) contributions to spatial versus temporal source (recency) retrieval, respectively. The goal of the current study was to determine if age-related decreases in temporal and spatial context retrieval are due to common or distinct changes in PFC function. To address this goal we conducted an event-related functional magnetic resonance imaging (fMRI) study in which young and older adults performed recognition, recency and spatial context retrieval tasks using face stimuli to identify event-related PFC regions associated with these retrieval tasks in both age groups. Our behavioural results indicated that older adults did not differ on recognition performance, but did exhibit a deficit in both context retrieval tasks, compared to young adults. The fMRI results suggest that age-related deficits in both spatial and temporal context retrieval may be linked to functional changes in right dorsolateral and left medial anterior PFC (APFC) function. In addition, based on brain-behaviour correlations in older adults, our results imply that older adults attempt to compensate for these deficits by engaging left dorsolateral PFC during spatial context retrieval and right APFC during temporal context retrieval.

1. Introduction

Compared to young adults, healthy older adults maintain the ability to recognize previously encountered stimuli or events (item recognition memory); but, exhibit a significant reduction in the ability to recollect the temporal and spatial contextual details of their past personal experiences (temporal and spatial context retrieval, respectively) (Tulving, 1972; Schacter et al., 1991, 1994; Craik, 1994; Wegesin et al., 2002). These age-related reductions in context memory retrieval can have a marked effect on seniors' quality of life. For example, temporal context memory allows us to keep track of the time in which past events occurred (e.g., when you took a prescribed medication) and to recollect the relative temporal order of past events (e.g., the order in which you took a series of prescribed medications). Spatial context memory allows us

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to recollect the spatial location in which past events occurred (e.g., where you parked your car). Thus, reductions in temporal and spatial context retrieval can impair the daily functioning of older adults; making it critical to understand the neurobiological correlates of these memory reductions in healthy older adults.

Functional neuroimaging studies of young adults have shown that in addition to the importance of the medial temporal lobe (MTL) and its role in episodic memory encoding and retrieval (Tulving and Markowitsch, 1998; Burgess, 2002; Suzuki, 2003; Johnson, 2004), the prefrontal cortex (PFC) also plays a crucial role in performing cognitive control processes, critical for item recognition, temporal context retrieval and spatial context retrieval (Tulving et al., 1994; Henson et al., 1999a, 1999b; Buckner, 2003; Dobbins et al., 2003; Nyberg et al., 2003; Rugg et al., 2003; Rajah and McIntosh, 2006; Rajah et al., 2008). Moreover, recent neuroimaging studies of young adults have reported laterality differences in PFC activation: item recognition and temporal context retrieval tasks engage various right PFC regions whereas spatial context retrieval and other context retrieval tasks engage left PFC regions (Cabeza et al., 2000; Dobbins et al., 2003; Mitchell et al., 2004; Rajah et al., 2008; Rajah and McIntosh, 2006). For example, in an event-related functional magnetic resonance imaging (fMRI) study in which subjects performed recognition (old/new) and spatial-source (SS) (left/right) memory tasks for abstract visual shapes, Slotnick et al. (Slotnick et al., 2003) reported greater activity in left lateral and anterior PFC (APFC) during correct SS judgements compared to correct item recognition judgements. Left lateral PFC activation has also been reported during spatial context retrieval of pictorial stimuli (Mitchell et al., 2004) and during verbal list context retrieval (Dobbins et al., 2003). In contrast, in a recent event-related fMRI study we conducted, subjects were scanned while performing verbal recency and recognition tasks (Rajah and McIntosh, 2006); although both tasks engaged right dorsolateral PFC (DLPFC) activation, the recency tasks activated right DLPFC to a greater degree than recognition tasks. We also observed similar right-lateralized DLPFC activation during temporal context retrieval of face stimuli versus face recognition in a recent fMRI study (Rajah et al., 2008); suggesting that these PFC laterality effects in young adults are not stimulus-based, but reflect differences in the PFC-related cognitive control processes engaged during spatial versus temporal context retrieval (Dobbins et al., 2003; Mitchell et al., 2004; Rajah et al., 2008).

Therefore, based on the functional neuroimaging studies of young adults one would predict that some of the age-related deficits in spatial versus temporal context retrieval may be mediated by functional changes in *different* PFC regions. Specifically one may assume that age-related deficits in temporal context retrieval may be linked to changes in right lateral PFC function and age-related deficits in spatial context retrieval may be linked to changes in left lateral PFC function. However, to date, no functional neuroimaging study has directly examined this question. In fact, the few studies that have used functional neuroimaging to investigate age-related changes in the neural correlates of context memory retrieval, support the hypothesis that a common change in right PFC function may underlie the context memory retrieval deficits observed in older adults. For example, Cabeza et al. (2000) conducted a positron emission tomography (PET) study in which young and older adults performed verbal recognition and temporal context retrieval (recency) tasks. They found that young adults performed better than older adults during recency tasks and, during recency tasks both age groups activated left DLPFC, but only young adults engaged right APFC. In a recent fMRI study we conducted on verbal recognition and recency memory in young and older adults, we found older adults activated *right* DLPFC to a *greater degree*, compared to young adults, during both retrieval tasks. Morever, this increased right DLPFC activation correlated with improved recognition memory performance, but not with improved recency performance, in older adults. This suggests that even when older adults engaged right PFC to a greater degree than young adults, it was not sufficient for maintaining context retrieval abilities at a level equivalent to young adults. Therefore, these two studies suggest that age-related deficits in temporal context retrieval may be linked to changes in right PFC function.

There is also indirect evidence that age-related deficits on other context retrieval tasks may be associated with changes in right PFC function. For example, in an auditory source memory PET study, Cabeza et al. (2002) found during source retrieval young adults and low-performing older adults engaged right DLPFC, whereas high-performing older adults engaged left DLPFC. This result is also consistent with the view that there are limitations in right lateral PFC function in older adults that are related to context memory retrieval deficits. In addition, this result indicates that older adults may engage the homologous left PFC region to successfully compensate for a deficit in right PFC function (Cabeza, 2002; Cabeza et al., 2002). This finding has been formalized as the hemispheric asymmetry reduction in older adults (HAROLD) model by Cabeza (2002).

Recently, Duarte et al. (2008) conducted an fMRI study in which both young and older adults performed spatial and temporal context retrieval within the same experimental session. Duarte et al. (2008) found that a group difference in right lateral PFC activity was related to deficits in objective context memory judgement, collapsed across spatial and temporal context. However, because no direct comparison between PFC activation differences between temporal versus spatial were examined, and separate group-by-task interactions for temporal versus spatial context retrieval were not presented, there remains no direct evidence that age-related deficits in different context retrieval tasks, such as temporal and spatial context retrieval tasks, are mediated by similar or different changes in PFC function.

Therefore, to date, there is indirect support for the hypothesis that a common change in right PFC function with age may be associated with the age-related behavioural deficits observed in many context memory retrieval tasks. This is surprising, since one would assume from the young adult literature that age-related reductions in these different context memory tasks should also be related to changes in different PFC regions (Rugg et al., 1999; Cabeza et al., 2000; Dobbins et al., 2003; Mitchell et al., 2004; Rajah and McIntosh, 2006; Rajah et al., 2008). To directly determine if age-related deficits in different context retrieval tasks, such as spatial and temporal context retrieval tasks, are mediated by a common