

Neural indices of improved attentional modulation over middle childhood

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ABSTRACT

The ability to control the focus of attention relies on top-down modulation of cortical activity in areas involved in stimulus processing, and this ability is critical for maintaining items in working memory in the presence of distraction. Prior research demonstrates that children are less capable of focusing attention, relative to adults, and that this ability develops significantly during middle childhood. Here, using fMRI and a face/scene working memory task adapted from Gazzaley et al. (2005a,b), we compared top-down modulation in 15 children (aged 8–13) and 15 young adults (aged 19–26). Replicating prior results, in young adults, attention to scenes modulated activity in the parahippocampal place area (PPA). In addition, modulation of PPA activity increased as a function of age in children. PPA activity was also related to performance in this group, on the working memory task as well on a test of subsequent memory. Dorsolateral PFC also demonstrated increasing task-specific activation, as a function of age, in children. The present findings support the idea that children's reduced ability to maintain items in working memory, especially in the presence of distraction, is driven by weaker top-down modulation of activity in areas involved in stimulus processing.

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1. Introduction

Working memory, the capacity to maintain and manipulate information, particularly in the presence of distraction, depends critically on attentional control (Baddeley, 1998). In fact, the contents of working memory can be conceptualized as active internal representations maintained within the focus of attention (Cowan, 1995), and this viewpoint is supported by neuroimaging studies that have identified a mechanistic overlap between

attention and working memory (Awh and Jonides, 2001). The ability to control the focus of our attention allows us to maintain in working memory those aspects of the environment that are relevant to our goals, and to devote fewer resources to processing environmental cues that are not goal-relevant. This ability waxes and wanes over the lifespan; indeed, in both children (Harnishfeger and Bjorklund, 1994) and older adults (Hasher and Zacks, 1988), the ability to maintain relevant information in working memory is hindered by suboptimal selective attention. Prior research on the development of working memory has demonstrated that the ability to maintain items in the absence of distraction, and the neural substrates of this ability, are established very early in childhood (Diamond et al., 1994). However, there is protracted development of working memory, into adolescence and even adulthood, as it involves large item loads, manipulation of items, or main-

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tenance in the presence of distraction (Luna et al., 2004; Scherf et al., 2006; Geier et al., 2009). For recent reviews of this literature, see Bunge and Wright (2007) and Luna et al. (2010). Protracted development of attentional control is likely to be a major cause of the protracted development of working memory.

There is strong neurophysiological evidence that attentional control is mediated by *top-down* (or *goal-based*) modulation of activity in brain regions involved in stimulus processing (Desimone and Duncan, 1995; Miller and Cohen, 2001). This evidence comes from single-cell physiology (Moran and Desimone, 1985), electroencephalography (Hillyard et al., 1973), and neuroimaging (Corbetta et al., 1990; Pessoa et al., 2003). This body of research has demonstrated that activity in cortical regions involved in the representation of particular classes of stimuli increases as a result of top-down shifts of attention toward the relevant stimulus class. This mechanism of top-down modulation supports working memory, as well as attention, by favoring the effective encoding of relevant information (Rainer et al., 1998; Ploner et al., 2001; Vogel et al., 2005). Numerous studies have implicated frontal and parietal regions in top-down attentional control (Pessoa et al., 2003). Lateral prefrontal cortex (PFC), in particular, has been linked to selective attention tasks where relevant and irrelevant stimuli compete for attention (Rossi et al., 2009; Iba and Sawaguchi, 2003; Everling et al., 2002).

Gazzaley, D'Esposito, and colleagues have previously demonstrated that younger adults exhibit enhanced activation of relevant visual association areas in response to stimuli to be maintained in working memory, and reduced activity in response to distracting stimuli (Gazzaley et al., 2005a,b). In addition, they have demonstrated the functional relevance of these activation changes for working memory performance. Their work has focused on the top-down modulation of activation in two brain regions: the fusiform face area (FFA) and the parahippocampal place area (PPA). FFA has been identified as a region that is particularly sensitive to the observation of faces (Kanwisher et al., 1997). PPA, by contrast, has been shown to be particularly sensitive to the observation of buildings and outdoor scenes (Epstein and Kanwisher, 1998).

Gazzaley and colleagues sought to test whether activation in these brain regions that process faces or scenes would be modulated by instructions to attend to either of these stimuli. In the face-scene working memory task, participants were instructed to view a sequence of four images: two faces and two scenes. Following a delay, they viewed a probe stimulus and indicated whether or not it matched one of the target items. In the “Attend Face” condition, they were instructed to attend only to the faces, as they would always receive a face stimulus as a probe. Likewise, in the “Attend Scene” condition, participants were instructed to attend only to the scenes, as they would always receive a scene stimulus as a probe. In the “Passive View” condition, they were instructed to passively view the stimuli, as they would never be asked to make a recognition memory judgment at the end of the trial, but rather to respond to a leftward or rightward arrow stimulus by pressing one of two buttons.

Within the right FFA, the instruction to attend to faces produced increased activation during cue presentation relative to passive viewing. Similarly, within the PPA, the instruction to attend to scenes produced increased cue-related activation relative to passive viewing. Gazzaley et al. argued that these effects result from *top-down attentional enhancement*. In the PPA, the researchers also found evidence of *reduced* activation when participants were asked to attend to the faces as compared with passive viewing. Gazzaley et al. argued that these effects result from *top-down attentional suppression*. Further, they showed that a region in left lateral PFC was highly correlated with PPA during attention to scenes, and that the strength of this coupling correlated with the magnitude of attentional modulation in PPA, suggesting that this region biases activity levels in PPA (Gazzaley et al., 2007).

In a follow-up study, Gazzaley and colleagues used the same fMRI paradigm to examine selective attention in older adults, aged 60–72 (Gazzaley et al., 2005a,b). Compared to younger adults, older adults demonstrated diminished modulation of PPA. This difference was driven by reduced suppression of activity associated with irrelevant information; specifically, older adults did not show reduced activation of left PPA for “Attend Face” relative to “Passive View” trials. Enhancement of activity associated with relevant information (“Attend Scene” > “Passive View”) was similar in older and younger adults. This inability to suppress activation of left PPA was correlated with impaired performance on the working memory task. These results supported the “inhibitory deficit hypothesis” (Hasher and Zacks, 1988), suggesting that age-related decline in working memory capacity may be driven specifically by decline in the ability to suppress irrelevant information.

Here, we sought to use the same fMRI paradigm to assess the effectiveness of top-down attentional modulation in children, both in terms of its neural signature as well as its consequences for performance. There is a rich behavioral literature showing that children experience greater interference from distracters than do young adults, which affects their performance on tasks that present competing stimuli (Bjorklund and Harnishfeger, 1990; Ordaz et al., 2010). Given the parallels between the behavioral findings for children and older adults, we posited that children, like older adults, would demonstrate reduced modulation of visual association areas. Previous studies have demonstrated that attentional control improves over the course of middle childhood (Rueda et al., 2004), and that children, relative to adults, show reduced activation in frontal and posterior brain regions associated with attentional control (Konrad et al., 2005). Similar changes have been observed with respect to working memory and interference control, with age-related improvements in performance and changes in brain activation, particularly in lateral PFC and posterior parietal cortex during task performance (Kwon et al., 2002; Olesen et al., 2007; Velanova et al., 2009; Luna et al., 2010). However, it is not yet known whether children exhibit reduced modulation of visual association areas relative to young adults during performance of a task requiring selective attention to visual stimuli.

Although FFA and PPA continue to mature through childhood and adolescence (Golarai et al., 2007, 2010),

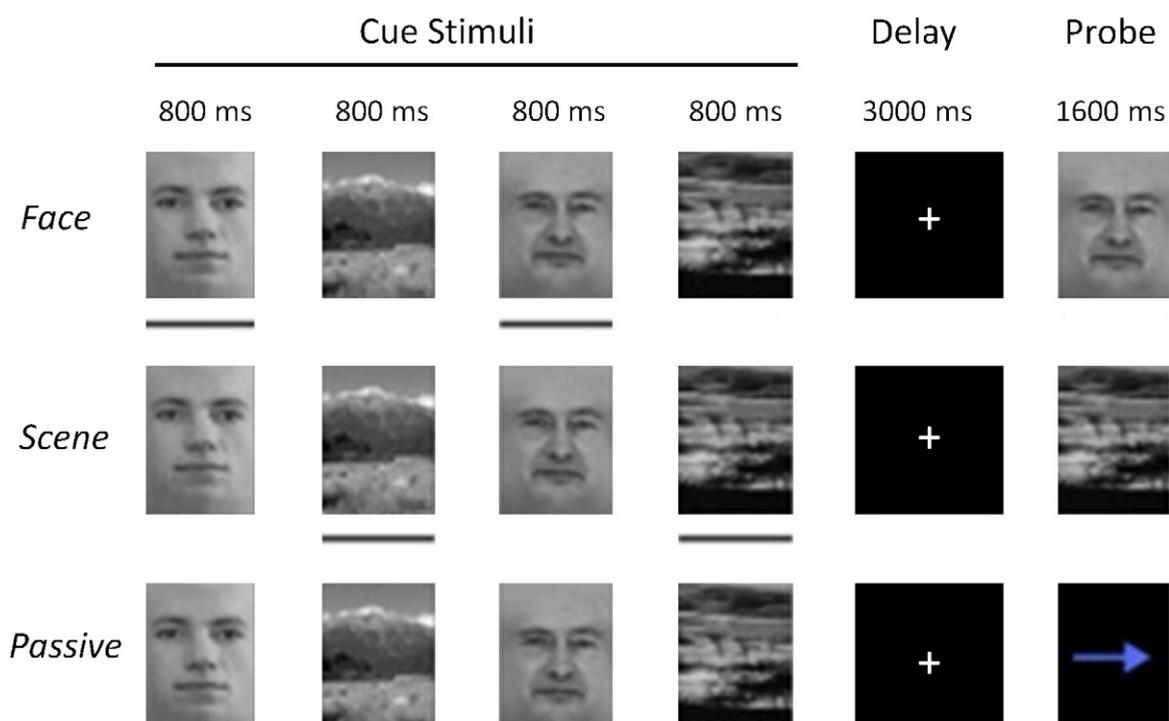


Fig. 1. A depiction of the experimental task, with sample stimuli. There were three task conditions: *Face* (attend faces and ignore scenes), *Scene* (attend scenes and ignore faces), and *Passive* (passively view stimuli).

these regions can be identified reliably in young children using functional localizer tasks (Scherf et al., 2007). Here FFA and PPA were isolated in each subject by means of a simple localizer task involving separate presentation of faces and scenes. For evidence of top-down modulation, we looked for increased activation in PPA for Scene relative to Face trials, and for increased activation in FFA for Face relative to Scene trials. The status of activity during Passive trials in each brain region helps to clarify whether modulation is mainly due to enhanced processing of the to-be-attended stimuli, reduced processing of the to-be-ignored stimuli, or both.

2. Materials and methods

To examine top-down attentional modulation in children, we collected fMRI data from children and young adults as they performed a task that we adapted from the task used by Gazzaley et al. (2005a,b, 2008) for use in children.

2.1. Participants

Data from 15 typically developing children aged 8–13 (6 males, $11.5 \pm .43$) and 15 young adults aged 19–26 (8 males, 21.9 ± 2.3) were included in the analyses. Each age between 8–13 and 19–26 was represented in the sample. An additional two adults participated in the study, but were excluded from analysis due to technical difficulties. An additional seven children were excluded from the study: six because of excessive head movement, and one for failing to follow the task instructions. All children

and adults were recruited from the Davis and Sacramento areas. Participants were compensated \$10 per hour for their participation. Informed consent was acquired from all participants in accordance with the Institutional Review Board at the University of California at Davis or the Committee for Protection of Human Subjects at the University of California at Berkeley.

2.2. Experimental task

Participants were scanned while performing three different 40-trial task blocks across three 7.8-min scanning runs (see Fig. 1). Run order was counterbalanced across participants and between groups. Before each scanning run, subjects were instructed to either (1) remember faces and ignore scenes (*Face* condition), (2) remember scenes and ignore faces (*Scene* condition), or (3) passively view both faces and scenes (*Passive* condition). Each trial started with the successive presentation of two face and two scene pictures, in pseudo-random order (with order counterbalanced across trials). Each image was presented for 800 ms, followed by a blank screen for 200 ms. Presentation of these stimuli was followed by a 3-s delay period, after which a probe stimulus was presented for 1600 ms. The probe stimulus was always a face image for the *Face* condition and a scene image for the *Scene* condition, and for both of these conditions participants were instructed to indicate via left/right button press if the probe image was present in the set of images presented at the beginning of the trial. For the *Passive* condition, the probe stimulus was an arrow and participants were instructed to press either the left or right button in accordance with the direction of the arrow. Pre-

sentation of the probe stimulus was followed by a jittered fixation period of between 2 and 10 s, with a distribution determined by an optimal sequencing program (optseq2) designed to maximize estimation efficiency (Dale, 1999).

The task used here was modified from a paradigm used previously in adults (Gazzaley et al., 2005a,b). The delay period in this study was considerably shorter (3 s rather than 7 s) and the probe period was slightly longer (1.6 s rather than 1 s). These modifications were intended to render the working memory task easier for children, and to limit the amount of time that they needed to stay still in the scanner.

In addition to the main face-scene working memory task, participants also performed a face-scene functional localizer task. The purpose of this task was to localize the FFA and PPA – or, more specifically, FFA and PPA voxels involved in face or scene working memory – in each individual subject. In the localizer task, participants were presented with alternating 20-s blocks of face or scene stimuli (10 blocks of each type) and were instructed to attend to the stimuli and press a button whenever the current stimulus repeated the immediately preceding stimulus.

2.3. Long-term memory testing

Following completion of the fMRI task, participants were given a surprise recognition memory test outside the scanner. The purpose of this was to test whether the attentional instructions influenced long-term retention of to-be-remembered versus to-be-ignored items differently in adults and children. The test was comprised of 192 images (96 faces and 96 scenes), half of which had been seen during the fMRI session. Images were presented on a computer screen and participants were instructed to respond using a 4-point scale whether they had seen the image previously and their confidence. Stimuli that had been used as probes in the fMRI task were not used in the long-term memory test. Previously viewed stimuli in the memory test were taken equally from each condition in the fMRI task (*Face, Scene, Passive*).

2.4. Scan procedure

Imaging was performed using an 8-channel phased-array coil on a 3-T Siemens Trio MRI scanner (Siemens Medical Solutions, Erlangen, Germany) at the University of California at Davis Imaging Research Center (Sacramento, CA). Children were introduced to the scanner environment with a mock scanner, where they were trained to lie still. Prior to fMRI data acquisition, all participants were provided with explicit task instructions. Task stimuli were presented using Presentation software (Neurobehavioral Systems, Inc.), and were projected to a screen, which participants could view from within the scanner by means of a mirror. Participants responded via button box, held in the right hand. Inside the scanner, but prior to scanning, participants practiced using the button box to respond to a set of sample problems.

After acquisition of a T2 localizer scan, four functional runs were collected (TR=2000 ms, TE=25 ms, 34 axial slices, no interslice-gap, 3.4 mm × 3.4 mm × 4 mm voxels,

flip angle=90°, field of view=220 mm), including three runs of the working memory task and one run for the localizer task. A gradient-echo echo-planar pulse Prospective Acquisition Correction (3D-PACE) sequence was used to minimize motion artifacts by prospectively adjusting scan parameters throughout a run on the basis of real-time assessment of head motion (Siemens Medical Solutions) (Thesen et al., 2000). Four volumes from the start of each functional scan were removed from analysis to account for magnetic field equilibration. Following the functional scans, high-resolution three-dimensional T1 MPRAGE anatomical images were acquired.

2.5. fMRI data preprocessing and analysis

fMRI data were analyzed using SPM5 (Wellcome Department of Cognitive Neurology, London, UK). Functional volumes from each participant were corrected for interleaved slice acquisition, and then were translated using a rigid-body motion correction. Functional images were then normalized to an EPI template using a 12-parameter affine transformation and resampled to 3 mm × 3 mm × 4 mm voxels. The SPM EPI template has been validated for use in normalization of brain volumes for children aged 6 and up (Burgund et al., 2002). After normalization, functional images were smoothed using an 8 mm full-width at half maximum isotropic Gaussian kernel.

Statistical analyses were performed using the general linear model in SPM5. For the localizer task, separate block regressors for the face and scene blocks were convolved with SPMs canonical hemodynamic response function (HRF), and then fit to each subject's data to obtain parameter estimate (beta) images for each condition. Face and Scene beta images were then contrasted, and these contrast images submitted to group-level analysis, in order to identify group maxima within right FFA (for Faces > Scenes) and within left and right PPA (for Scenes > Faces). For each subject, the local maximum nearest the group FFA maximum (42, -51, -20) was identified as the center of a subject-specific FFA ROI. Similarly, the local maxima nearest the group PPA maxima at (-24, -48, -12) and (27, -51, -12) were identified as centers of subject-specific left and right PPA ROIs. In all cases, subject-specific ROIs were defined as spheres that included the center voxel along with the surrounding six voxels.

For the main task, data analysis was conducted using a finite impulse response (FIR) model in SPM5. This choice was dictated by the need to isolate cue-related activation (in which visual stimuli were similar across conditions, but attentional demands differed) from probe period activation (in which the visual stimulus varied as a function of condition). The FIR model does not convolve the underlying neural model with an HRF. Instead, it creates a series of stick functions for each event (spanning multiple timepoints) and then obtains a parameter estimate for each timepoint, for each condition. Our FIR model included 8 timepoints, spanning the 16 s after the start of each correct trial. In our examination of cue-related activation, we restrict our analysis to the third FIR timepoint (4–6 s), which should correspond to the peak of the BOLD response associated with the appearance of the cue stimulus, for children and

Table 1

Accuracy and response time results for Adults and Children. Standard errors are shown in parentheses.

Group	Accuracy (%)			Response time (s)		
	Scene	Passive	Face	Scene	Passive	Face
Adults	91.1 (2)	99.7 (0)	87.7 (2)	.94 (.03)	.56 (.02)	.95 (.04)
Children	77.5 (4)	99.6 (0)	75.9 (4)	1.03 (.04)	.63 (.02)	1.02 (.03)

adults (Richter and Richter, 2003). We also report activation at the sixth timepoint as a proxy for probe-related activation. The advantage of the FIR approach over the standard convolution with a canonical HRF is that the estimate of cue-related activation (i.e. FIR timepoint 3), which depends only on data obtained between 4 and 6 s post-onset, cannot be affected by activation induced by the subsequent probe, which appears at 7 s post-onset.

In addition to the task conditions, six parameters, describing participants' motion, were also included in the model. The FIR model was used for both exploratory whole-brain as well as ROI analyses. For single-subject voxelwise analyses, beta images were obtained for each FIR timepoint, for each condition, and contrast images were formed as differences between these beta images. For a given contrast and timepoint of interest, appropriate single-subject contrast images were submitted to a *T*-test to obtain a group contrast image and associated *T*-map. These *T*-maps were thresholded at $p < .001$ (uncorrected), with an extend threshold of $k > 10$ voxels, to produce cluster activation images.

Functional ROIs of the FFA and PPA were obtained from the localizer task, as described above. Additional functional ROIs were obtained based on contrast activation at timepoint 3 of the FIR analysis for the face-scene working memory task. For each ROI, data were averaged across all voxels in the region to produce a single timeseries per region. These ROI timeseries were then submitted to FIR analysis, as above, producing a single parameter estimate (beta value) per FIR timepoint per condition per region. Beta values corresponding to the third timepoint were submitted to second-level analyses (ANOVAs) within SPSS.

3. Results

3.1. Behavioral performance

To assess participants' performance on the working memory task, we submitted accuracy scores (Table 1) to a 3 (condition: *Face*, *Scene*, or *Passive*) \times 2 (group: Adult or Child) mixed analyses of variance (ANOVA). Overall, children performed worse than adults ($F_{1,28} = 10.1, p = .004, 84\%$ versus 93% correct, respectively), though performance of both groups was at ceiling (>99%) for *Passive* trials. There were no significant differences in performance between *Face* and *Scene* conditions, for either group. There were significant positive correlations between age and WM performance in children for both the *Face* ($r^2 = .20, p < .05$) and *Scene* ($r^2 = .43, p = .004$) conditions (Fig. 2).

Response times were analyzed in a similar manner. Adults, with a mean response time of 820 ms, were marginally faster than children ($p = .06$), with a mean response time of 890 ms. The group \times condition interaction

was not significant ($F < 1$). For both groups, responses to *Passive* trials were faster than responses to either *Face* or *Scene* trials ($p < .001$).

To assess participants' long-term memory, we submitted familiarity ratings (Table 2) to a 4 (condition: *Attended*, *Passive*, *Ignored*, or *New*) \times 2 (group) mixed ANOVA, separately for scenes and faces. For scenes, the overall effect of condition was highly significant ($F_{3,84} = 15.3, p < .001$), but the group \times condition interaction was not ($p = .24$). Both adults and children indicated the highest level of familiarity with to-be-attended scenes, an intermediate level of familiarity with passively viewed scenes, and the least familiarity with to-be-ignored scenes (i.e. scenes that had been presented on *Face* trials). Both groups rated to-be-attended and passively viewed scenes, but not to-be-ignored scenes, as significantly more familiar than new scenes (adults: p 's $< .001$, children: p 's $< .05$). Notably, the effect of attention on scene memory (i.e. *Attended Scene* – *Ignored Scene*) was positively correlated with age in the child group ($r^2 = .32, p = .03$), as were raw memory scores for the *Attended Scene* ($r^2 = .40, p = .01$) and *Passive Scene* ($r^2 = .32, p = .03$) conditions. Adults demonstrated a stronger effect of top-down enhancement (*Attended Scene* – *Passive Scene*) on scene memory than did children ($p = .04$), but there was no appreciable difference in the effects of top-down suppression (*Passive Scene* – *Ignored Scene*).

For faces, there was again a significant overall effect of condition ($F_{3,84} = 8.3, p < .001$) and no interaction between condition and group ($F < 1$). Both children and adults reported greater familiarity for to-be-attended faces than for passively viewed faces (adults: $p = .006$, children: $p = .02$) or ignored (adults: $p = .13$, children: $p = .04$). However, for both groups, familiarity ratings for old faces were not significantly different from familiarity ratings for new faces, suggesting negligible long-term retention of the face stimuli (despite the fact that working memory accuracy was well above chance).

3.2. Whole-brain comparisons: attention to scenes versus attention to faces

Initial exploratory analyses focused on the contrast between the *Scene* and *Face* conditions. Our primary interest is in cue-related activation (i.e. FIR timepoint 3), though, as a point of comparison, we also report probe-related activation (i.e. FIR timepoint 6).

During the cue period, bilateral PHG and bilateral pre-cuneus were more active when participants were cued to attend to the scenes than the faces (Table 3A and Fig. 3A, left). There were no significant group differences with respect to the *Scene*–*Face* contrast, as revealed by a whole-brain two-sample *T*-test. All of the regions activated by

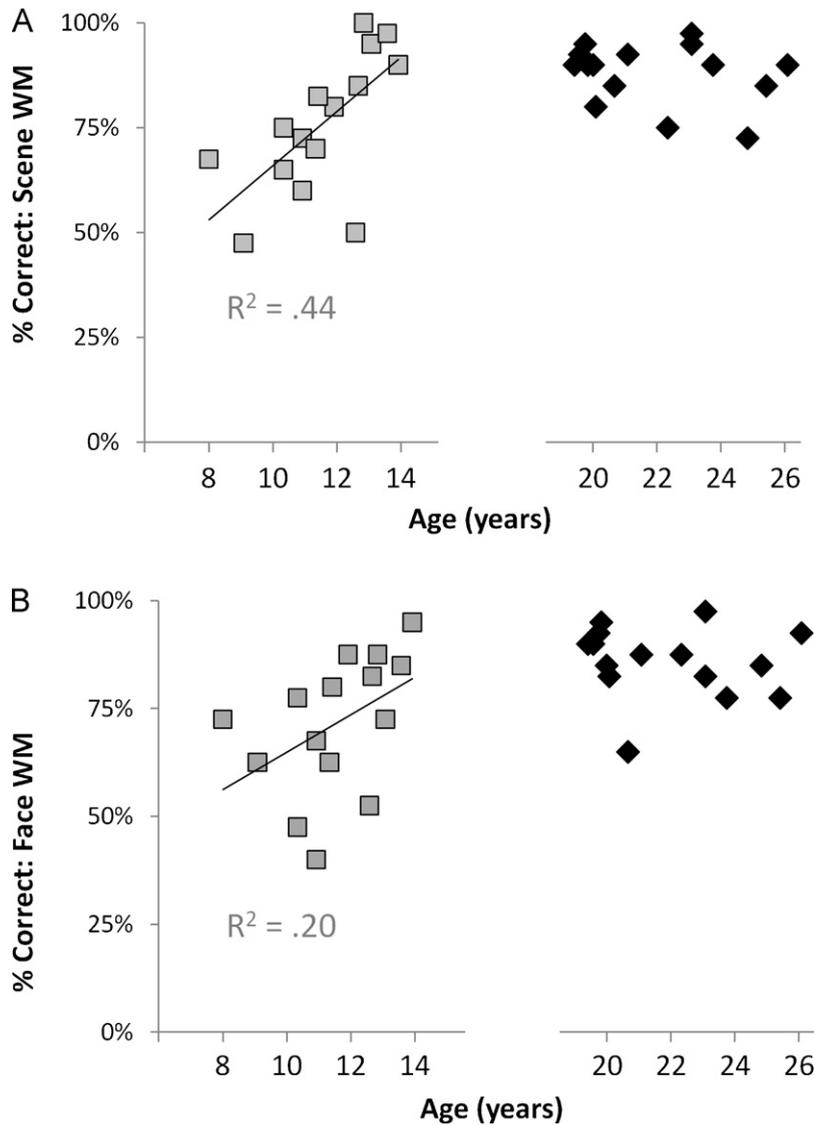


Fig. 2. Regression of working memory performance with age, showing improved performance on scene (A) and face (B) working memory as a function of age in children, and adult-like performance among the older children in the group.

Scene–Face during the cue period were also activated by *Scene–Face* at the probe (Fig. 3B), which produced additional activation extending in to the lingual and middle occipital gyri.

When participants attended to faces rather than scenes, the only significant cue-related activation was observed in the posterior cingulate gyrus (Table 3B). There were no significant group differences with respect to this contrast. While there was no activation of the fusiform gyrus

associated with the cue, this region was activated by the *Face–Scene* contrast for the probe.

3.3. PPA and FFA: targets of top-down modulation

To focus on the probable targets of top-down modulation in this task, we next examined the PPA and FFA ROIs obtained from the functional localizer task. Of particular interest is whether and to what extent the effects of atten-

Table 2

Average familiarity ratings from the long-term memory test. Parentheses show standard error.

Group	<i>Scene</i>				<i>Face</i>			
	Attend	Passive	Ignore	New	Attend	Passive	Ignore	New
Adults	2.71 (.14)	2.45 (.13)	2.25 (.14)	2.23 (.11)	2.1 (.09)	2.47 (.11)	2.58 (.09)	2.69 (.07)
Children	2.46 (.14)	2.40 (.13)	2.26 (.14)	2.23 (.11)	2.77 (.09)	2.62 (.12)	2.64 (.10)	2.75 (.07)

Table 3

Activation clusters associated with Scene versus Face contrasts. All clusters that survive thresholding at $p < .001$ (uncorrected), with a 10-voxel extent threshold, are reported. In addition, FWE-corrected p -values are reported for each cluster. PHG = parahippocampal gyrus, LG = lingual gyrus, SOG = superior occipital gyrus, MOG = middle occipital gyrus, SPL = superior parietal lobe, MFG = middle frontal gyrus, IFJ = inferior frontal junction, MTG = middle temporal gyrus, and STG = superior temporal gyrus.

Region	x, y, z	Z (voxel)	cluster size (# voxels)	p-Value (corr. cluster)
<i>(A) Scene > Face (cue) All Subjects</i>				
Left PHG	-27, -45, -16	4.73	103	.001
Right PHG	27, -36, -16	3.79	51	.036
Left precuneus, SPL	-15, -69, 52	4.51	253	<.001
Right SOG, MTG	24, -57, 24	4.43	213	<.001
Left posterior cingulate	-15, -54, 16	4.40	40	.08
Left MFG	-45, 33, 16	3.58	36	.11
<i>(B) Face > Scene (cue) All Subjects</i>				
Posterior cingulate gyrus	-3, -51, 28	3.92	92	.002
Right STG	60, -51, 8	3.98	44	.06
<i>(C) Scene > Passive (cue) All Subjects</i>				
Left precuneus, SPL	-15, -69, 52	5.60	684	<.001
Right precuneus, SPL	20, -60, 56	5.51	660	<.001
Left IFJ (MFG/precentral)	-36, 0, 36	4.92	370	<.001
Right IFJ (MFG/precentral)	39, 3, 36	4.67	302	<.001
Left MOG/MTG/fusiform	-48, -63, -4	4.51	133	.001
Left MFG, IFG	-36, 27, 24	4.61	44	.02
<i>(D) Face > Passive (cue) All Subjects</i>				
Left precuneus, SPL	-24, -69, 32	4.58	248	<.001
Right precuneus, SPL	27, -69, 40	4.04	207	<.001
Left IFJ (precentral/MFG)	-42, -3, 36	4.14	89	.005
Right IFJ (precentral/MFG)	39, 0, 40	4.85	202	<.001
Left MOG/MTG/fusiform	-51, -63, -4	5.00	203	<.001
Right MTG/MOG/fusiform	48, -54, 8	4.48	136	<.001

tion on activity modulation, previously observed in adults, is present in children.

Within bilateral PPA (Fig. 4A), both children and adults exhibited attentional modulation during the cue period, exhibiting greater activation for *Scene* trials than for *Face* trials (Fig. 4B; adults: $F_{2,28} = 11.9, p < .001$; children: $F_{2,28} = 3.2, p = .05$; 87% of adults (13/15) and 66% of children (10/15) exhibited this pattern). Adults also demonstrated significant enhancement (*Scene > Passive*), and children demonstrated marginal enhancement, but only in left PPA (adults: $F_{1,14} = 8.1, p = .01$; children: $F_{1,14} = 4.2, p = .06$; 87% of adults versus 80% of children exhibited this pattern). There was no significant condition \times group interaction in either left or right PPA (F 's < 1). Neither group exhibited significant attentional suppression (*Passive > Face*) of the PPA.

To investigate development of top-down modulation, we probed for correlations between PPA activation and age in children. Significant age-related increases were observed for both top-down modulation (*Scene-Face*; $r^2 = .28, p = .04$) and top-down enhancement (*Scene-Passive*; $r^2 = .31, p = .03$). These effects were driven by a highly significant age-related increase in PPA activation for *Scene* trials ($r^2 = .56, p = .001$) in the absence age-related changes for *Face* or *Passive* trials (Fig. 4C).

In children, in addition to correlating with age, PPA activation on *Scene* trials also correlated with performance, for both scene working memory ($r^2 = .46, p = .006$; Fig. 5A) and scene long-term memory ($r^2 = .49, p = .004$; Fig. 5B). In adults, by contrast, although the trends were in the same direction as in children, there were no significant correlations between PPA activation and either working memory or long-term memory performance.

As with PPA, investigation of the right FFA ROI confirmed the success of the localizer task, insofar as there was a large effect of condition (*Face > Scene, Passive*) associated with the probe, in both children and adults. However, in the FFA, neither group demonstrated an effect of attentional modulation during presentation of the cue stimulus (adults: $F_{2,26} < 1$, children: $F_{2,26} = 1.1$). Nevertheless, for adults, though not for children, there was a significant correlation between face working memory performance and FFA cue-related activation for the *Face-Scene* contrast ($r^2 = .21, p = .04$), demonstrating that top-down modulation of FFA did occur, at least in the better-performing adult participants.

3.4. Sources of top-down modulation

To identify additional regions that were modulated by attentional demands during the cue period, we examined the *Scene > Passive* and *Face > Passive* contrasts across all subjects (Table 3C and D and Fig. 6A). Activation in bilateral inferior frontal junction (IFJ), and in bilateral SPL was observed for both contrasts. In addition, activation with a left DLPFC peak (-36, 27, 24), spanning the inferior frontal sulcus, was observed for *Scene > Passive* across all subjects.

We next probed explicitly for differences between adults and children in top-down control by submitting *Scene > Passive* and *Face > Passive* cue contrast images from both groups to a voxel-wise, two-sample t -test. No significant clusters emerged from this analysis (we note, however, that when the threshold was lowered to $p < .005$, a cluster in left lateral PFC (-48, 18, 8) was observed for *Scene > Passive*).

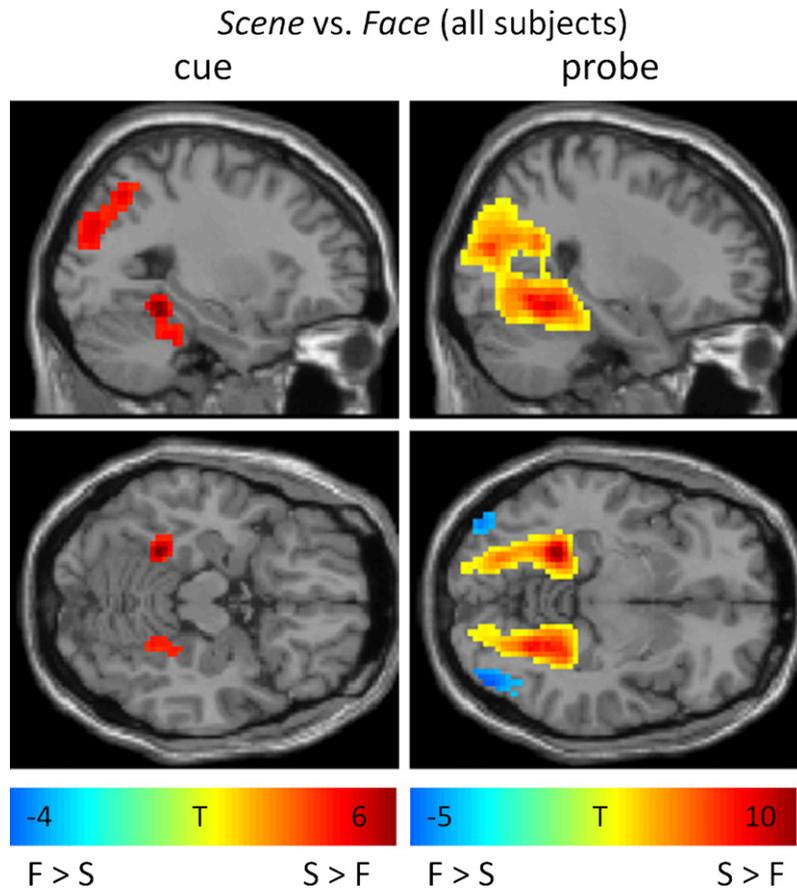


Fig. 3. Scene versus Face contrast images for the entire group of participants ($N=30$), thresholded at $p < .001$ (uncorrected) with a 10-voxel extent threshold. (A) Contrast activation associated with the cue (FIR timepoint 3). (B) Contrast activation associated with the probe (FIR timepoint 6).

Because DLPFC has been previously identified as a primary locus of top-down control (Gazzaley et al., 2007), we selected the DLPFC ROI (obtained from the *Scene > Passive* contrast across all subjects) for further analysis. First, we probed for a group \times condition interaction associated with the cue. Although there was a trend toward greater activation for scenes in adults than in children, this effect was not significant ($p = .2$). Next, the relation between DLPFC function and age in the child group was examined by correlating cue-related *Scene–Passive* contrast values with age (Fig. 6B). This correlation proved to be highly significant ($r^2 = .37$, $p = .008$): older children engaged DLPFC more strongly during attention to scenes than younger children.

Although session order was counterbalanced in our task, across subjects and between groups, we sought to ensure that none of our reported results might be due to session order effects. Thus, we conducted a follow-up analysis testing for correlations between session order (represented as the position of the *Scene* session) and each of our reported behavioral and brain measures. Only long-term memory for scenes was even marginally correlated with session order ($p = .09$); for all other reported measures, there was no correlation (all p 's $> .4$).

4. Discussion

Evidence from the current study suggests that top-down enhancement of the PPA develops over the course of middle childhood. Between the ages of 8 and 14, increasing age was associated with increasing activation of bilateral PPA, but only when the task goals required attending to scene stimuli. Replicating prior studies, adults demonstrated strong enhancement of PPA when attention to scenes was required. While younger children appear to be markedly different than young adults, in terms of their capacity for top-down modulation of PPA, these differences have largely if not entirely disappeared by the age of 14. However, a more precise characterization of the developmental trajectory of PPA enhancement will require further study, with more individuals from the age range in question and, ideally, longitudinal tracking of individuals.

PPA activation in children was correlated both with scene working memory and long-term memory for attended scenes. Because all of these variables were correlated with age among the children, we cannot conclude definitively that PPA activation is causally related to scene memory. A larger sample would be needed to test whether the brain-behavior correlations hold after regressing out the effects of age.

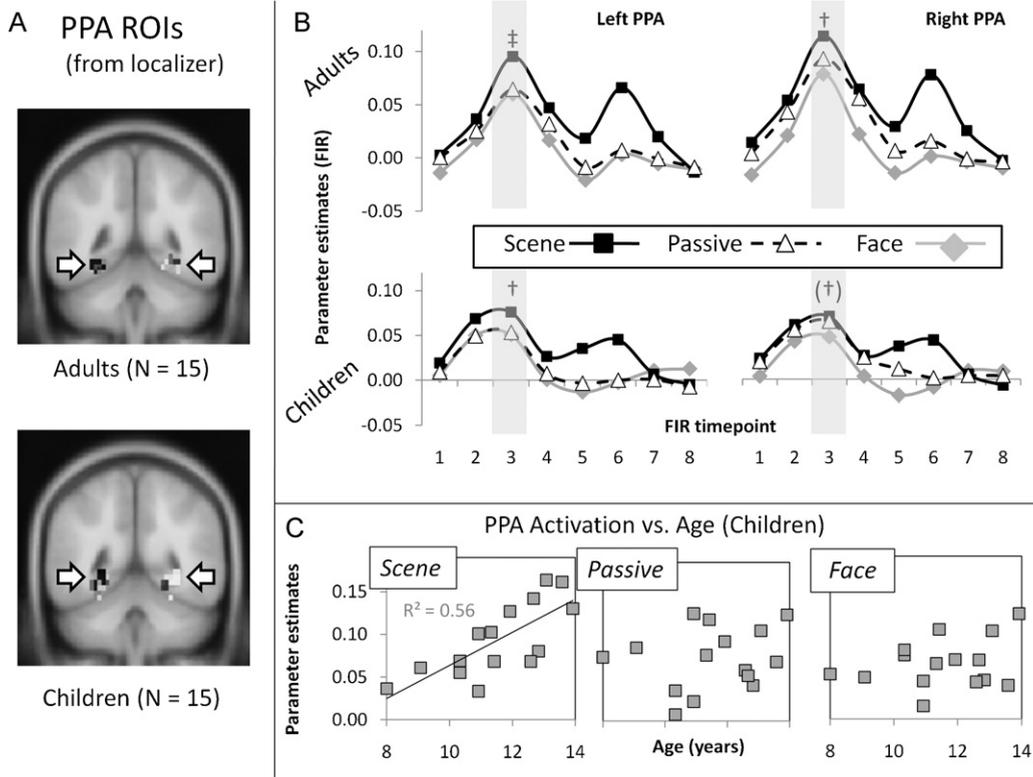


Fig. 4. (A) Subject-specific parahippocampal place area (PPA) regions of interest obtained from the localizer task. (B) BOLD activation (finite impulse response) timecourses from parahippocampal place area (PPA) regions of interest, for adults and children. Statistical differences between conditions were assessed at timepoints 3 and 6, corresponding to cue-related and probe-related activation peaks. Significant effects are marked with † (*Scene > Face*) or ‡ (*Scene > Face, Passive*). Parentheses indicate a marginally significant effect. (C) Bilateral PPA activation (cue-related) versus age in children, for each experimental condition. Trendline indicates the presence of a significant correlation (see text).

Some prior studies have observed top-down suppression as well as top-down enhancement of PPA (Gazzaley et al., 2005a,b). We observed enhancement of PPA, but failed to observe significant suppression. The lack of suppression effects could be due to differences, relative to the earlier studies, in the instructions provided to participants or in participants' strategies. But examination of the results from another recent study (Rissman et al., 2009) suggests an alternative explanation – that suppression happens later than enhancement – too late, in fact, to be detected using our short-delay-period design. In an earlier study (Gazzaley et al., 2005a,b), which involved a delay period of seven rather than 3 s, it was observed that suppression effects

were entirely absent during cue encoding and early delay, and only became apparent in association with the later part of the delay period. There is a hint of this in data from the current study; for both left and right PPA, numerical suppression effects are observed in adults and children at later timepoints, but this effect is not significant and is confounded with the appearance of the probe stimulus. Thus, in order to examine development of top-down suppression abilities, a follow-up investigation involving longer delay periods will be required.

Comparing the developmental pattern observed here in children to the pattern of age-related decline observed previously in older adults is complicated by the lack of any

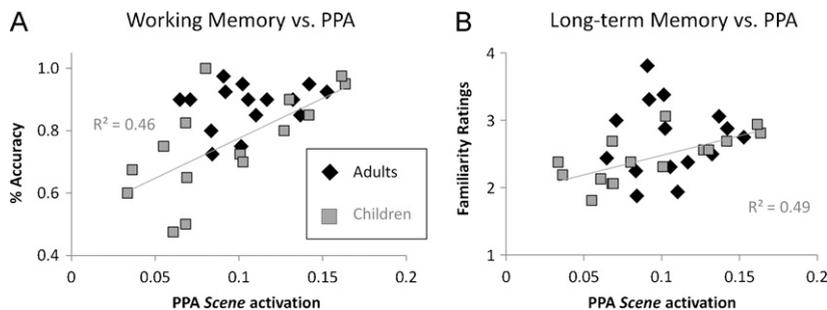


Fig. 5. (A) Correlation between working memory performance and PPA activation, for *Scene* trials. (B) Correlation between long-term memory responses for attended scenes and *Scene* trial PPA activation. All activation values are cue-related, taken from the third FIR timepoint.

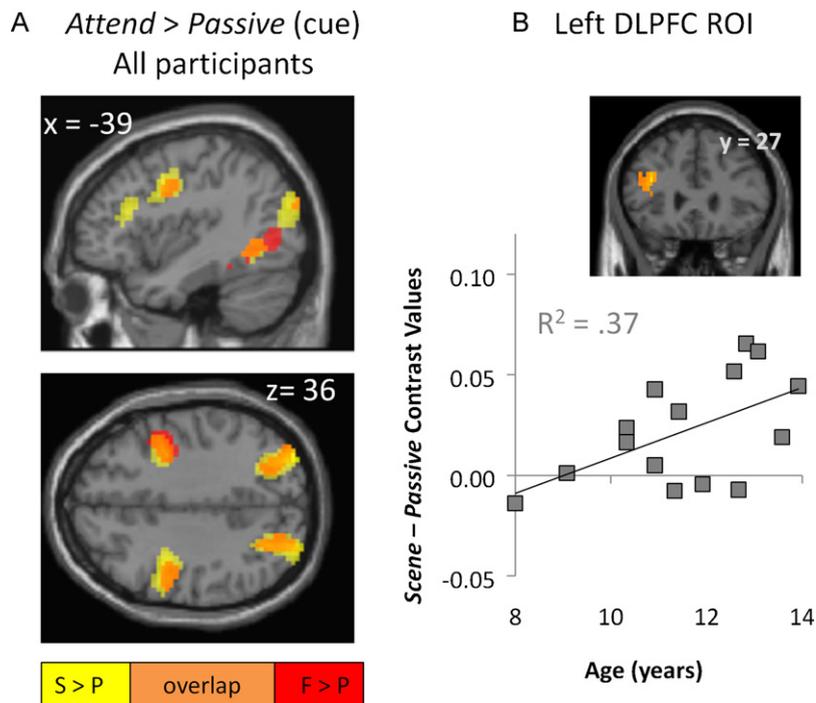


Fig. 6. Contrast images for *Scene/Face > Passive (cue)*, thresholded at $p < .001$ (uncorrected) with a 10-voxel extent threshold. (A) Separate effects of *Scene > Passive* (yellow) and *Face > Passive* (red), with overlap in orange. (B) Correlation of DLPFC selective enhancement (*Scene - Passive cue*) with age.

clear suppression effect for either age group in the current study. It is not possible to determine, based on the present results, whether and to what extent children exhibit a suppression deficit similar to that seen in older adults. Given prior behavioral evidence that children (Harnishfeger and Bjorklund, 1994) as well as older adults (Hasher et al., 1991) are more susceptible to interference than young adults, it remains likely that such a deficit exists. However, it appears from the current results that young children differ from older adults in one important respect: where older adults demonstrate enhancement at a level similar to young adults, young children do not.

Although we found that adults with better working memory performance did modulate FFA, we did not observe reliable top-down modulation of FFA across the whole group. This could mean that FFA is less susceptible to top-down modulation than PPA—perhaps because face recognition is a more automatic process than scene examination. Our FFA ROI was clearly sensitive to the presentation of faces, so it seems unlikely that the lack of effect is due to the region selection. It is the case that, in prior studies that looked at both PPA and FFA, top-down modulation of FFA has been weaker and less reliable than that of PPA (Gazzaley et al., 2005a,b); in fact, in a number of previous studies using a similar task paradigm, the focus of investigation has been limited to PPA for this reason (Gazzaley et al., 2008; Rissman et al., 2009). Thus, the lack of an effect in FFA is perhaps not very surprising or informative. A better understanding of the conditions under which robust and reliable modulation of FFA can be produced should facilitate further investigation of the development of this capacity.

In children, the age-related increase in PPA enhancement was matched by an age-related increase in the selective activation (for attention to scenes versus passive viewing) of lateral PFC. This finding is consistent with many prior studies on the development of cognitive control, which have repeatedly demonstrated a reduction in selective activation of lateral PFC in children relative to adults (e.g. Konrad et al., 2005; Kwon et al., 2002; Crone et al., 2006a,b). Other regions commonly associated with top-down control, including IFJ (Derrfuss et al., 2004) and SPL (Yantis and Serences, 2003; Silvanto et al., 2009), were similarly activated across adults and children.

As in prior work from our group on the development of working memory and cognitive control processes, we found that children age 8–13 generally engage the same set of brain regions as adults, or a subset thereof, rather than engaging an entirely different network (Crone et al., 2006a,b; Paz-Alonso et al., 2008). In the one study for which we have observed important qualitative differences in activation between children and adults on a cognitive control paradigm (Bunge et al., 2002), we interpreted this finding, together with supporting evidence, as reflecting a shift in cognitive strategy. In the present study, as in others (Scherf et al., 2006; Crone et al., 2006a,b; Ofen et al., 2007) we observed quantitative differences in the pattern of activation in lateral PFC and in key regions involved in the task. These findings are broadly consistent with the idea that strengthening of long-range connections between PFC and other brain regions results in more effective top-down modulation of task-related processing (Fair et al., 2007; Lebel et al., 2008).

Developmental changes in neural activation patterns may be related to concurrent changes in brain structure. Changes in cortical thickness occur throughout childhood, with different brain regions demonstrating different developmental trajectories (Shaw et al., 2008). DLPFC, which appears to be a major locus of top-down modulation, demonstrates particularly delayed maturation in terms of cortical thickness (Gogtay et al., 2004). Over the course of middle childhood, myelination processes result in increasing white matter volume (Giedd, 2004) and increasing tract coherence (Barnea-Goraly et al., 2005). It is highly likely that these white-matter changes have a positive impact on the potential for top-down modulation, and help to explain the reduced modulation observed in younger children. Further investigation of the link between structural and functional development is an important goal for future research.

In summary, the present results suggest that top-down modulation of PPA, mediated by lateral PFC, develops over the course of middle childhood. Attention-related prefrontal activation and the associated enhancement of PPA activation are reduced in younger children compared with older children and young adults. Notably, although we are unable to draw firm conclusions about top-down suppression in the current study, the observed reduction of top-down enhancement in younger children also contrasts with the suppression-specific deficit previously observed in older adults, indicating that the development of top-down attentional modulation may follow a different trajectory than its eventual decline.

Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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