Neural activation patterns of successful episodic encoding: Reorganization during childhood, maintenance in old age

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ABSTRACT

The two-component framework of episodic memory (EM) development posits that the contributions of medial temporal lobe (MTL) and prefrontal cortex (PFC) to successful encoding differ across the lifespan. To test the framework's hypotheses, we compared subsequent memory effects (SME) of 10–12 year-old children, younger adults, and older adults using functional magnetic resonance imaging (fMRI). Memory was probed by cued recall, and SME were defined as regional activation differences during encoding between subsequently correctly recalled versus omitted items. In MTL areas, children's SME did not differ in magnitude from those of younger and older adults. In contrast, children's SME in PFC were weaker than the corresponding SME in younger and older adults, in line with the hypothesis that PFC contributes less to successful encoding in childhood. Differences in SME between younger and older adults were negligible. The present results suggest that, among individuals with high memory functioning, the neural circuitry contributing to successful episodic encoding is reorganized from middle childhood to adulthood. Successful episodic encoding in later adulthood, however, is characterized by the ability to maintain the activation patterns that emerged in young adulthood.

1. Introduction

Episodic memory (EM) emerges and increases during childhood (e.g., Schneider and Pressley, 1997) and deteriorates in aging (e.g., Rönnlund et al., 2005). On the surface, children in middle childhood and older adults show comparable memory levels, with both groups performing worse than younger adults (Li et al., 2004). However, direct lifespan comparisons of neural correlates of EM are entirely lacking, leaving an untested assumption that neural mechanisms underlying memory in children and older adults are the same, given their similarities in performance (but see behavioral comparisons by Brehmer et al., 2007; Fandakova et al., 2013; Shing et al., 2008). Therefore, lifespan studies are strongly needed in the field of developmental cognitive neuroscience, which has

tended to focus either on comparisons on the lower end (children vs. young adults) or the higher end (younger vs. older adults) of the developmental spectrum. Here, we examined the neural correlates of subsequent-memory effects (SME), defined as differences in fMRI activation between subsequently remembered and omitted trials during encoding, in 10–12 years old children, younger adults between 21 and 26 years, and older adults above 60 years of age. Our focus was to compare SME within the memory systems of the various age groups when they operate successfully to form durable memory representation.

According to the two-component framework of EM development, the ontogeny of EM reflects interactions between associative and strategic components (Shing et al., 2010; Shing et al., 2008; Werkle-Bergner et al., 2006). The associative component refers to binding mechanisms that integrate features of episodes into coherent representations (Treisman, 1996; Zimmer et al., 2006), and the strategic component refers to cognitive-control processes that aid and regulate memory functions (Simons and Spiers, 2003). In line with established conceptions of EM (Eichenbaum, 2002;

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Moscovitch, 1992; Simons and Spiers, 2003) and meta-analyses of fMRI studies on SME (Kim, 2011; Spaniol et al., 2009), we assume that the lateral PFC and MTL (particularly the hippocampus, HC) support strategic and associative components of EM, respectively. The HC and associated structures contribute to the formation of memory representations, particularly establishing associations between features (e.g., Davachi, 2006). Lateral PFC, on the other hand, supports cognitive control processes in service of memory (Fletcher and Henson, 2001), such as implementation of attention selection processes in the VLPFC and organization of information in working memory in the DLPFC (e.g., Blumenfeld and Ranganath, 2007).

Both PFC and MTL undergo profound reorganization in childhood (Johnson, 2001; Nelson, 2001) and aging (Buckner, 2004; Cabeza et al., 2004). The structural integrity of PFC (particularly the dorsolateral regions) undergoes maturational changes well into adolescence. On the other hand, MTL regions mature at faster rates particularly in the first few years of life (Gogtay et al., 2006; Sowell et al., 2003). Therefore, we assume that successful memory formation in children should rely more on the associative component of MTL and less on the strategic component of PFC that is still developing (Ofen, 2012; Shing et al., 2010; but see Ghetti and Bunge, 2012). Thus far, results are mixed regarding MTL differences between childhood and young adulthood in SME, with some studies finding age differences (e.g., Ghetti et al., 2010) and others not (e.g., Ofen et al., 2007). This stands in contrast to the more consistent age differences found in PFC across development. Therefore, our empirical investigation will shed light on this topic.

On the other hand, lower EM performance in aging is assumed to reflect senescent changes in the associative as well as strategic components (Shing et al., 2010). Gray matter differences are especially pronounced in both HC and PFC regions (Fjell et al., 2009; Raz et al., 2005; but see Raz et al., 2010 for lack of longitudinal change in PFC). However, findings regarding functional alterations in these regions during episodic encoding in old age have been mixed. In part, the inconsistencies across studies may reflect the heterogeneity of memory functioning in old age (Persson et al., 2011; Raz et al., 2010; Rönnlund et al., 2005). This partly gave rise to a maintenance view on EM proposed by Nyberg et al. (2012), underscoring the notion that preserved brain functioning is the primary characteristic of successful memory aging. While this view focuses on between-person differences, a within-person aspect of maintenance would suggest that, among healthy older adults, successful episodic encoding should engage both the associative and strategic components optimally, reflecting a state that is youth-like. Therefore, our study aimed to shed lights on the mixed findings by comparing age groups across the lifespan to identify their commonalities and differences in neural mechanisms contributing to successful memory formation.

Importantly, in contrast to most SME studies that tested memory with a recognition procedure, we opted for cued recall in which participants studied word pairs (e.g. dog-crown) and subsequently had to recall the target (crown) when shown the cue (dog). This required individuals' memory system to operate at its best during encoding in order to form strong, distinctive memory representations that can be recalled later on. In younger adults, compared to recognition, cued-recall imposes stronger demands on both PFC and MTL (Habib and Nyberg, 2007; Staresina and Davachi, 2006). Based on our framework, we expected that SME in children, relative to younger and older adults, would rely more on MTL and less on PFC regions. In contrast, SME-related activation of healthy older adults should be largely similar to those of younger adults. This is because the neural circuitry contributing to SME, particularly for forming strong memory representations, should not alter fundamentally in healthy aging (cf. Maillet and Rajah, 2014). As a secondary goal, we also explored potential age differences in func-

tional connectivity in EM networks. Thus far little is known about memory-related connectivity in children, while older adults seem to show increased connectivity in fronto-temporal networks for successful memory encoding (Dennis et al., 2008; Oh and Jagust, 2013). Therefore, in addition to functional activation, our analyses will extend the two-component framework of EM lifespan development to examine MTL-PFC interactions.

2. Methods

2.1. Participants

This fMRI study was part of a larger scale EM training study. The initial sample consisted of 95 children aged 10–12 years (fifth-graders in the German Gymnasium education track), 49 younger adults aged 21–26 years (university or college students), and 165 older adults aged 63–74 years (retired community dwellers living in Berlin). These participants took part in a screening session and were invited to participate in the fMRI study if they fulfilled all of the following criteria: (a) a minimum raw score of 34 correctly solved symbols on the digit symbol test (maximum score 94; Wechsler, 1955); (b) recalling at least 3 word pairs from a list of 10 pairs; and additionally for adults only (c) more than 27 points on the Mini-Mental State Exam (maximum score 30; Folstein et al., 1975); (d) 30 points or higher on the CES-D scale on depression (Radloff, 1977). The first two criteria were established after extensive piloting and were adopted to increase the likelihood that our scanned participants would produce enough remembered trials for the fMRI analyses.

56 children, 35 younger adults, and 55 older adults fulfilled the screening criteria and participated in the fMRI assessment. These participants were right-handed, native German speakers, and reported not having neurological or psychiatric disorders (e.g. Alzheimer, multiple sclerosis, Parkinson's disease, dyslexia, mood disorders etc.). For the current analysis of SME, three children had to be excluded due to excessive motion artifacts, and one younger adult due to technical error in scanning. Furthermore, we included only those participants who provided sufficient numbers of remembered as well as omitted responses for the fMRI analysis (i.e. a minimum of two runs with at least six trials per run; see Murphy and Garavan, 2005 on number of events for fMRI designs). Therefore, for the analyses below, we used data from 31 children (M_{age} = 11.09, SD_{age} = 0.39), 33 younger adults (M_{age} = 24.0, SD_{age} = 1.33), and 25 older adults (M_{age} = 66.8, SD_{age} = 2.15). As shown in Table 1, compared to the excluded sample, the final sample was positively selected on memory performance, particularly in the case of children and older adults. Within each age group, the excluded and final samples were comparable in terms of gender radio, performance on a marker test of crystallized intelligence (verbal knowledge; Lehrl, 1977), a marker test of fluid intelligence (digit symbol; Wechsler, 1955), and years of education. We found expected lifespan patterns with respect to crystallized and fluid intelligence, namely (a) a continuous increase in verbal knowledge across the lifespan, and (b) an inverted U-shaped lifespan function for the Digit Symbol scores, with children and older adults showing lowered performance in comparison to younger adults.

2.2. Materials and procedure

Stimuli were highly imaginable concrete German nouns paired together to form unrelated word pairs. Words were drawn from German norm databases and previous studies had established their comprehensibility for children of similar ages as those included here (see Brehmer et al., 2004, 2007; Hasselhorn et al., 1990; Shing et al., 2008). Screened by several raters, word pairs were checked