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Changes in the modulation of brain activity during context encoding vs. context retrieval across the adult lifespan

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ABSTRACT

Age-related deficits in context memory may arise from neural changes underlying both encoding and retrieval of context information. Although age-related functional changes in the brain regions supporting context memory begin at midlife, little is known about the functional changes with age that support context memory encoding and retrieval across the adult lifespan. We investigated how age-related functional changes support context memory across the adult lifespan by assessing linear changes with age during successful context encoding and retrieval. Using functional magnetic resonance imaging (fMRI), we compared young, middle-aged and older adults during both encoding and retrieval of spatial and temporal details of faces. Multivariate behavioral partial least squares (B-PLS) analysis of fMRI data identified a pattern of whole brain activity that correlated with a linear age term, and a pattern of whole brain activity that was associated with an age-by-memory phase (encoding vs. retrieval) interaction. Further investigation of this latter effect identified three main findings: 1) reduced phase-related modulation in bilateral fusiform gyrus, left superior/anterior frontal gyrus and right inferior frontal gyrus that started at midlife and continued to older age, 2) reduced phase-related modulation in bilateral inferior parietal lobule that occurred only in older age, and 3) changes in phase-related modulation in older but not younger adults in left middle frontal gyrus and bilateral parahippocampal gyrus that was indicative of age-related over-recruitment. We conclude that age-related reductions in context memory arise in midlife and are related to changes in perceptual recollection and changes in fronto-parietal retrieval monitoring.

Introduction

Healthy, age-related change in episodic memory is characterized by larger deficits in memory for the contextual features of items or events (context or source memory) relative to memory for the items or events themselves (item memory) (Spencer and Raz, 1995). Correct retrieval of specific context information relies on processes that relate contextual features together at encoding and retrieval (Mitchell and Johnson, 2009). Cognitive-behavioral evidence has shown that, relative to young adults (generally 18–35 yrs), older adults (generally 60 + yrs) have deficits in binding together contextual features of events at encoding (e.g., Chalfonte and Johnson, 1996) and/or in recollecting specific contextual features of events at retrieval (Mitchell et al., 2000; Johnson et al., 1993; Old and Naveh-Benjamin, 2008; Spencer and Raz, 1995). Thus, age-related declines in context memory may be associated with neural changes underlying both encoding (e.g., Dennis et al., 2008; Mitchell et al., 2000) and retrieval (McDonough et al., 2012; Mitchell et al., 2013) context information.

Functional neuroimaging studies of episodic memory in young adults have identified a core network of brain regions important for successful episodic memory encoding and retrieval (Cabeza and Nyberg, 2000; Lepage et al., 2000; Mitchell & Johnson, 2009; Nyberg et al., 1996; Tulving et al., 1994). Studies comparing context memory tasks (i.e., left/right spatial context decisions and recency/temporal context decisions) to item memory tasks (i.e., old-new recognition) have found that young adults generally perform worse on context vs. item memory tasks (e.g., Ekstrom and Bookheimer, 2007). Subsequent memory analysis of fMRI data indicates that there is increased activity in brain regions related to stimulus perception (i.e. ventral occipito-temporal cortices for visual stimuli), left VLPFC, and MTL regions, during successful context encoding, compared to item encoding (Awipi and Davachi, 2008; Cansino et al., 2002; Fan et al., 2003; Maillet and Rajah, 2014; Rugg et al., 2012; Uncapher et al., 2006). On the other hand, successful retrieval of contextual details has been related to increased activity in the core recollection network, compared to item recognition, which includes the hippocampus, parahippocampal cortex, secondary sensory processing regions (i.e. middle/superior temporal cortex for

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visual stimuli), inferior and superior parietal cortices, precuneus and medial PFC (Johnson et al., 2009; Leshikar et al., 2014; Newsome, Dulas and Duarte, 2012; Rajah et al., 2010; Rugg et al., 2012). In addition, several studies have reported increased bilateral DLPFC during context vs. item retrieval, which is thought to reflect greater involvement of post-retrieval strategic processing (Morcom and Rugg, 2012; Rajah et al., 2008; Rajah et al., 2010; Spaniol et al., 2009). Thus, in young adults, successful context memory places greater demands than item memory tasks on brain regions related to recollection-based episodic memory and cognitive control.

Functional neuroimaging studies comparing the neural correlates of context memory in young adults vs. older adults have reported age-group differences in context encoding activity (e.g., Dennis et al., 2008; Dulas and Duarte, 2012) and context retrieval activity (e.g., (Dulas and Duarte, 2012; McDonough et al., 2014; McDonough et al., 2012; Mitchell et al., 2013) in medial and lateral prefrontal cortex (PFC), medial temporal lobe (MTL), parietal cortices, and posterior occipital-temporal cortices. More recently, studies have shown that context memory decline arises as early as midlife (Cansino, 2009; Kwon et al., 2015). For example, in a previous study we used event-related fMRI to investigate similarities and differences in the neural correlates of context encoding and retrieval in middle-age adults vs. young adults. We observed marked differences in both ventral occipital temporal and PFC activity, primarily at retrieval, in middle-aged adults vs. young adults. This finding suggests that episodic memory decline, as measured by context memory, arises at midlife and continues into older age. However, to better inform our understanding of the functional brain changes underlying age-related episodic memory decline, it is necessary to examine the trajectory of functional brain changes during episodic memory task performance across the adult lifespan. A longitudinal study would be the best way to examine this issue. However, due to cost and feasibility, studies to date have used cross-sectional designs to examine the neural correlates of episodic memory in young adults, middle-aged adults and older adults (Cansino et al., 2015a,b; Filippini et al., 2011; Grady et al., 2006; Kennedy et al., 2012; Park et al., 2013). Several of these studies have used item memory paradigms to examine age-related changes in brain function and episodic memory (Grady et al., 2006; Kennedy et al., 2012; Park et al., 2013), despite evidence that item memory remains relatively intact until later life. As such, these studies may not have been sensitive at detecting functional changes associated with episodic memory decline in adulthood (Cansino, 2009; Rajah et al., 2010; Rajah and McIntosh, 2008). Recently, Cansino et al., conducted EEG and fMRI studies of context memory across the lifespan ato examine changes at encoding (Cansino et al., 2015a,b; Cansino et al., 2010) and at retrieval (Cansino et al., 2012; Cansino et al., 2015a,b). In their more recent fMRI studies, Cansino et al. have reported greater activation in PFC in young vs. older adults during encoding, and greater right occipital cortex activity older vs. young adults during retrieval (Cansino et al., 2015a,b). This is interesting, given that others have reported decreased occipital cortex activation with age, and increased PFC activity with age during successful item encoding and retrieval (Grady et al., 2006; Kennedy et al., 2012; Park et al., 2013). These between-study differences may be due to the use of different memory tasks and/or the use of different analysis methods. For example, Cansino and colleagues identified group differences in brain activity during successful vs. unsuccessful context encoding/retrieval by conducting within group young adults, middle-aged adults and older adults analyses followed by subsequent between-group comparisons in regions identified per group. In contrast, other studies have used subjects' age as a continuous variable to examine linear increases and decreases in brain activity across the lifespan during successful memory encoding (Kennedy et al., 2012; Liu et al., 2013; Park et al., 2013), or during encoding plus retrieval (Grady et al., 2006). To help clarify amongst the alternative possibilities it would be important to conduct a study examining context encoding and retrieval across the adult lifespan by examining both continuous linear changes in brain function with age, and post-hoc comparisons of age-groups. This is one goal of the current study. An additional goal of the current study is to examine brain activity related to successful context encoding *and* retrieval, in the same fMRI session, across the adult lifespan. To our knowledge, no study to date has done this.

Therefore, in the current study, young, middle-aged and older adults will undergo fMRI scanning while encoding and retrieving spatial and temporal contextual features from episodic memory. Multivariate partial least squares (PLS) will be used to investigate similarities and differences in whole brain patterns of activity during successful context encoding and retrieval across the adult lifespan. This analysis will help identify linear age-related changes in brain function related to context memory decline with age. In addition, we will conduct post-hoc comparisons of encoding and/or retrieval related activity in peak activation foci identified by the PLS analysis to determine if there are any non-linear effects in brain activity, and if activity in middle-aged adults differed from young adults and/or older adults. Using this cross-sectional lifespan approach, we aim to identify linear and non-linear patterns of functional brain change with age at encoding and retrieval; and determine how age-related changes in brain activity at encoding relate to changes observed at retrieval.

Methods

Participants

One hundred and twelve right-handed adults between the ages of 19–76 yrs (mean age = 46.61 yrs; 75 females; mean years of formal education [EDU] = 15.75 yrs) with no history of neurological or psychological illness or family history of Alzheimer's disease were recruited for the study. Having no family history of Alzheimer's disease was defined as the absence of any blood relatives with probable Alzheimer's disease type dementia (Hayden et al., 2009). Of the 112 participants tested 41 were young adults (age range 19–35 yrs, mean age = 26.20 yrs, 26 females, mean EDU = 16.10 yrs), 32 were middle-aged adults (age range 40–58 yrs, mean age = 48.50 yrs, 24 females, mean EDU = 15.47 yrs), and 39 were older adults (age range 60–76 yrs, mean age = 66.51 yrs, 25 females, mean EDU = 15.62 yrs). Handedness was confirmed using the Edinburgh Inventory for Handedness, and age groups did not differ in level of education.

Participation involved two separate test sessions, conducted on different days. During the first session, participants completed a neuropsychological assessment (i.e., the Mini-International Neuropsychiatric Interview (MINI), inclusion cut-off ≤2; the Folstein Mini Mental State Examination (MMSE), exclusion cut-off <27; the Beck Depression Inventory (BDI), exclusion cut-off <15; the California Verbal Learning Task (CVLT) exclusion cutoff was based on the recommendations by Norman et al. (2000); correct delayed free recall, cued recall and recognition >12/16 for young, 11/16 for middle aged and 9/16 for older adults) (Norman, Evans, Miller, & Heaton, 2000); the American National Adult Reading Test (NART), inclusion cut-off ≤2.5 SD), and completed a practice session of the context memory tasks in a mock MRI scanner. One-way ANOVAs with post-hoc comparisons of young, middle-aged and older age groups were conducted on MMSE, BDI, CVLT, and education (yrs) to ascertain if there were any significant differences between age groups on these measures. Additional medical exclusion criteria included having a history of diabetes, having untreated cataracts and glaucoma, smoking >40 cigarettes a day; and having a current diagnosis of high cholesterol levels and/or high blood pressure left untreated in past six months.

All participants were paid. Informed consent was obtained from all participants, and protocol was approved by ethics board at the Faculty of Medicine, McGill University.

Behavioral methods

Only participants who met our neuropsychological inclusion/exclusion criteria and who were able to perform above chance on the practice