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Development of deactivation of the default-mode network during episodic memory formation

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ABSTRACT

Task-induced deactivation of the default-mode network (DMN) has been associated in adults with successful episodic memory formation, possibly as a mechanism to focus allocation of mental resources for successful encoding of external stimuli. We investigated developmental changes of deactivation of the DMN (posterior cingulate, medial prefrontal, and bilateral lateral parietal cortices) during episodic memory formation in children, adolescents, and young adults (ages 8–24), who studied scenes during functional magnetic resonance imaging (fMRI). Recognition memory improved with age. We defined DMN regions of interest from a different sample of participants with the same age range, using resting-state fMRI. In adults, there was greater deactivation of the DMN for scenes that were later remembered than scenes that were later forgotten. In children, deactivation of the default-network did not differ reliably between scenes that were later remembered or forgotten. Adolescents exhibited a pattern of activation intermediate to that of children and adults. The hippocampal region, often considered part of the DMN, showed a functional dissociation with the rest of the DMN by exhibiting increased activation for later remembered than later forgotten scene that was similar across age groups. These findings suggest that development of memory ability from childhood through adulthood may involve increased deactivation of the neocortical DMN during learning.

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Introduction

The ability to form detailed memories for facts and events is essential for education and for everyday life, and increases from childhood to adulthood (Cycowicz et al., 2001; Ghetti and Angelini, 2008; Mandler and Robinson, 1978). Successful memory formation in adults is correlated with activations in a number of brain regions, including the prefrontal cortex (PFC) and the medial temporal lobe (MTL) (Brewer et al., 1998; Wagner et al., 1998). Activations in these regions are also correlated with successful memory formation in children (Chai et al., 2010; Ghetti et al., 2010; Ofen, 2012; Ofen et al., 2007). Activations in these regions are greater during encoding of items that are subsequently remembered compared to those that are subsequently forgotten. In adults, deactivations of a different set of brain regions, including midline regions such as the posterior cingulate cortex (PCC) and lateral parietal cortices, are also associated with successful memory encoding (Daselaar et al., 2004). The amplitude of deactivation in these regions is greater for items that are later remembered than for items that are later forgotten.

Here we asked whether deactivation or suppression of those brain regions during memory formation undergoes maturation between childhood and adulthood.

Brain regions exhibiting deactivation during successful memory encoding in adults overlap with regions of the default-mode network (DMN), a network of brain regions commonly deactivated during tasks that demand external attention (Raichle et al., 2001). The DMN is consistently comprised of the PCC, medial prefrontal cortex (MPFC), and left and right lateral parietal cortices (LLP and RLP) (Raichle et al., 2001), and also frequently extends to the hippocampal region bilaterally (Buckner et al., 2008) The DMN may be activated in internal- and self-oriented processing (Buckner et al., 2008). Suppression of the DMN, on the other hand, appears to be functionally important for successful operation of cognitive processes that demand attention to the environment. For example, better sustained attention is associated with more deactivation of the DMN (Lawrence et al., 2003), whereas momentary lapses in attention are associated with reduced task-induced deactivation of the DMN (Lawrence et al., 2003; Weissman et al., 2006). Greater working memory demands provoke both increased activation in cognitive control regions (e.g., PFC) and also increased deactivation in the DMN (McKiernan et al., 2003). Task-induced deactivation of the DMN may signal the suppression of attention to one's own thoughts or feelings and promote the allocation of mental and neural resources to tasks involving external stimuli (Anticevic et al., 2012;

Whitfield-Gabrieli et al., 2009). In the case of episodic memory formation, more deactivation of the DMN may enhance resources allocated to memory encoding of external stimuli and thus better long-term memory.

Development of the DMN has been studied using resting-state fMRI, and although there is considerable evidence that the DMN develops from childhood through adulthood, methodological issues have made uncertain the specific nature of that development. Some studies suggest that long-range correlations among the DMN components grow markedly from childhood through young adulthood (Barber et al., 2013; Fair et al., 2007, 2008; Supekar et al., 2009, 2010). Other studies, noting evidence that differences in head movement have major influences on the analysis of resting-state connectivity (Power et al., 2012; Van Dijk et al., 2012; Yan et al., 2013) and that such movement declines precipitously with age, have controlled for such movement and have reported far smaller developmental effect of DMN correlations (Satterthwaite et al., 2012; Chai et al., submitted). Developmental effects for DMN may be more robust when anticorrelations between the DMN and cortical areas involved in cognitive control are considered (Barber et al., 2013; Chai et al., submitted).

Based on evidence of DMN deactivation during memory encoding in adults and the maturation of DMN in resting-state, here we examined whether or not there were developmental changes related to deactivation of the DMN during memory encoding that predicted subsequent memory. Prior studies of such development in children and adolescents relative to adults have focused exclusively on activations related to successful memory formation, and not deactivations. For scenes, there were developmental increases in PFC and parietal activations for the successful encoding of well-remembered scenes (Ofen et al., 2007), and a similar finding for the successful retrieval of memory for scenes (Ofen et al., 2012). MTL activations were associated with successful encoding and retrieval, but did not change with age (Ofen et al., 2007, 2012). Other studies, however, have reported developmental differences in MTL activation related to memory formation for specifically complex scenes (Chai et al., 2010) or contextual information (Ghetti et al., 2010). Thus, there are findings of both early maturation in which memory-related activations are adult-like in childhood, and also late maturation in which memory-related activations grow through young adulthood. Here we investigated the development of task-induced deactivation of the DMN during memory formation in a reanalysis of previously published data (Ofen et al., 2007) that examined the normal development of activations related to successful memory formation, in healthy children, adolescents and adults from ages 8 to 24.

Methods

Participants

Fifty-two volunteers, ages 8 to 24 years, were recruited from the Stanford University community and provided informed consent as indicated by a Stanford University IRB-approved protocol. All participants were right-handed, had normal or corrected-to-normal vision, with no history of psychiatric or neurological disorder. Two participants were excluded as a result of motion artifacts during scan (maximum head movement during the fMRI task exceeded 3 mm). In addition, two participants were excluded due to incomplete data. We present data from the remaining 48 participants (mean age = 15.7 ± 4.5, 25 females). Analyses were performed on three age groups: children (ages 8–12, $N = 16$), adolescents (ages 13–17, $N = 18$) and adults (ages 18–24, $N = 14$)). All participants were tested on a standardized speed of processing (SOP) test (Visual Matching, Woodcock-Johnson III (Woodcock et al., 2001)). Age-normed scores on that test did not differ among the groups (F(2,45) = 2.45, p > .1), suggesting the validity of cross-sectional comparison in this sample.

Memory task

Participants viewed 125 indoor and 125 outdoor scenes during a scanned study phase that was followed by a recognition memory test. During scanning, each picture was presented for 3 s with 1 s of inter-trial interval. Participants made "indoor" or "outdoor" judgments to each scene by pressing a button on the button box. Trials with incorrect or no responses were excluded from the analyses (error trials). The study phase was divided into five sessions, each with 50 scenes. After the scanning session, participants were given a self-paced recognition test of the 250 scenes studied during the scanning session and 250 new scenes. If the participant responded "old" to a scene, they were further asked to indicate if they "actually remembered" the scene (R) or if the scene "just looks familiar" (Know, K). Adjusted memory accuracy was calculated by subtracting the false alarm rate ("old" responses to new pictures) from the hit rate ("old" responses to studied pictures). In addition to the overall accuracy (Hits − FA), accuracy for "R" and "K" trial types was calculated separately, by subtracting the corresponding false alarm rate from the hit rate for R or K trial types (R accuracy: $R - FA_R$; K accuracy: $K / (1 - R) - FA_K$, adjusted for being mathematically constrained by R responses). If a "new" response was given to a studied scene, the trial was classified as a "forgotten" trial (F).

Imaging procedure

MRI data were acquired in a 1.5 T GE scanner. T1-weighted whole-brain anatomy images (256×256 voxels, 0.86-mm in-plane resolution, 1.2-mm slice thickness) were acquired prior to the functional scans. Functional images were acquired using T2*-sensitive two-dimensional gradient-echo sequence in 24 contiguous, 6-mm slices parallel to the line connecting the anterior and posterior commissures, with 2 s repetition time, 60 degree flip angle, 64×64 voxels, and 3.75 mm in-plane resolution. The first two volumes of each run were discarded.

fMRI analysis

Functional imaging data were analyzed in SPM8 (Department of Imaging Neuroscience, London, UK). Functional images were slice-time corrected and motion corrected. The anatomical image was coregistered to the mean functional image that was created during motion correction. Functional images were then spatially normalized to the T2 Montreal Neurological Institute (MNI) template, and smoothed with a 6-mm Gaussian kernel. Data were inspected for artifacts and motion using custom software (http://www.nitrc.org/projects/artifact_detect/). First-level analysis was performed with a general linear model (GLM) with regressors for R, K, and F and error trials. Additional regressors accounted for head movement (3 translation, 3 rotation parameters) and outlier scans (images in which average intensity deviated more than 3 SD from the mean intensity in the session or in which movement exceeded 0.5 mm in translation or 0.01° in rotation from the previous image). Each outlier scan was represented by a single regressor in the GLM, with a 1 for the outlier time point and 0 s elsewhere. There was a significant age-group difference in the number of outlier images (F(2,47) = 5.3, p = .009). Children had more outliers (mean = 15.9 ± 11.7) than both adults (5.7 ± 10.5) and adolescents (7.3 ± 6.4) (children vs. adults: t(28) = 2.6, p = .016; children vs. adolescents t(32) = 2.7, p = .011). Adolescents and adults did not differ in the number of outliers (t(30) = .6, p > .5).

DMN region of interest (ROI) analysis

We examined activations during R and F conditions in four independently defined neocortical default-mode regions of interests: MPFC, PCC, LLP, and RLP created as 15 mm spheres around peak coordinates from an independent developmental resting-state fMRI study (Chai