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Structural brain correlates of associative memory in older adults

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ABSTRACT

Associative memory involves binding two or more items into a coherent memory episode. Relative to memory for single items, associative memory declines greatly in aging. However, older individuals vary substantially in their ability to memorize associative information. Although functional studies link associative memory to the medial temporal lobe (MTL) and prefrontal cortex (PFC), little is known about how volumetric differences in MTL and PFC might contribute to individual differences in associative memory. We investigated regional gray-matter volumes related to individual differences in associative memory in a sample of healthy older adults ($n = 54$; age $= 60$ years). To differentiate item from associative memory, participants intentionally learned face–scene picture pairs before performing a recognition task that included single faces, scenes, and face–scene pairs. Gray-matter volumes were analyzed using voxel-based morphometry region-of-interest (ROI) analyses. To examine volumetric differences specifically for associative memory, item memory was controlled for in the analyses. Behavioral results revealed large variability in associative memory that mainly originated from differences in false-alarm rates. Moreover, associative memory was independent of individuals' ability to remember single items. Older adults with better associative memory showed larger gray-matter volumes primarily in regions of the left and right lateral PFC. These findings provide evidence for the importance of PFC in intentional learning of associations, likely because of its involvement in organizational and strategic processes that distinguish older adults with good from those with poor associative memory.

Introduction

Episodic memory (EM) is the conscious remembrance of events and relations between events situated in time and place (Tulving, 1972). Within EM, a distinction can be made between remembering single items (e.g., a name, an object, or a word) versus associated information (e.g., face–name, object–location, or word–sound pairs; Davachi, 2006). Although item memory remains relatively well preserved in aging, older adults' associative memory is markedly impaired (Chalfonte and Johnson, 1996; Naveh-Benjamin, 2000). The associative-deficit hypothesis, which attributes age-related EM deficits to problems in encoding and retrieving associated information (Naveh-Benjamin, 2000), has been supported by numerous studies using different materials (e.g., word–word, word–font, face–name, object–location, and object–object combinations; Old and Naveh-Benjamin, 2008).

In addition to mean age-related alterations in performance, individual differences in EM increase in aging (Lindenberger, 2014; Lindenberger et al., 2013). Both cross-sectional and longitudinal studies reveal greater inter-individual variability in EM functioning in older compared to younger adults (Christensen et al., 1999; Morse, 1993; Wilson et al., 2002). With regard to memory for associative information, greater variability has been reported for older compared to younger adults and for associative compared to item memory (Dennis et al., 2008; Glisky et al., 2001; Kilb and Naveh-Benjamin, 2011; Naveh-Benjamin, 2000; Naveh-Benjamin et al., 2009; Rajah et al., 2010a).

Only few studies have systematically investigated the neural underpinnings of these individual differences. Magnetic resonance imaging (MRI) studies show that EM functioning in general draws on medial–temporal lobe (MTL) and lateral prefrontal (PFC) structures (Buckner et al., 1999; Cabeza, 2006; Dickerson and Eichenbaum, 2010; Mayes et al., 2007; Simons and Spiers, 2003; Van Petten, 2004). Findings from functional MRI studies have linked associative memory to hippocampal and item memory to parahippocampal activity, and reported greater PFC activity for associative than for item memory (Blumenfeld et al., 2011; Lepage et al., 2003; Staresina and Davachi, 2008; Westerberg et al., 2012). Structural MRI studies are less conclusive. Equivocal findings have been observed regarding the association between hippocampal volume and item memory (Hackert et al., 2002; Kalpouzos et al., 2009; Köhler et al., 1998; Rosen et al., 2003; for a review see Van Petten, 2004). Structural studies investigating associative

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memory are generally less common. To our knowledge, only one study examined both item and associative memory (using a word–pair recognition paradigm) from early to late adulthood with a ROI-based approach including the hippocampus (HC), entorhinal cortex, and lateral PFC (Rodrigue and Raz, 2004). Findings revealed a positive relation between hippocampal volume and associative memory across age. Shing et al. (2011) examined associative memory in relation to hippocampal subfield volumes in older adults and found a positive correlation between the CA3–4 and dentate gyrus subfields and memory performance. However, another study focused on differences between younger and older adults by comparing the relation of hippocampal volume to associative memory in each age group, and found a positive relation between gray-matter volume and associative memory in younger, but not older, adults. These data were interpreted to mean that older adults might depend less on HC, but rely more on frontal regions when intentionally learning associations (Rajah et al., 2010a; see Rajah et al., 2010b for supporting functional results).

Although the relation of MTL and PFC gray-matter volumes to item and associative memory is still ambiguous, there is consensus on the functions these regions serve. The MTL, especially the HC, is important for binding single items together. Hence, we expect structural gray-matter volume differences in the hippocampal region to be one underlying source of inter-individual differences in associative memory in older adults. The lateral PFC is known to enhance binding through control operations (Fletcher et al., 2000) and strategy use (Kirchhoff and Buckner, 2006; Kirchhoff et al., 2014), which facilitates item-item binding (Dunlosky and Hertzog, 1998; Naveh-Benjamin et al., 2007). In healthy aging, the PFC undergoes structural and functional changes accompanied by increased inter-individual variability in volume (Lindenberger, 2014; Lindenberger et al., 2013; Raz et al., 2005). Given that also differences in strategic processes might underlie individual differences in associative-memory performance, we hypothesize that individual differences in binding are, in part, explained by volumetric differences in PFC. However, to date no structural MRI study has investigated associative memory in a sample of older adults specifically in relation to PFC. Hence, the contribution of gray-matter volume in PFC to individual differences in associative memory remains unknown.

We investigated whether inter-individual differences in PFC and MTL volumes account for inter-individual differences in associative memory in a sample of healthy older adults. To differentiate the relative contribution of brain structures to item and associative memory, a recognition task that captures both memory for single items and associated information was used.

Methods

Participants

Data were collected within the *Swedish National Study on Aging and Care in Kungsholmen (SNAC-K)*, a population-based study targeting people 60 years and older living in the Kungsholmen district in central Stockholm. The current sample was taken from a cohort added in 2010–2013 (wave 4 in SNAC-K). All 678 participants in this new cohort were 60 years old and randomly selected from population registries. The examination in SNAC-K took about six hours and consisted of three parts: a nurse interview, a medical examination, and a neuropsychological testing session. In addition to the standard cognitive test battery of SNAC-K (Laukka et al., 2013), this cohort was also assessed with an item-associative-memory task. A subsample of 57 individuals participated in an MRI assessment. The sample for this study included cognitively healthy persons with data on MRI and the item-associative memory task. Participants were screened for microvascular lesions, cerebral infarcts, and motion artifacts by two independent and experiences raters. Three participants in the MRI sample were excluded due to missing data on the item-associative memory task; thus the final sample consisted of 54 participants (30 females; mean years of education = 15.3; see Table 1). The selection bias of the MR subsample relative to the whole sample was positive but small (effect size of selectivity < .29 in a number of cognitive variables, including the item-associative memory task, Mini-Mental State Examination (MMSE), episodic memory, perceptual speed, semantic memory, and educational background).

Material and procedure

Item-associative-memory task (IAMT)

The IAMT was administered at the end of the neuropsychological testing session. During encoding, participants saw 24 face–scene picture pairs on a computer screen. Each pair was presented for 4 s with a fixed inter-stimulus interval of 1 s. The face stimuli were male and female, old and young faces, exhibiting either a neutral or happy expression (Ebner et al., 2010). Scene stimuli were colored photographs of indoor and outdoor scenes (Chen and Naveh-Benjamin, 2012). Subjects were instructed to memorize both the single pictures and their combinations. The encoding phase was followed by a distractor task, in which subjects had to count backwards from 89 in steps of two for one minute.

Immediately following the distractor task, three self-paced recognition tasks were administered: two item-memory and one associative-memory task with their order counterbalanced across participants. In each item-memory task (one for the faces and one for the scenes), subjects saw 16 single pictures (i.e., 16 faces and 16 scene pictures), of which eight had been studied during encoding. The remaining eight new pictures served as lures. Participants were instructed to indicate whether they had seen a particular face or scene picture in the encoding phase by pressing the buttons “yes” or “no” on a computer keyboard. In the associative-memory task, subjects saw 16 face–scene pairs of which all had been previously presented. However, half of the pairs were intact (old), whereas the other half was recombined (composed of faces and scenes that appeared in the study phase, but not together). Again, subjects indicated whether or not they had seen a particular face–scene combination during encoding by pressing a “yes” or “no” button on the computer keyboard (see Fig. 1). Each face or scene appeared in only one of the three tests.

Free-recall task

To control for differences in task difficulty between item and associative memory in the IAMT, a separate and more difficult item-memory task was assessed and used as regressor in the analyses. Here, participants studied 16 concrete Swedish nouns, presented in black on a 14.5 × 21 cm white paper. Each word was shown and read out aloud by the experimenter. Immediately after presentation of the last word in the series, participants were asked to free recall the words orally (Laukka et al., 2013).

Table 1
Demographic and cognitive measures of the study sample.

Variable		Mean	SD
Age (years)		60.47	.21
Education (years)		15.30	3.17
MMSE score		29.20	1.00
Item memory (scenes)	H	6.87	1.03
	FA	0.04	1.25
	H-FA	6.83	1.06
Item memory (faces)	H	6.85	1.00
	FA	1.81	.19
	H-FA	5.04	1.48
Associative memory	H	6.50	1.23
	FA	3.31	2.05
	H-FA	3.19	2.56
Free recall	H	8.56	1.62