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Left caudal middle frontal gray matter volume mediates the effect of age on self-initiated elaborative encoding strategies

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ABSTRACT

Aging is associated with decreased self-initiated use of effective elaborative encoding strategies. Little is currently known regarding what factors drive age differences in self-initiated encoding strategies. The present research investigated whether age differences in prefrontal gray matter integrity contribute to age differences in self-initiated elaborative encoding strategies. The relationships between age, prefrontal regional gray matter volumes, and overall use of self-initiated elaborative encoding strategies were examined in healthy younger and older adults. Gray matter volume was calculated from structural MRI scans using Freesurfer. Encoding strategy use was assessed by retrospective item-by-item strategy self-reports given after a verbal intentional encoding task. Left caudal middle frontal gray matter volume mediated the effect of age on overall self-initiated use of elaborative encoding strategies. This suggests that age-associated declines in prefrontal gray matter integrity significantly contribute to age-associated declines in effective encoding strategies.

1. Introduction

Older adults' episodic memory is impaired relative to younger adults' (for a review see Balota et al., 2000), especially when no explicit instruction is given on how to encode studied information (i.e., unsupported intentional encoding; Hultsch et al., 1990; Sanders et al., 1980). Prior research suggests that age differences in self-initiated use of memory strategies during encoding contribute to age differences in episodic memory (Hertzog et al., 1998; Kirchhoff et al., 2012; Verhaeghen and Marcoen, 1994). When asked, older adults report using elaborative encoding strategies less frequently than younger adults during unsupported intentional encoding (Hertzog et al., 1998; Naveh-Benjamin et al., 2007; Verhaeghen and Marcoen, 1994). Elaborative encoding strategies rely on complex, highly effortful cognitive processes, such as thinking about the meaning of studied items, purposefully forming detailed visual images, and/or relating studied items to each other or one's personal experiences (Craik and Lockhart, 1972; Kirchhoff et al., 2013; Richardson, 1998). Some common examples of elaborative encoding strategies include visual imagery, sentence generation, story generation, and personal relevance (Camp et al., 1983; Kirchhoff et al., 2012; Naveh-Benjamin et al., 2007). Non-elaborative strategies are simpler and require less controlled processing to initiate and maintain (Kirchhoff et al., 2013). Common examples include rote repetition (i.e., verbal rehearsal) and concentration (Kirchhoff et al., 2012; Naveh-Benjamin et al., 2007; Verhaeghen and Marcoen, 1994). Use of elaborative encoding strategies results in a greater ability to learn presented material than use of non-elaborative encoding strategies (Camp et al., 1983; Geiselman et al., 1982; Martin et al., 1965; Shaughnessy, 1981). Older adults are also more likely than younger adults to report not using any strategy to learn new information (Devolder and Pressley, 1992; Kirchhoff et al., 2012; Rowe and Schnore, 1971).

Importantly, age differences in encoding strategy use are not due to older adults' inability to use elaborative encoding strategies. Instructing or training older adults to use elaborative encoding strategies can increase their use of the strategies and improve their memory performance (Kirchhoff et al., 2012; Miotto et al., 2014; Naveh-Benjamin et al., 2007). Thus, age differences in spontaneous encoding strategy use are most likely due to age differences in the ability to self-initiate complex, effortful strategies rather than impairment in older adults'

Abbreviations: CVLT-II, California Verbal Learning Test-II; FDR, false discovery rate; MPRAGE, magnetization-prepared rapid gradient echo; PFC, prefrontal cortex; ROI, region of interest

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ability to effectively use them.

Little is currently known about what factors contribute to age differences in self-initiated use of elaborative encoding strategies. One important factor may be age differences in prefrontal function. Prior research has shown that prefrontal cortex plays an important role in supporting self-initiated use of elaborative encoding strategies. Individuals with prefrontal lesions report using elaborative encoding strategies less frequently than healthy controls during unsupported intentional encoding. They also report not using any encoding strategy at all more frequently than healthy controls (Gershberg and Shimamura, 1995). However, like healthy older adults, individuals with frontal lobe lesions can effectively use elaborative strategies during encoding when instructed to do so (Hirst and Volpe, 1988). Individual differences in brain activity in prefrontal cortex during unsupported intentional encoding have been shown to be positively correlated with individual differences in self-initiated encoding strategy use in younger adults (Kirchhoff and Buckner, 2006). Training older adults to use elaborative semantic encoding strategies leads to changes in prefrontal brain activity during unsupported intentional encoding which are positively correlated with behavioral improvements in self-initiated semantic encoding strategy use and memory performance (Kirchhoff et al., 2012). Structural neuroimaging research has shown that prefrontal cortex is one of the brain regions most affected by age (for reviews see Lockhart and DeCarli, 2014; Raz and Rodrigue, 2006), and negative associations between age and prefrontal gray matter volume have consistently been reported (Jernigan et al., 2001; Raz et al., 1997). Taken together, this prior research suggests that age-associated declines in prefrontal integrity may significantly contribute to age-associated declines in effective encoding strategies.

To begin to test the contribution of declines in prefrontal integrity to declines in effective encoding strategy use in older adults, we recently examined the relationships between age, prefrontal regional gray matter volumes, and semantic clustering during free recall on the California Verbal Learning Test (CVLT-II; Delis et al., 2000) in a large adult lifespan dataset (Kirchhoff et al., 2014). Semantic clustering scores (Bousfield, 1953) from the CVLT are the most common measure of self-initiated elaborative memory strategy use in the clinical psychology and cognitive neuroscience literatures. The scores measure the degree to which individuals consecutively report semantically related words during free recall after studying an unstructured word list. The degree of clustering is thought to reflect self-initiated semantic strategy use during encoding and/or retrieval (Schmitt et al., 1981; Weist, 1972). We found that gray matter volume in left caudal middle, right rostral middle, and left inferior frontal regions mediated the effect of age on semantic clustering. These results are consistent with the proposed contribution of age-associated declines in prefrontal integrity to age-associated declines in effective encoding strategies. However, a significant limitation of using semantic clustering scores to measure self-initiated strategic processing is that it is not possible to determine whether semantic clustering is driven by purposeful memory strategy use during encoding, recall, both encoding and recall, or neither memory stage. For example, semantic clustering during recall could reflect relatively automatic, non-purposeful grouping of semantically-related words rather than self-initiated use of elaborative memory strategies in some individuals. Thus, further research is needed to directly investigate whether there is a significant link between age differences in self-initiated elaborative encoding strategy use found in behavioral research and age differences in prefrontal integrity found in structural neuroimaging research.

The primary goal of the current study was to investigate whether age differences in prefrontal integrity make a significant contribution to age differences in effective encoding strategies by examining whether prefrontal regional gray matter volumes mediate the effect of age on self-initiated elaborative encoding strategies. Strategy use was assessed by retrospective item-by-item strategy self-reports following a verbal unsupported intentional encoding task. This allowed us to measure the frequency of self-initiated elaborative memory strategy use *specifically during encoding*. Based upon our prior work (Kirchhoff et al., 2014), we hypothesized that gray matter volume in left caudal middle, right rostral middle, and left inferior frontal cortex would mediate the effect of age on overall self-initiated use of elaborative encoding strategies in this study. Relationships between gray matter volume and encoding strategy use were also examined in prefrontal exploratory regions of interest (ROIs) because it is possible that prefrontal regions beyond those identified in our prior structural neuroimaging study mediate self-initiated use of elaborative encoding strategies.

2. Material and methods

2.1. Participants

Thirty-eight younger (mean age = 25.0, range = 18–35, 20 female) and thirty-eight older (mean age = 70.4, range = 65–80, 23 female) adults participated in this study. All participants were right-handed native English-speakers with normal or corrected-to-normal vision. They reported no significant neurological history or active psychiatric conditions and were not taking any psychiatric medications. Participants were also screened for head injuries, untreated hypertension, heart disease, diabetes, kidney disease, thyroid conditions, chemotherapy treatments, and alcoholism. Older adults underwent screening for dementia using the Short-Blessed (Katzman et al., 1983). They all had weighted error scores less than seven (M = 1.3, SD = 1.5, Range = 0–4), indicating that they were non-demented. Study procedures were approved by the Human Studies Committees of Saint Louis University, the University of Missouri - St. Louis, and Washington University in St. Louis. Informed consent was obtained in accordance with their guidelines.

2.2. Neuropsychological assessment of cognitive function

A neuropsychological testing session was conducted prior to the MRI scanning session (range 0–32 days) to characterize participants' crystallized intelligence (Vocabulary subtest of the Wechsler Adult Intelligence Scale - Third Edition, WAIS-III; Wechsler, 1997), verbal fluency (FAS; Spreen and Strauss, 1991), semantic fluency (Animal Naming Test; Spreen and Strauss, 1991), working memory capacity (Computation Span; McCabe et al., 2010), and processing speed (Digit Symbol-Coding subtest of the WAIS-III; Wechsler, 1997).

2.3. Memory tasks

2.3.1. Unsupported intentional encoding task

An unsupported intentional encoding task was performed during three fMRI scans that occurred within the same scanning sessions as the structural MRI scans. Stimuli were 108 four to seven letter English words selected from the MRC Psycholinguistic Database (Wilson, 1988). Half of the words were concrete (e.g., paper) and half were abstract (e.g., power). Word lists were counterbalanced across participants and were matched for word frequency, length, and syllable count.

The unsupported intentional encoding scans had a block design and started with a 36 s fixation block, during which a plus sign was displayed in the center of a screen. The initial fixation block was followed by an intentional encoding task block that lasted 72 s, during which eighteen words were presented one at a time for 3750 ms in the center of a screen. Each word was immediately followed by a fixation plus sign presented for 250 ms. A second fixation block then occurred for 28 s, and was followed by an additional 72 s intentional encoding task block and then a final 28 s fixation block. Participants were instructed to carefully study each word and were told that their memory for the words would be tested later. However, they were not instructed to use any specific strategy or strategies to study the words, so they could study the presented words using any method that they chose. To ensure