As Working Memory Grows: A Developmental Account of Neural Bases of Working Memory Capacity in 5- to 8-Year Old Children and Adults

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Abstract

■ Working memory develops slowly: Even by age 8, children are able to maintain only half the number of items that adults can remember. Neural substrates that support performance on working memory tasks also have a slow developmental trajectory and typically activate to a lesser extent in children, relative to adults. Little is known about why younger participants elicit less neural activation. This may be due to maturational differences, differences in behavioral performance, or both. Here we investigate the neural correlates of working memory capacity in children (ages 5–8) and adults using a visual working memory task with parametrically increasing loads (from one to four items) using fMRI. This task allowed us to estimate working memory capacity limit for each group. We found that both age groups increased the activation of frontoparietal networks with increasing working memory loads, until working memory capacity was reached. Because children's working memory capacity limit was half of that for adults, the plateau occurred at lower loads for children. Had a parametric increase in load not been used, this would have given an impression of less activation overall and less load-dependent activation for children relative to adults. Our findings suggest that young children and adults recruit similar frontoparietal networks at working memory loads that do not exceed capacity and highlight the need to consider behavioral performance differences when interpreting developmental differences in neural activation. ■

INTRODUCTION

Working memory or the ability to temporarily maintain a limited set of information across delays and in the face of interfering information (Baddeley, 2003; Kane, Bleckley, Conway, & Engle, 2001) shows a remarkably protracted developmental trajectory, with performance parametrically improving across early and middle childhood (Kharitonova, Martin, Gabrieli, & Sheridan, 2013; Simmering, 2012; Cowan, Morey, AuBuchon, Zwilling, & Gilchrist, 2010; Riggs, McTaggart, Simpson, & Freeman, 2006; Espy, Kaufmann, McDiarmid, & Glisky, 1999; Luciana & Nelson, 1998) and with subsequent increases in performance throughout adolescence (Tamnes et al., 2013; Conklin, Luciana, Hooper, & Yarger, 2007; Luna, Garver, Urban, Lazar, & Sweeney, 2004; Luna & Sweeney, 2004). Capacity for memory itself, as opposed to auxiliary processes, such as encoding efficiency or ability to filter out irrelevant items, appears to be driving the change across childhood (Cowan, AuBuchon, Gilchrist, Ricker, & Saults, 2011; Cowan et al., 2010).

Visual working memory capacity is severely limited: Even healthy adults are unable to maintain more than four (~3 to 5) items in an actively accessible state (Vogel, McCollough, & Machizawa, 2005; Vogel & Machizawa, 2004; Cowan, 2000). Working memory capacity (k) can be estimated by a simple formula: $k = S * (H - F)$, where S is the size of the array, H is the observed hit rate, and F is the false alarm rate (Cowan, 2000). It is generally observed that the k estimate increases as a function of increasing working memory load, until capacity is reached, at which point the estimate of k will plateau or even decline (possibly due to encoding processes being inefficient when too many items need to be encoded at once). Using this estimate of working memory capacity, previous studies have demonstrated that 7-year-olds are able to maintain 1.5 items, whereas adults, on average, are typically able to maintain approximately four items (Cowan et al., 2010, 2011; Vogel et al., 2005; Vogel & Machizawa, 2004). Thus, across middle and late childhood, the capacity to actively maintain information in working memory increases at least twofold.

Very little is also known about the neural substrates supporting working memory in early childhood and about whether lower working memory capacity observed in younger ages is reflected in neural activation patterns. In general, the neural substrates that support working memory in adults, namely the lateral prefrontal and parietal regions (D'Ardenne et al., 2012; Todd & Marois,

2004; Courtney, Petit, Maisog, Ungerleider, & Haxby, 1998; D'Esposito et al., 1995; Jonides et al., 1993), mirror the developmental trajectory of behavior in terms of both structure and function. These "higher-order" association regions reach structural maturity later than the "lower-order" somatosensory and visual regions (Lenroot & Giedd, 2006; O'Donnell, Noseworthy, Levine, & Dennis, 2005; Gogtay et al., 2004; Sowell, Thompson, Tessner, & Toga, 2001). Importantly, structural maturity, both in terms of cortical thickness (Kharitonova et al., 2013; Sowell, 2004) and volume (Tamnes et al., 2013) in the prefrontal and parietal regions, is associated with improved performance on working memory tasks.

Functional neuroimaging studies paint a similar picture with regard to involvement of these regions in working memory tasks. In adults, a network of prefrontal, parietal, and anterior cingulate regions is reliably activated in working memory contexts (D'Ardenne et al., 2012; Todd & Marois, 2004; Osaka et al., 2003; Courtney et al., 1998; D'Esposito et al., 1995; Jonides et al., 1993), and activation in these regions increases with increasing working memory load (Rypma, Prabhakaran, Desmond, Glover, & Gabrieli, 1999; Barch et al., 1997; Braver et al., 1997). In children and adolescents, many studies find activation in similar frontoparietal and cingulate networks (Mürner-Lavanchy et al., 2014; Spencer-Smith et al., 2013; Geier, Garver, Terwilliger, & Luna, 2009; Tsujii, Yamamoto, Masuda, & Watanabe, 2009; Ciesielski, Lesnik, Savoy, Grant, & Ahlfors, 2006; Klingberg, 2006).

Despite these similarities, there are also important differences in patterns of activation across adults and children, and both the specific pattern and source of these differences are currently unresolved. Specifically, we do not yet know how differences in behavioral performance that are associated with development reflect neural activation differences.

Many studies report less activation in children than in adults in regions that typically activate in response to performing a working memory task (Thomason et al., 2009; O'Hare, Lu, Houston, Bookheimer, & Sowell, 2008; Olesen, Macoveanu, Tegnér, & Klingberg, 2007; Scherf, Sweeney, & Luna, 2006). The amount of activation in these regions generally increases with age (O'Hare et al., 2008; Klingberg, Forssberg, & Westerberg, 2002; Kwon, Reiss, & Menon, 2002), mirroring well-observed improvements in behavioral performance. In contrast, other studies report more diffuse patterns of activation in children in working memory tasks (Geier et al., 2009; Scherf et al., 2006), consistent with the idea that neural activation becomes progressively more focused with development (Durston et al., 2006). Finally, some studies report a qualitatively different set of regions that are involved in supporting working memory in childhood relative to adulthood (Finn, Sheridan, Kam, Hinshaw, & D'Esposito, 2010; Ciesielski et al., 2006), suggesting a possible compensatory role in children's immature neural systems.

One interpretation for the different levels of activation of working memory networks at younger ages and the recruitment of compensatory regions lies in developmental immaturity: Neural regions that support task performance at older ages may simply be too immature to be fully active at younger ages, and therefore, compensatory regions must activate to support task performance. On the other hand, younger children tend to perform the same tasks at lower accuracy levels and thus maintain fewer items in working memory than older children and adults. Hence, lower levels of activation may also reflect an effectively lower load that is being maintained earlier in development. Without a task that parametrically manipulates working memory load in the same way across different age groups, it is impossible to determine if differences in activation are due to differences in age or differences in effective load. This difficulty is compounded by the manner in which working memory ability is generally tested: Activation to encoding or maintaining a low-load stimulus is compared to encoding and maintaining a high-load stimulus. The use of this comparison inherently contains the assumption that, when an individual is confronted with more stimuli, they must necessarily be able to maintain more stimuli in working memory. The theory of capacity confronts this idea: If one's capacity is only 1.5 items, then it may not matter how many stimuli are presented; only one or two will be encoded and maintained.

Here we attempt to adjudicate between several possible explanations for age-related increases in activation in the working memory network by examining differences in activation in response to parametrically increasing working memory loads in children and adults. Both groups were administered an identical task with four different working memory loads. Parametrically manipulating working memory load in the same task in children and adults allowed us to begin answering the critical question of whether changes in neural activation as a function of development represent qualitative changes in neural activation, quantitative changes, or both. Specifically, if maturational differences drive lower levels of activation in children, then these differences in typical working memory networks should be observed even when levels of performance across age groups are comparable. In contrast, if differences in activation reflect behavioral performance differences, then comparing conditions performed with comparable accuracy should elicit comparable levels of activation. Importantly, this performance-based account suggests that largest increases in neural activation should be observed for working memory loads that just precede working memory capacity (k), with no subsequent neural increase in activation for trials exceeding working memory capacity limit.

Most existing studies of the neurodevelopment of working memory have focused on older children and adolescents (typically ages 7 and up). However, early

childhood is a critical period in terms of observed structural changes in brain regions relevant to executive functions, including working memory (Walhovd, Tamnes, & Fjell, 2014; Tamnes et al., 2013). We know that working memory capacity increases across childhood (e.g., Simmering, 2012; Riggs et al., 2006; Luciana & Nelson, 1998) and that by age 8 children are able to maintain half of the number of items in working memory compared to adults (1.5 vs. 3.0 items; Cowan et al., 2010, 2011); however, we do not know yet how neural activation patterns relate to developmental changes in working memory across in early and middle childhood. This is the first study, to our knowledge, examining the neural correlates of working memory development in children as young as 5 years.

We examine changes in neural activation as a function of age and increasing working memory load both in the whole brain and in three a priori defined ROIs. The ROIs include the caudal middle frontal gyrus, the superior parietal cortex, and the rostral ACC: regions that typically activate in response to increasing working memory demands and performance monitoring in older children and adults.

Middle Frontal and Superior Parietal Cortex

The middle frontal gyrus and superior parietal cortex are classical regions supporting working memory maintenance in adults (D'Ardenne et al., 2012; Todd & Marois, 2004; Osaka et al., 2003; Courtney et al., 1998; D'Esposito et al., 1995; Jonides et al., 1993), with activation increasing with increasing load (Gould, Brown, Owen, & Howard, 2003). Here we are able to examine changes in activation in these regions due to both the actual load within each age group and the inferred or "effective" load, by observing activation at each group's capacity limit.

Rostral ACC

Rostral ACC (rACC) is typically activated in response to the need to monitor the environment for conflicting information (Botvinick, Cohen, & Carter, 2004). This region is also important for online monitoring of task performance (Carter et al., 1998). Even though our task did not contain any explicit conflicting information, the need to monitor incoming information for difficulty was high, particularly for children who had more difficulty with this task. Therefore, we expected to observe rACC activation in response to load increases on this task.

METHODS

Participants

This study included 22 children and 20 adults. Two children did not complete the study because they did not feel comfortable in the scanner environment; their data are not included in the analyses. The final sample thus included 20 children (M age = 6.92 years, SD = .87; range = 5.2–8.6 years; 12 girls) and 20 adults (M = 24.7 years, SD = 3.8, range = 19–35 years; 12 women). All participants were typically developing and had no neurological or MRI contraindications including being unconscious for more than a few minutes, having known head trauma, having nonremovable metal, or claustrophobia. These data were collected as part of a larger study, in which we additionally collected EEG data, BOLD response to an interference control task, and several behavioral and/or questionnaire measures on a larger group of typically developing children and children meeting criteria for ADHD. These data will be reported elsewhere. No child in the current study met criteria for ADHD.

Here we examine age-related change in activation in children who are younger than previously reported in fMRI studies. Because of this, one concern is that the selection criteria for younger participants were different than that for adult participants. Our groups were matched on sex (12 female, 8 male in both groups); however, to further address this possibility, we additionally report group differences (adults vs. children) for IQ and the number of movement or signal change-related outliers using two sample t tests.

Procedure

All participants came to the Center for Brain Imaging at Harvard University. Child participants came with their legal guardian for two sessions: a mock scanning session and a real scanning session. Adults came for a single scanning session. Researchers explained mock and real scanning and testing procedures to parents and children, answered questions, and then provided written consent documents. The child's parent or legal guardian provided written consent before the mock scanning session, which preceded the scanning session by at least 1 day but not more than 1 week. Adult participants consented before the scanning session. All procedures were approved by the institutional review board at Harvard University and Boston Children's Hospital and were conducted in accordance with the Helsinki declaration on human participants.

Mock Scan Session

All children first participated in a preliminary session where they lay in a mock brain scanner, listened to recordings of the sounds they would hear in the scanner, and participated in a training paradigm that taught them to lie still. During this training, they watched a movie while their head motion was monitored using a motion detector. If they moved their head more than 3–4 mm during the movie, the movie paused to indicate they had moved too much. The movie continued once they were still again. This training and experiencing the mock

scanner took approximately 30 min. Children also practiced the task they would perform in the real scanner while lying in the mock scanner. We collected data from each child's task performance during the mock and actual scan. During the mock scan, we were able to collect 64 trials of the working memory task; during the actual scan, we were able to collect 40 trials. Because of reduced number of trials and the unfamiliar environment of the scanner, the data collected during the behavioral session is a more reliable estimate of each child's working memory ability (k); thus, our k estimates are derived from the behavioral session.

Behavioral Testing

As part of the larger study, each child completed the matrix reasoning subscale of the Wechsler Preschool and Primary Scale of Intelligence. To screen for IQ in adults, each adult completed the matrix reasoning subtest of the Wechsler Abbreviated Scale of Intelligence in an online (nonstandard administration) format.

Working Memory Task

The working memory task was adapted from Cowan et al. (2011). In this task (Figure 1), children were first shown a cue for 500 msec, which indicated that the memory trial was beginning. Next, they were shown a visual array of several circles (1, 2, 3, or 4) within a 3 × 4 grid for 750 msec (encoding), they maintained this array in working memory for a delay of 1700 msec, after which they made same/ different judgments about the color a single shape (probe), presented for 2000 msec. Each trial was followed by an intertrial interval of 500–4500 msec, jittered for an event-related design, with an exponential distribution of frequencies of each jitter (e.g., 40% of trials were followed by 500 msec, 40% by 2500, and 20% by 4500; Ollinger, Corbetta, & Shulman, 2001; Ollinger, Shulman, & Corbetta, 2001; Miezin, Maccotta, Ollinger, Petersen, & Buckner, 2000).
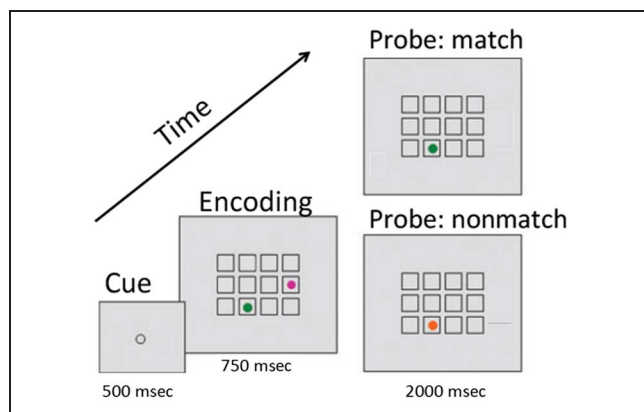

Figure 1. Working memory task. The delay between the encoding and probe screens was 1700 msec.

On 50% of trials, the color of the shape remained the same (match trials), while on the remaining 50% of trials, the color of the probe changed (nonmatch trials). Location of the probe stayed constant across the encoding and probe periods.

Children practiced this task until their accuracy on the practice set reached at least 75% correct, which on average took 1.7 attempts (SD = 1.2). Only three children failed to meet the 75% accuracy criterion during practice. After meeting this criterion, 64 trials of this task (16 per load) were administered in the mock scan session that preceded the scan session. On the day of the fMRI scan, a single run of this task that included 40 trials (10 per each load) and lasted approximately 5 min was administered during fMRI scanning. Accuracy rates were similar across the mock and scan sessions; the only difference was observed in Load 3 trials, which were performed less accurately during the scan (M = .56, SEM = .05) than the mock session (M = .68, SEM = .04), p = .01. This difference was present only for children; no significant differences were found for adults, all ps > .4.

MRI Data Acquisition

All MRIs were acquired at the Center for Brain Science at Harvard University on a 3-T Siemens Tim Trio MRI system (Berlin, Germany). Anatomical scans (T1-weighted multi-echo MPRAGE volumes) are acquired for anatomical co-registration with fMRI (repetition time [TR] = 2530 msec, echo time = 1640–7040 msec, flip angle = 7°, field of view = 220 mm^2, 176 slices, in-plane voxel size = 1 mm^3; iPAT = 3 to reduce acquisition time). To reduce motion artifacts, a navigator echo was used before the onset of the scan acquisition, slices were compared to this echo online, and up to 20% of slices that did not align with the navigator echo were reacquired. BOLD signal was obtained using a gradient-echo T2*-weighted EPI sequence (echo time = 30 msec, TR = 2000 msec, flip angle = 90°, bandwidth = 2300, echo spacing = 0.5, field of view = 192 × 192, matrix size = 64 × 64, resulting in in-plane resolution of 3 mm × 3 mm). Slices were acquired positioned parallel to the AC–PC line by an automatic algorithm (AAscout) using noninterleaved acquisition. Before each scan, four images were acquired and discarded to allow longitudinal magnetization to reach equilibrium. PACE, an online prospective motion correction algorithm, was included to reduce the effect of motion artifacts on data collection; however, non-PACE motion-corrected raw data were used in all analyses because online motion correction is not as reliable as standard motion correction techniques.

Data Analysis

fMRI Data Analysis

Processing and statistical analysis of fMRI data were performed using Nipype, a Python-based software framework

that incorporates components of several fMRI data analysis packages (nipy.sourceforge.net/nipype/). Following reconstruction of images into 3-D space, realignment and slice timing correction were run simultaneously using a 4-D slice timing correction and realignment algorithm to correct for participant movement within the scanner. Next, artifact detection (ART tool; web.mit.edu/swg/software.htm) was used to identify which frames or TRs we should exclude from the overall analysis; these frames are referred to as "outliers." Outliers were defined as fluctuations in signal that exceed three standard deviations from the mean in signal intensity or 2 mm of movement (in any of six movement directions: x, y, z and roll, pitch, yaw). Outliers were excluded from our data by creating unique covariates for each outlier image and including them in the general linear model. Finally, a 6-mm FWHM isotropic smoothing kernel was used to smooth the data.

Identification of BOLD activation to the task was performed using the FMRIB Software Library (FSL; Jenkinson, Beckmann, Behrens, Woolrich, & Smith, 2012). The task was modeled in an event-related design. We used different covariates for working memory maintenance (cue, encoding, delay) and recall (probe). For maintenance we had four conditions (four loads), and for probe we had eight conditions (four loads across both match and nonmatch trials). Working memory maintenance was modeled as one event, and recall was modeled separately. These covariates were entered into a general linear model. Nuisance covariates for motion parameters, including outliers (from artifact detection), were also included in this general linear model. Covariates were checked for multicolinearity, and all correlation coefficients were less than .35. For this study, we examined encoding and delay-related BOLD activation (acquired during the cue, encoding, and delay phases of the task). Intertrial interval was not explicitly modeled and thus constituted an implicit baseline. Next we directly contrasted BOLD-related activity in one type of trial with the other (e.g., encoding Load 2 > encoding Load 1) or with the implicit baseline. These individual level contrasts were input into a group level analysis. A one-sample t test was performed across participants within each group (children/adults) separately to identify significant activation for each condition of interest. A two-sample t test was performed to compare activation between children and adults for each load and task period separately. Clusters are reported if they reached significance at $p < .05$, corrected using a cluster level correction for multiple comparisons implemented in FSL, with a voxel level significance of $z > 2.3$.

To examine a priori hypotheses concerning neural recruitment across age and task performance, we used an ROI analysis. We examined working memory load-dependent activity in three ROIs: the caudal middle frontal gyrus, the superior parietal cortex, and the rACC. All ROIs were identified structurally using the FreeSurfer

image analysis suite (surfer.nmr.mgh.harvard.edu). First, each participant's structural and functional data were coregistered using bbregister, an alignment technique used by FreeSurfer in the normalization process (freesurfer.net/fswiki/bbregister#Description). For each participant, functional data were extracted within their FreeSurfer region corresponding to each ROI. This method allowed for the use of independently defined structural ROIs without relying on regions that had been normalized to group space.

FreeSurfer processing includes motion correction of a volumetric T1-weighted image, removal of nonbrain tissue using a hybrid watershed/surface deformation procedure (Ségonne et al., 2004); automated Talairach transformation, previously validated in pediatric populations (Burgund et al., 2002); and segmentation of the subcortical white matter, deep gray matter volumetric structures, and cortical gray matter using gyral and sulcal landmarks. FreeSurfer morphometric procedures have demonstrated good test–retest reliability across scanner manufacturers and field strengths (Han et al., 2006). In addition, these procedures have been successfully used in studies of children as young as 4 years (Ghosh et al., 2010). Using FreeSurfer, we defined 148 cortical regions (74 for each hemisphere) according to the 2005 Desikan–Killiany Atlas (Desikan et al., 2006) within each participant.

The ROI analysis was conducted using REX on unstandardized beta values from the first-level general linear model analysis (web.mit.edu/swg/software.htm). To examine changes in neural activation as a function of increasing working memory load, we ran repeated-measures ANOVAs with four levels (Loads 1, 2, 3, and 4) separately for children and adults. Polynomial contrasts were used for the load variable, such that we were able to examine linear, quadratic, and cubic effects of load on activation. We also tested whether differences in activation between Loads 1 and 2 (2 > 1 contrast) and Loads 2 and 4 (4 > 2 contrast) were significantly different from 0 (suggesting a load-dependent increase in activation) for each ROI and each group, using one-sample t tests. Finally, we ran a 4 (Load of 1, 2, 3 or 4) × 2 (child vs. adult) mixed within/between measures ANOVA to directly compare levels of activation across the age groups. Because children and adults had different levels of movement and IQ scores, repeated-measures ANOVAs were conducted while controlling for the number of motion outliers and IQ scores. Because we did not have a priori hypotheses about activations in right versus left hemispheres, we averaged across both hemispheres in the ROI analyses. Finally, to examine whether there were age-associated changes in neural activation in children, we examined the effect of age at the time of scan on amount of activation for each of the four loads in our three ROIs, controlling for IQ and motion outliers, using linear regression.

Motion

We were concerned that increased head motion in the child group might have contributed to any group differences in neural activation. Thus, we implemented multiple ways of accounting for differences in motion-related artifacts. First, we included movement covariates and outliers in our initial individual subject analysis. Second, we included the number of motion outliers each participant had as a covariate for our between-subject analyses. Finally, we tested to see if the number of motion-related outliers in the child group was significantly correlated to the amount of neural activation in the three ROIs.

Behavioral Data Analysis

Average accuracy and k estimates were calculated at each load for children and adults separately. k is an estimate of working memory capacity that has been used in previous studies with children and adults (Cowan et al., 2010; Cowan, 2000) to estimate the number of items that participants hold in mind. In the current study, we ran a 4 (Load 1, 2, 3 or 4) × 2 (child vs. adult) mixed within/between measures ANOVA separately on the accuracy and the k values. We also examined whether there were significant load effects in the two groups separately to ensure that the task was challenging enough for adults (in terms of accuracy) and to check whether the two groups differed in their working memory capacity (in terms of k).

RESULTS

Behavioral Data

IQ and Motion

Adults ($M = 13.75$, $SD = 1.6$) had higher scaled matrix reasoning scores than children ($M = 12.1$, $SD = 3.1$), $t(38) = 2.1$, $p = .04$. Adults ($M = 1.8$, $SD = 1.4$) also had significantly fewer motion outliers than children ($M = 16.5$, $SD = 17.0$), $t(38) = 3.9$, $p < .001$.

Accuracy

We observed a main effect of both Load and Age group on accuracy (Figure 2A). When performance was collapsed across load, children's accuracy ($M = .70$, $SD = .02$) was lower than that for adults ($M = .94$, $SD = .02$), $F(1, 38) = 50.6$, $p < .001$. In addition, accuracy collapsed across groups decreased as a function of Load, $F(3, 114) = 16.1$, $p < .001$. There was a marginal Load × Age interaction, $F(3, 114) = 2.3$, $p = .08$, such that the rate of change in accuracy across loads was marginally stronger for children. However, each group showed a significant linear Load effect even when examined by themselves (adults: $F(1, 19) = 21.4$, $p < .001$; children: $F(1, 19) = 15.0$, $p = .001$). Given the high level of overall accuracy for adults, we examined the effect of Load separately for
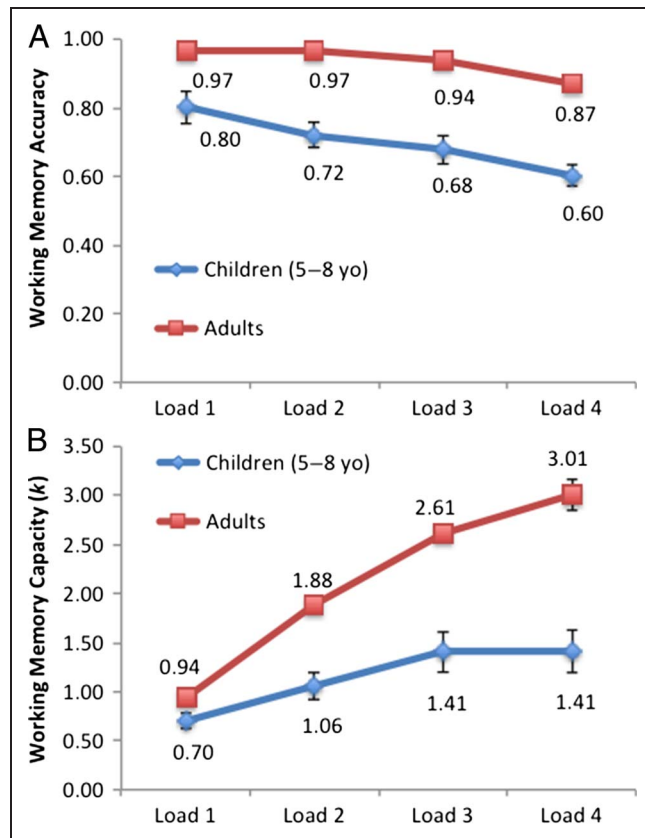

Figure 2. Performance (A: accuracy, B: k estimates) on the working memory task from the behavioral session, for children and adults, as a function of working memory load. Error bars reflect the standard errors of the mean, calculated for each trial type within age group.

each group in an effort to ensure that the task was sensitive to working memory demands in both age groups.

Working Memory Capacity (k)

Similar to accuracy, there was a significant main effect of Age group and Load on k values (Figure 2B). Children had lower k estimates than adults, $F(1, 38) = 45.5$ $p < .001$. The values of k estimate increased as a function of load, $F(3, 114) = 15.5$, $p < .001$. We observed a significant Age group × Load interaction, such that the increase in k was steeper for adults than for children, $F(3, 114) = 14.7$, $p < .001$. This finding is consistent with the hypothesis that capacity limit was reached at a different load for children and adults. For children, the k-estimate trajectory plateaued after Load 2, with both Load 3 and Load 4 eliciting estimates of 1.41 items maintained in working memory. In contrast, k values increased linearly from 1 to 4 for adults. As described above, a plateau in k values across load was expected once capacity was achieved, suggesting that children in our sample could maintain between one and two items in their working memory. The fact that adult's k trajectory did not plateau suggests that the task demands did not exceed adults' working memory capacity.

Age Effects

A four-way (Load: 1, 2, 3, 4) repeated-measures ANOVA with IQ as a covariate showed a marginal effect of Age year (5–8 years old) on accuracy, $F(3, 15) = 2.8$, $p = .08$, such that children become marginally more accurate with age. There was no significant effect of Age on the k estimate, $F(31, 145) = 2.0$, $p = .16$, and no interaction between Age year and Load, both $ps > .5$. In subsequent analyses, we examine changes in activation as a function of age within the child group.

fMRI Data

Whole-brain Analysis

All analyses are for the cue/encoding/delay phase of each working memory trial. We first examined activation as a function of increasing working memory load for both children and adults separately to identify patterns of neural recruitment with increasing load for the two groups of participants. Given the apparent difference in working memory capacity between children and adults, we additionally report activation for children and adults separately for direct contrasts between Load 2 and Load 1 (2 > 1) and Load 4 and Load 2 (4 > 2). Neural recruitment that supports successful working memory performance regardless of age should be similar between adults and children for the 2 > 1 contrast and should differ for the 4 > 2 contrast, because our behavioral analysis (k values) indicate that children are, on average, not encoding more items between Loads 2 and 4, even though they are presented with more items at encoding (Figure 3; Tables 1 and 2). Next, we directly contrasted activation in children and adults at each load, as well as examined activation patterns at each load for each age group (Figures 4 and 5; Tables 3 and 4).

Adults. Consistent with the existing literature, adults recruited distributed regions in the middle frontal and superior parietal regions, bilaterally, as load increased. This was true for the 2 > 1 contrast and the 4 > 2 contrast, suggesting that adults' increased capacity allowed them to recruit areas supporting working memory in a parametric, linear way across our working memory loads.

Children. Similar to adults, children recruited distributed regions in the middle frontal and superior parietal regions. Children showed enhanced parietal, occipital, and prefrontal activation for encoding at 2 > 1 contrast, but no activation differences were found when comparing Loads 2 and 4. This is consistent with children's more limited in working memory capacity ($k = 1.4$ items) and suggests that children do not up-regulate their neural activity for trials that exceed their working memory capacity.

Adults > children. When activation at each load was directly compared between adults and children, adults activated more lateral prefrontal and dorsal anterior cingulate regions (mostly on the left). For Load 4 (which exceeded children's working memory capacity), adults additionally activated bilateral BG and superior parietal regions.

Figure 3. BOLD activity from increasing working memory load for both adults and children, for the right hemisphere (RH; A: lateral surface, B: medial surface) and the left hemisphere (LH; C: lateral surface, D: medial surface). The contrasts (Load 4 > Load 2 and Load 2 > Load 1) are shown on a representative inflated FreeSurfer surface. Areas are shown if they survive cluster level correction at $p < .05$. Please refer to Table 1 for a list of significant activations for these contrasts (and for individual loads relative to implicit baseline).
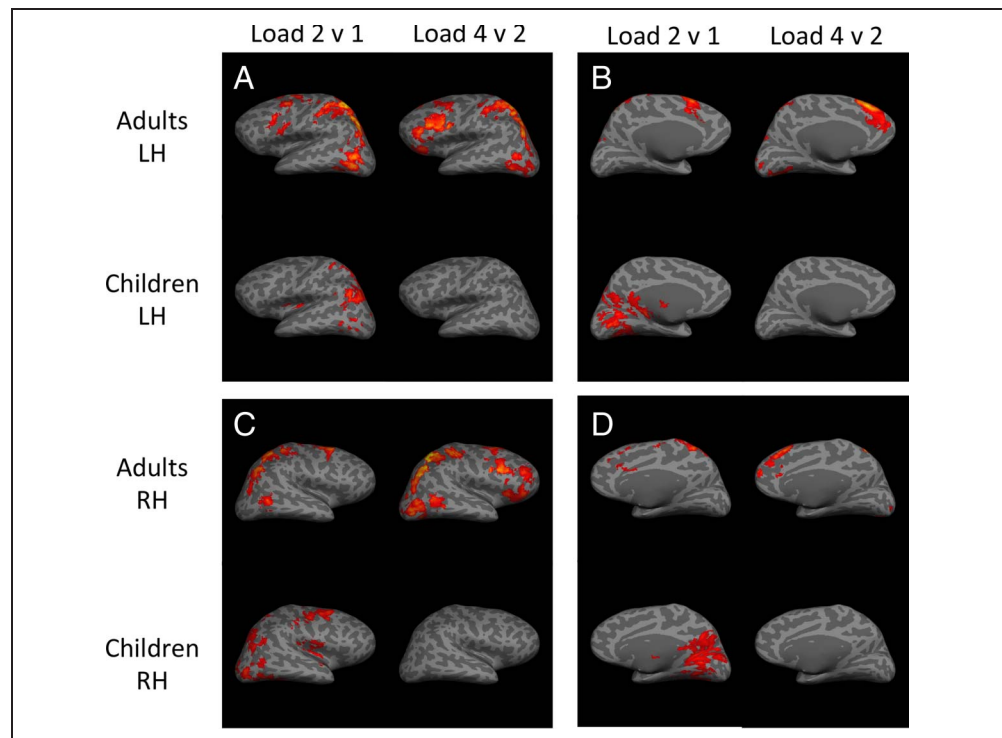
Table 1. Areas of Significant Activation across Working Memory Loads, for Adults

	Region	x	y	z	z-Value
Load 1	Lateral occipital (R)	38	20	32	6.38
	Middle frontal gyrus[1] (R & L)	34	64	65	4.84
	Superior frontal gyrus[1] (R & L)	49	67	64	4.48
Load 2	Lateral occipital (R & L)	32	22	33	6.12
	Putamen (L)	55	68	41	5.10
Load 3	Lateral occipital (R & L)	32	23	31	6.49
	Middle frontal gyrus[1] (R & L)	34	63	64	5.19
	Superior frontal gyrus[1] (R & L)	41	63	70	4.86
	Putamen (L)	55	68	42	5.57
Load 4	Lateral occipital (R & L)	32	22	33	6.29
	Putamen/caudate[1] (R)	35	72	39	5.06
	Middle frontal gyrus[1] (R)	26	79	45	3.50
Load 4 vs. 2	Lateral occipital gyrus (R)	33	27	62	5.31
	Superior frontal gyrus[1] (R & L)	48	74	59	4.84
	Middle frontal gyrus[1] (L)	29	64	64	4.44
	Lateral occipital gyrus (L)	57	27	51	4.48
	Inferior frontal gyrus (R)	25	78	38	3.69
Load 2 vs. 1	Superior parietal lobule (R)	35	33	64	4.88
	Superior parietal lobule (L)	54	29	63	5.13
	Middle frontal gyrus (L)	59	60	63	4.38

Contrasts were calculated relative to implicit baseline, except when two different loads were contrasted (two bottom rows).

[1]Part of the same cluster.

Children > adults. In contrast to previous findings (e.g., Thomason et al., 2009; O'Hare et al., 2008; Klingberg et al., 2002; Kwon et al., 2002), we found a number of regions that were more active for children relative to adults, across all loads, including areas in the PFC. This finding is consistent with the notion that children use distinct neural networks to solve the same task, which has been suggested elsewhere in the context of working memory (Finn et al., 2010; Scherf et al., 2006). In particular, we observe activation in rostral superior frontal regions and in inferior parietal cortex/angular gurus on the lateral surface. On the medial surface, children appeared to recruit posterior cingulate and ventromedial prefrontal regions relative to adults. Overall, prefrontal activations in children were more rostral when neural recruitment was directly compared to adults.

ROI Analysis

To further explore the differences in neural recruitment across the two age groups in solving the same working memory task, we examined three independently identi-fied ROIs described above: superior parietal cortex, caudal middle frontal gyrus, and rACC (Figure 6).

Superior parietal. Adults showed a linear increase in activation with increasing load, $F(1, 19) = 15.6$, $p = .001$ (quadratic and cubic contrasts were not significant, both ps > .4). In adults, the differences in activation between Load 2 and Load 1 (2 > 1) and between Load 4 and Load 2 (4 > 2) were significantly greater than 0, both ps < .03, consistent with the linear increase. Children, similarly, showed a marginal linear increase in activation with increasing load, $F(1, 17) = 3.2$, $p = .09$ (ps for quadratic and cubic contrasts > .6); however, 2v1 and 4v2 comparisons did not significantly differ from 0, both ps > .2. A direct comparison of age groups showed no significant difference in amount of activation across children and adults, $F(1, 36) = 2.4$, $p = .13$. In children, there was no association between age and activation of the superior parietal region across any of the four loads, all ps > .26.

Caudal middle frontal. Adults showed a significant linear increase in activation as a function of increasing load, $F(1, 17) = 4.3$, $p = .05$; quadratic ($p = .1$) and cubic contrasts ($p = .85$) were not significant. The largest increase in recruitment by load for adults was between Loads 2 and 4: Only the differences in activation between Load 4 and Load 2 (4 > 2) was significantly greater than 0,

Table 2. Areas of Significant Activation across Working Memory Loads, for Children

	Region	x	y	z	z-Value
Load 1	Lateral occipital (L)	51	18	32	4.28
	Lateral occipital (R)	36	20	31	3.90
	Inferior parietal (R)	28	27	51	3.27
Load 2	Lateral occipital (R & L)	32	28	33	5.3
	Middle frontal gyrus (R)	28	60	60	5.07
	Thalamus (R & L)	34	50	35	4.06
Load 3	Lateral occipital (R)	27	30	31	4.72
	Lateral occipital (L)	61	37	29	4.55
	Superior frontal gyrus (R & L)	44	92	46	3.58
Load 4	Lateral occipital (R)	32	28	33	5.53
	Lateral occipital (L)	61	37	29	5.08
	Middle frontal gyrus (R)	29	61	60	4.7
Load 4 vs. 2	–	–	–	–	–
Load 2 vs. 1	Lateral occipital (L)[1]	58	26	50	3.75
	Posterior cingulate (L)[1]	52	42	37	3.59
	Inferior parietal (L)[1]	64	30	46	3.58

Contrasts were calculated relative to implicit baseline, except when two different loads were contrasted (two bottom rows).

[1]Part of the same cluster.

Figure 4. BOLD activity contrasting children and adults, in the left hemisphere, across each of the four working memory loads versus implicit baseline. Activations are shown on a representative inflated FreeSurfer surface, if they survive cluster level correction at $p < .05$. Please refer to Table 2 for a list of significant activations for each load.
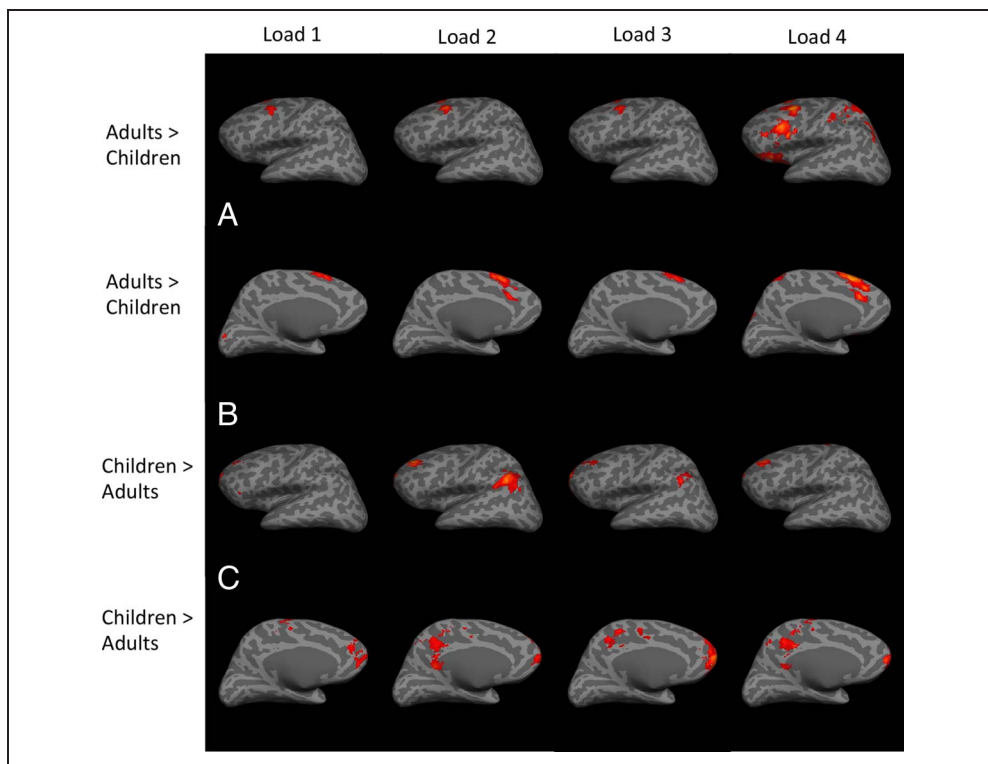
$t(19) = 2.3$, $p = .032$. Children also showed a marginally significant linear effect of Load on activation, $F(1, 17) = 3.7$, $p = .07$; quadratic ($p = .47$) and cubic ($p = .13$) contrasts were not significant. In contrast to adults, the largest increase recruitment by load for children was between

Loads 1 and 2: Only the differences in activation between these loads ($2 > 1$) was marginally greater than 0, $t(19) = 1.8$, $p = .086$. There was no difference in overall levels of activation across groups, $F(1, 36) = 1.0$, $p = .32$. In children, there was also no association between age and

Figure 5. Lateral surface BOLD activity in children and adults, across each of the four working memory loads relative to implicit baseline. Activations are shown on a representative inflated FreeSurfer surface, if they survive cluster level correction at $p < .05$. None of the regions show deactivation patterns, for either group. Please refer to Table 2 for a list of significant activations for each load.
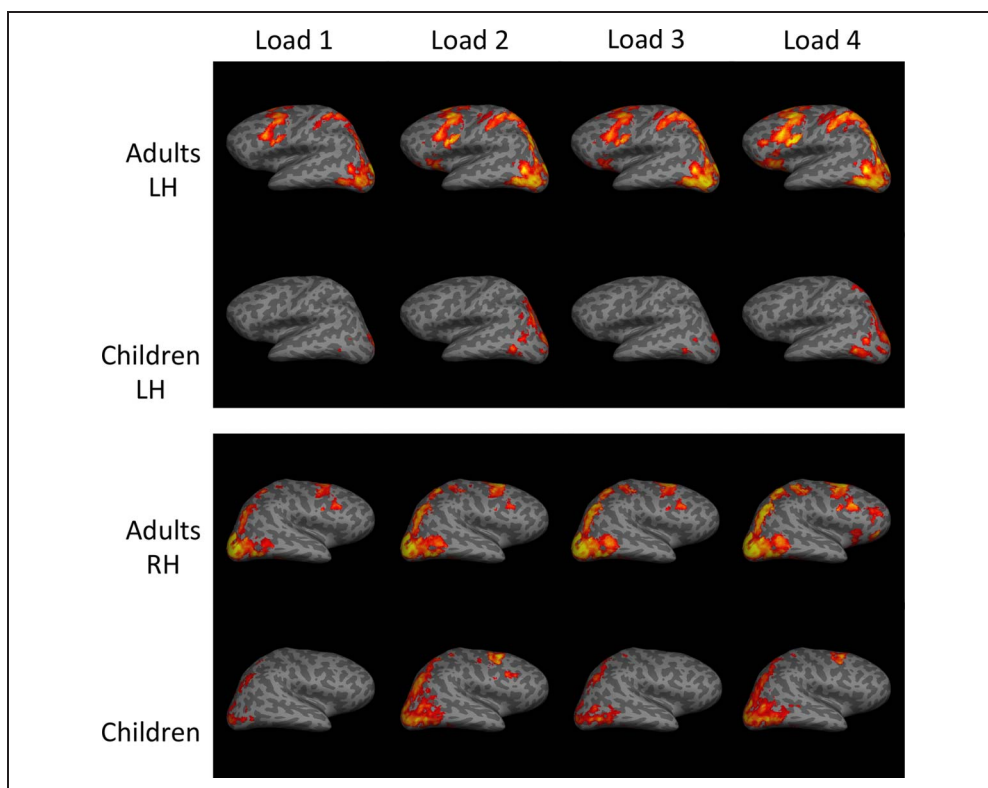
Table 3. Areas of the Brain that Were Significantly More Active for Adults, Relative to Children, across the Four Working Memory Loads

	Region	x	y	z	z-Value
Load 1	Lateral occipital (R & L)	27	17	44	3.98
	Superior frontal gyrus[1] (L)	49	66	65	3.73
	Middle frontal gyrus[1] (L)	65	63	64	3.64
Load 2	Superior frontal gyrus[1] (R & L)	32	64	67	4.12
	Middle Frontal Gyrus[1] (L)	59	62	62	3.97
Load 3	Middle frontal gyrus[1] (L)	69	62	61	3.52
	Superior frontal gyrus[1] (R & L)	48	67	67	3.5
	Lateral occipital cortex[2] (R)	27	17	44	3.69
	Inferior parietal[2] (R)	30	24	48	3.44
Load 4	Superior frontal[1] (R & L)	44	68	61	4.39
	Middle frontal gyrus[1] (L)	59	63	62	4.24
	Middle frontal gyrus (R)	33	64	65	4.33
	Superior parietal (L)	55	14	47	4.33
	Striatum[1] (L)	55	67	43	4.27
	Insula[1] (L)	59	75	35	3.93
	Striatum[2] (R)	35	72	39	4.12
	Insula[2] (R)	24	74	35	2.49

[1] Part of the same cluster.

[2] Part of the same cluster.

activation of the caudal middle frontal region across any of the four loads, all ps > .13.

Rostral ACC. Adults showed a linear effect of Load, such that activation of the rACC decreased with increasing, load, $F(1, 17) = 5.5$, $p = .03$ (quadratic and cubic contrasts were not significant, both ps > .8). Children showed marginal quadratic, $F(1, 17) = 3.1$, $p = .097$, and cubic, $F(1, 17) = 3.4$, $p = .083$, effects of load on activation, but not a linear contrast, $p = .78$. A direct contrast of loads was consistent with the cubic trend: The differences in activation between Load 2 and Load 1 (2 > 1) were marginally greater than 0, $t(19) = 2.1$, $p = .055$, whereas the difference in activation between Load 4 and Load 2 (4 > 2) was marginally less than 0, $t(19) = -2.1$, $p = .051$. When compared directly to each other, children ($M = 9.7$, $SE = 12.7$) showed a nonsignificant trend for activating the rACC more than adults did ($M = -23.3$, $SE = 12.7$), $F(1, 36) = 2.9$, $p = .10$. In children, there was also no association between age and activation of the rACC region across any of the four loads, all ps > .34.

ROI activation when performance levels are matched. To determine whether the observed differences in amount of activation across groups were due to differences in age or to differences in differences in task performance, we directly compared neural activity in the three ROIs for loads that elicited comparable accuracy: Load 4 in adults ($M = 87.3\%$ correct, $SD = .097$) and Load 1 in children ($M = 80.3\%$ correct, $SD = .21$), $t(38) = 1.3$, $p = .19$ (Figure 6). We observed different patterns for the three ROIs. In the superior parietal cortex, adults (at Load 4) elicited more activation than children (at Load 1), $p < .002$. In contrast, the rACC showed more activation for children (at Load 1) than for adults (at Load 4), $F(1, 36) = 6.5$, $p = .015$. The caudal middle frontal gyrus showed no difference between groups, $F(1, 36) = 2.0$, $p = .17$, when both groups were assessed at their working memory capacity.

DISCUSSION

The goal of this study was to examine the association between working memory capacity and neural activation in a sample of young children ages 5–8. We first sought to replicate previous findings, suggesting that estimates of working memory capacity (k) in children were significantly lower than adults' estimates. Next, we tested (1) whether neural substrates supporting working memory in childhood differed from those supporting mature working memory processes and (2) whether these differences could be attributed to the differences in behavioral capacity limits.

Table 4. Areas of the Brain that Were Significantly More Active for Children, Relative to Adults, across the Four Working Memory Loads

|	Region	x	y	z	z-Value
Load 1	Rostral superior frontal gyrus (R & L)	40	94	49	3.76
	Superior parietal lobule[1] (R)	33	45	69	3.40
	Posterior cingulate[1] (R)	45	49	59	3.07
	Inferior frontal gyrus (L)	70	84	34	3.51
Load 2	Rostral superior frontal gyrus (R & L)	51	88	55	4.38
	Posterior cingulate (R & L)	39	39	53	3.92
	Angular gyrus (L)	71	33	51	4.14
Load 3	Rostral superior frontal gyrus (R & L)	45	93	45	4.77
	Angular gyrus (L)	76	36	53	4.08
	Posterior cingulate (R & L)	45	53	58	3.93
	Angular gyrus (R)	15	46	60	3.77
Load 4	Rostral superior frontal gyrus (R & L)	45	92	46	4.26
	Posterior cingulate (R & L)	39	39	54	4.24

[1] Part of the same cluster.
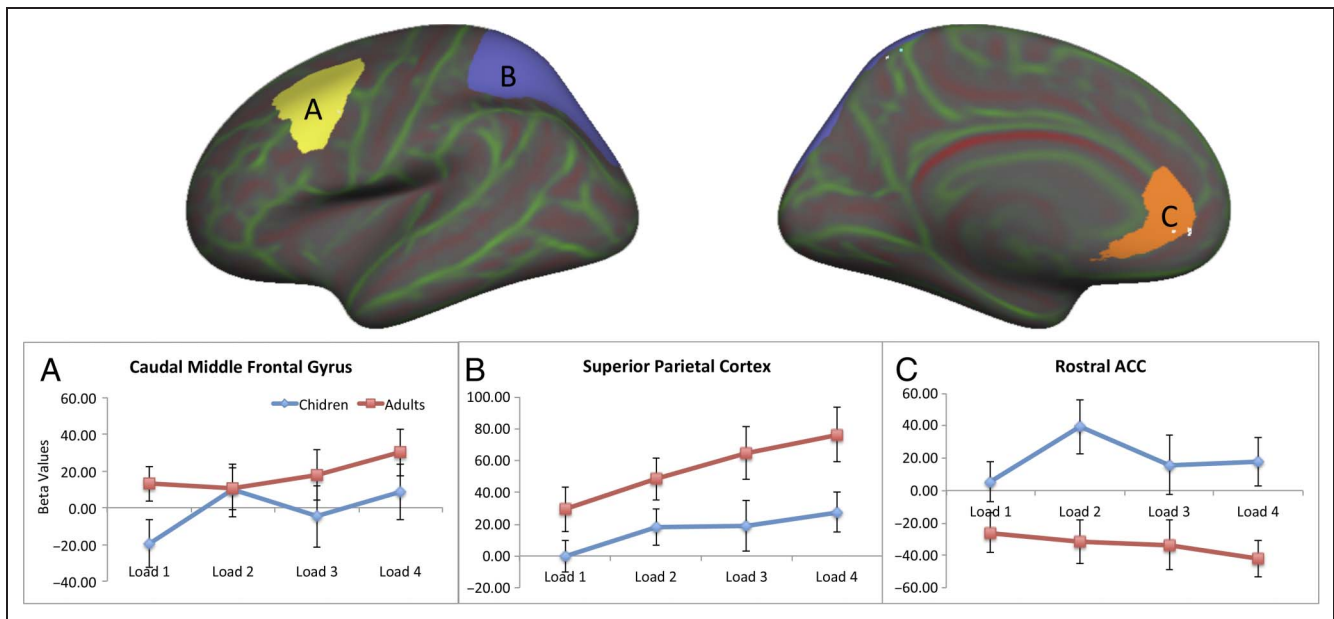
Figure 6. ROI results for children and adults, overlayed on a representative inflated FreeSurfer surface, for each of the three ROIs. Beta values were extracted from activation collapsed across right and left hemispheres. Error bars represent 1 *SEM* in each direction.

We found that consistent with previous studies (Cowan et al., 2010, 2011; Riggs et al., 2006) adults can remember at least twice as many items (3+ items) as children (1.4 items). Additionally, although many groups have found that working memory abilities (and degree of associated neural activation) change substantially across early and middle childhood (Spencer-Smith et al., 2013; Simmering, 2012; Tsujii et al., 2009; Klingberg, 2006; Riggs et al., 2006), we did not observe differences in working memory capacity limit (k) or neural activation across ages 5–8. This lack of age-related differences likely stems from our relatively narrow age band. As our study was not designed to investigate this question further, follow-up work is needed to better understand age-related changes in capacity limits and neural activation associated with working memory performance within childhood itself.

Importantly, we found similar distributed frontoparietal networks activated in response to our task in children and adults. However, important differences were observed in terms of the amount of activation in response to increasing working memory demands across groups. Across all four loads, adults reliably showed an increase in activation across the middle frontal gyrus and the superior parietal cortex, with significant increases in activation for Load 4, relative to Load 2. In contrast, children only up-regulated the recruitment of these regions for Load 2, relative to Load 1, with no further increase in recruitment at Load 4 (which exceeded their working memory capacity limit). This pattern in recruitment across load was observed in both the whole brain (4 > 2; 2 > 1) and ROI analyses. These patterns of activation are consistent with the interpretation that both groups recruit typical neural systems necessary to perform this working memory task, but only until capacity limit is reached, with neural activation levels plateauing at that point. This suggests that differences in the extent of neural activation across development stems at least in part from differences in behavioral performance abilities: Children do not up-regulate neural activation at loads that exceed their working memory capacity limits.

Our paradigm allowed us to shed additional light on the question of whether differences in children and adults' activation patterns are due to maturation or due to performance differences by comparing activation patterns for conditions that elicited comparable levels of behavioral performance across groups (Load 1 for children and Load 4 for adults). This analysis revealed that when controlling for accuracy in this way, young children and adults did not differ in the extent of activation in the middle frontal gyrus, consistent with the conclusion that differences in middle frontal gyrus activation were due at least in part to differences in performance abilities across groups.

However, not all regions were activated similarly by both groups when capacity was held constant. In contrast to the middle frontal gyrus ROI, the superior parietal ROI showed increased activation for adults relative to children even when controlling for differences in performance, consistent with the findings of Thomason et al. (2009). The whole-brain analysis revealed other differences in activation that appeared unrelated to working memory capacity differences across age groups. When children and adults were directly compared at each load, adults consistently activated a region in the left middle frontal gyrus more than children regardless of memory load. Finally, across all loads, whole-brain analyses revealed that children activated a more anterior middle frontal region, whereas adults activated a more posterior middle frontal region in response to encoding demands. These differences

in neural recruitment, which were not load-dependent, may account for adults' enhanced accuracy when collapsed across all loads. These differences (particularly, the anterior/posterior differences) might also reflect differences in strategy or way in which the task was solved by children versus adults. Simpler and more perceptual working memory tasks often rely on more caudal regions, whereas more complex tasks requiring abstract reasoning require the maturity of more rostral prefrontal regions (Reynolds, O'Reilly, Cohen, & Braver, 2012; Badre & Wagner, 2007). Because our task was more difficult for children, it is not altogether surprising that they relied on more anterior prefrontal regions to solve it.

Finally, ACC region was more active in children than in adults across all loads, even when controlling for differences in accuracy. There are at least two interpretations for this finding and future research needs to adjudicate between these possibilities. ACC activates in response to conflict processing in executive functions tasks (Botvinick et al., 2004) and in response to error monitoring (Carter et al., 1998). Because the task overall was more difficult for children than for adults, it is possible that children were overall more aware of the errors they made, thus showing an increase in ACC activation. However, a substantial body of work suggests that children are less aware of making errors (e.g., Santesso, Segalowitz, & Schmidt, 2006), making this explanation less likely.

 Alternatively, our findings are consistent with the growing evidence that ACC plays a more general role in the development of cognitive control in childhood, relative adulthood. We observed that the level of ACC activation in response to conflict on the Simon task was negatively associated with age in children 5–10 years old (Sheridan, Kharitonova, Martin, Chatterjee, & Gabrieli, 2014), suggesting a critical role of this region in executive control earlier in childhood. Others found that ACC was more active in 6-year-old children than in adults for a categorical *n*-back task, but not more active in 10-year-olds than in adults (Ciesielski et al., 2006). The surface area of the right ACC predicted performance on the incongruent trials of the Flanker task, but only for participants younger than the age of 12 (Fjell et al., 2012). Others have observed that specific sulcal patterns of ACC are selectively associated with performance on a Stroop task in children at ages 5 and 9 (Borst et al., 2014; Cachia et al., 2014; Gould et al., 2003). It may be that for children younger than 8 years, a group historically understudied using fMRI, ACC plays a more general role in supporting task performance across executive functioning tasks, without a specific focus on conflict processing. Longitudinal studies that start in early childhood will help to elucidate the role that ACC plays in the development of working memory and cognitive control.

Our study has several limitations. First, we examined children under the age of 8 and adults over the age of 18; thus, although we can robustly identify the presence of developmental differences in neural recruitment and in behavioral performance, we can do less to explicate

precisely how these differences emerge and change over time. Second, when working with young children, the possibility that increased head movement in the child sample may account for findings is always present. We attempted to account for this potential confound in several ways. First, we included movement covariates and outliers in our initial individual subject analysis. Second, we included the number of outliers each participant had as a covariate for our between-subject analyses. Third, we found no significant correlation between the number of motion outliers during scanning and the amount of activation for any of our three ROIs, all Rs < .4. Finally, it is likely that a variable-like movement would introduce noise into the data and thus elicit either overall reductions in activation for the sample with more movement or specific increases in activation across all conditions along the edges of the brain or ventricles (where fluctuations in signal are greatest). Instead, we observe increases in activation for children in areas that are not at the edge of the brain and are highly linked to task condition and behavioral capacity limits. An additional limitation stems from the fact that this is not a longitudinal study; thus, the developmental trends observed here could potentially be the result of unmeasured third variables between groups. We have attempted to account for this possibility by matching groups on gender and covarying IQ in all our analyses.

Several previous investigations of neural development supporting working memory have concluded that adults recruit working memory-related regions in a load-dependent manner more so than children (Thomason et al., 2009; O'Hare et al., 2008). We also observed some evidence for this claim, particularly in the whole-brain analysis, where adults activated frontoparietal networks to a larger extent than children, across all loads. Other groups have focused on the observation that children recruit distinct areas than adults in support of their working memory performance (Finn et al., 2010; Ciesielski et al., 2006). We also observed evidence for this claim: Regardless of load, children recruited the rostral middle frontal region and ACC to support working memory performance. Nevertheless, the majority of our findings support the idea that children and adults share a similar network of frontoparietal areas that support performance on visual–spatial working memory tasks. This network is increasingly recruited as more items are maintained in working memory, but only up to the individual's working memory capacity limit. Because working memory capacity differed substantially between our two groups and because we measured working memory at a variety of loads, we were able to observe this pattern of increasing recruitment of the working memory network until capacity was reached, and a more limited recruitment across most regions thereafter. The question of what drives differences in the extent of neural activation across development remains a critical one. We were able to shed some light on this issue, but future research should validate these observations through replication and extend them through the use of longitudinal paradigms.

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