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The relationships between age, associative memory performance, and the neural correlates of successful associative memory encoding

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ABSTRACT

Using functional magnetic resonance imaging, subsequent memory effects (greater activity for later remembered than later forgotten study items) predictive of associative encoding were compared across samples of young, middle-aged, and older adults (total N = 136). During scanning, participants studied visually presented word pairs. In a later test phase, they discriminated between studied pairs, "rearranged" pairs (items studied on different trials), and new pairs. Subsequent memory effects were identified by contrasting activity elicited by study pairs that went on to be correctly judged intact or incorrectly judged rearranged. Effects in the hippocampus were age-invariant and positively correlated across participants with associative memory performance. Subsequent memory effects in the right inferior frontal gyrus (IFG) were greater in the older than the young group. In older participants only, both left and, in contrast to prior reports, right IFG subsequent memory effects correlated positively with memory performance. We suggest that the IFG is especially vulnerable to age-related decline in functional integrity and that the relationship between encoding-related activity in right IFG and memory performance depends on the experimental context.

1. Introduction

Episodic memory—memory for unique events—is one of several cognitive domains in which performance declines with increasing age (Koen and Yonelinas, 2014; Nilsson, 2003; Old and Naveh-Benjamin, 2008; Rönnlund et al., 2005). A significant fraction of age-related variance in episodic memory performance is attributable to differences in the efficacy with which events are encoded into memory (see Craik and Rose, 2012 for review), and numerous studies have used functional neuroimaging in an effort to elucidate the neural underpinnings of the effects of age on episodic memory encoding. Most of these studies have used event-related functional magnetic resonance imaging (fMRI) in concert with the "subsequent memory procedure" (Paller and Wagner, 2002), examining age-related differences in neural activity predictive of successful or unsuccessful performance on a later memory test (e.g., de Chastelaine et al., 2011; Dennis et al., 2008; Duverne et al., 2009; Gutchess et al., 2005; Mattson et al., 2014; Miller et al., 2008; Morcom et al., 2003; Mormino et al., 2012; Park et al., 2013; see Maillet and Rajah, 2014 for review).

The findings from these studies are somewhat mixed but show some consistent trends. There is converging evidence for example that "negative" subsequent memory effects—where later remembered study items elicit relatively less activity than later forgotten items—are attenuated, and sometimes reversed, in older individuals (e.g., de Chastelaine et al., 2011; Duverne et al., 2009; Gutchess et al., 2005; Mattson et al., 2014; Miller et al., 2008; Mormino et al., 2012; Park et al., 2013). Consistent with these findings, in a recent published analysis of the present data set (de Chastelaine et al., 2015), we reported that although negative subsequent memory effects were reliable in young, middle-aged, and older age groups, there was a graded attenuation in the size of the effects with increasing age (young > middle-aged > older). We do not discuss these findings further here; however, instead, we focus on "positive" subsequent memory effects (henceforth, just "subsequent memory effects" or "encoding-related activity"), where study items that go on to be remembered on a later memory test elicit greater neural activity than items that are later forgotten (see Kim, 2011 for a review of relevant research in young adults).

Two fairly consistent trends emerge from studies examining the effects of age on subsequent memory effects: first, despite the vulnerability of the hippocampus to age-related volume reduction (see Raz and Rodrigue, 2006 for review), the weight of the evidence suggests that encoding-related activity in this region does not differ

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with age (e.g., de Chastelaine et al., 2011; Duverne et al., 2009; Miller et al., 2008; but see e.g., Dennis et al., 2008 for contrasting findings, and see Maillet and Rajah, 2014 for a review). Second, although the magnitude of subsequent memory effects in left lateral prefrontal cortex (PFC) also appears to differ little with age, the effects in homotopic regions of the right PFC have been reported to be greater in older than in young individuals (e.g., Duverne et al., 2009; Morcom et al., 2003), an example of age-related, right-frontal "over-recruitment" (Grady, 2012).

Findings of right frontal over-recruitment are open to multiple interpretations (Grady, 2012). According to one set of proposals, for example, the findings reflect engagement of neural regions that help to compensate for age-related decline in processing efficiency in other regions sufficient to support task performance in younger individuals (e.g., Cabeza, 2002; Reuter-Lorenz and Cappell, 2008; Reuter-Lorenz and Park, 2014). A second set of proposals suggests that, rather than facilitating task performance, over-recruitment harms it, reflecting age-related dedifferentiation of cortical specialization and an attendant decline in processing efficiency (e.g., Li et al., 2006). Another, related, proposal is that right frontal over-recruitment reflects age-related decline in the transcallosal inhibitory drive from the left hemisphere that suppresses activation of, and hence interference from, homotopic task-irrelevant cortical regions (e.g., Logan et al., 2002). Finally, it has been proposed that right frontal over-recruitment, at least as it is expressed in item-related activity (i.e., in the bold response elicited by study items relative to the inter-item baseline), is a consequence of age-related sampling bias (Nyberg et al., 2010; see also Pudas et al., 2013).

One possible way of arbitrating between these different proposals is to assess the relationship between right prefrontal activity and task performance. In studies of episodic memory encoding, this amounts to asking whether, as would be predicted by the simplest form of the "compensation hypothesis" described previously, memory performance in older individuals is positively correlated with the magnitude of right frontal subsequent memory effects. Three studies in which this question was addressed (de Chastelaine et al., 2011; Duverne et al., 2009; Miller et al., 2008; but see also Bangen et al., 2012) reported consistent findings: in each case, a reliable correlation between right frontal subsequent memory effects and memory performance was observed, but the direction was negative. That is, right frontal encoding-related activity was greater in those individuals with the poorest memories for the study items.

These findings are inconsistent with the most straightforward prediction of the compensation hypothesis of age-related right frontal over-recruitment and, on the face of it, are more supportive of the proposal that over-recruitment is detrimental for memory encoding. As was discussed by, among others, de Chastelaine et al. (2011) and Grady (2012) (see also Duverne et al., 2009), the findings are, however, compatible with other conceptualizations of age-related neural compensation. By one account (e.g., Düzel et al., 2011), it is those individuals most affected by aging, and hence with the lowest levels of performance, who engage compensatory mechanisms to the greatest extent. By an alternative account (de Chastelaine et al., 2011), right frontal over-recruitment reflects "partial" compensation—sufficient to support performance on the study task, but not to boost memory encoding. We return to this issue in the Discussion.

The aim of the present study was to gain further insight into the relationship between age, encoding-related neural activity, and memory performance. We used the same associative memory procedure as in our prior study of episodic encoding (de Chastelaine et al., 2011) on an independent sample of young, middle-aged and older participants. Associative memory is well suited to studies such as the present one because it is strongly dependent on the recollection of qualitative information (e.g., Mickes et al., 2010) and is highly sensitive to age (Old and Naveh-Benjamin, 2008). In our prior study, we investigated subsequent memory effects in samples of young ($n = 18$) and older ($n = 36$) individuals. We found that the magnitude of the effects in several regions, including left inferior frontal gyrus (IFG) and hippocampus, did not differ according to age group. In the older participants, we also found that subsequent memory effects in left and right IFG demonstrated reliable but opposite relationships with memory performance, such that there was a positive correlation for the left IFG and a negative correlation for the right IFG. We further reported that the integrity of the anterior corpus callosum, as this was indexed by fractional anisotropy (FA) estimated from diffusion tensor imaging (DTI), was both strongly age-dependent (replicating numerous prior reports, e.g., Head et al., 2004; Kochunov et al., 2012; O'Sullivan et al., 2001; Pfefferbaum et al., 2000) and positively correlated with the magnitude of subsequent memory effects in the right IFG. This latter finding is arguably inconsistent with the proposal that right frontal over-recruitment reflects age-related disruption of transcallosal inhibition (e.g., Logan et al., 2002).

The present study extends this prior work in 2 important ways. First, we used substantially larger samples of young and older participants than in the prior study (Ns of 36 and 64, respectively), affording greater statistical power with which to detect age-related differences in subsequent memory effects and examine the relationship between different facets of encoding-related activity and individual differences in subsequent memory performance. Thus, we were able to assess the generality of our prior finding that left and right frontal subsequent memory effects demonstrate opposite relationships with memory performance, and whether these or other relationships with performance differ with age. We were also able to assess the generality of a prior report that the magnitude of subsequent memory effects in the hippocampus is negatively correlated with subsequent associative memory accuracy in older individuals (Miller et al., 2008) and examine whether this finding extends to other age groups. Second, in addition to samples of young and older individuals, here, we also used a sample of middle-aged individuals ($n = 36$). This age range has been relatively neglected in studies examining the effects of age on the neural correlates of episodic memory (we are aware of only 3 prior papers describing encoding-related activity in this population: de Chastelaine et al., 2015; Kwon et al., 2015; and Park et al., 2013). The inclusion of middle-aged individuals provides a more continuous sampling of encoding-related activity across the life span than can be achieved with an extreme age-groups approach, and hence provides additional insight into the profile of any age-related differences.

2. Materials and methods

Additional methodological information can be found in de Chastelaine et al. (2015), where a complementary analysis of the present fMRI data set is reported (see Introduction).

2.1. Participants

Participants were 36 young (18–29 years; M = 22 years; standard deviation [SD] = 3.0 years; 17 female), 36 middle-aged (43–55 years; M = 49 years; SD = 3.4 years; 17 female), and 64 older adults (63–76 years; M = 68 years; SD = 3.6 years; 35 female). The participants were recruited from the city of Dallas and surrounding communities and comprised samples wholly independent of those participating in our previous study (de Chastelaine et al., 2011). All participants were in good health, had no history of cardiovascular, neurologic, or psychiatric disease, and were not taking central nervous system–active medication. The participants were right-handed, had learned English before age 5, and had normal or corrected-to-normal vision. Exclusion criteria based