Neurocognitive development of the ability to manipulate information in working memory

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The ability to manipulate information in working memory is a key factor in cognitive development. Here, we used event-related functional MRI to test the hypothesis that developmental improvements in manipulation, relative to pure maintenance, are associated with increased recruitment of dorsolateral (DL) prefrontal cortex (PFC) and superior parietal cortex. Three age groups (8–12 years old, 13–17 years old, and 18–25 years old) performed an object-working memory task with separate maintenance and manipulation conditions. We found that 8- to 12-year-olds did not perform the task as well as adolescents or adults, particularly on trials requiring manipulation in addition to maintenance. In this study, no age differences were observed in the activation profile of ventrolateral PFC, a region associated with online maintenance. In contrast, unlike the older participants, 8- to 12-year-olds failed to recruit right DL PFC and bilateral superior parietal cortex during the delay period for manipulation relative to maintenance. This group difference was observed specifically during the delay period, while participants reordered items in working memory, and could not be accounted for by group differences in performance. Across participants, activation levels in right DL PFC and superior parietal cortex, but not ventrolateral PFC, were positively correlated with performance on manipulation trials. These results indicate that increased recruitment of right DL PFC and bilateral parietal cortex during adolescence is associated with improvements in the ability to work with object representations.

prefrontal cortex | children | executive function | intelligence

Working memory, or the ability to keep information in a highly accessible state (1), improves over the course of childhood (2–4). The ability to keep information in mind is essential for a variety of cognitive abilities, including reading, mathematical calculation, and problem-solving (5, 6), and working memory capacity predicts school performance (7). Developmental changes in the ability to maintain information online are observed in school-aged children (e.g., 8). However, these changes are more dramatic when children must manipulate, or work with, this information (9, 10). In this study, we focus on the neural substrates that support developmental changes in the ability to manipulate information in working memory.

The finding that children have particular difficulty on tasks involving manipulation could be explained in several ways. One possibility is a unitary account (e.g., 11), whereby general improvements in working memory occur over childhood, and challenging working memory tasks, which often involve manipulation, are associated with protracted behavioral changes. Another possibility is a process-specific account of working memory development, following up on the neuroscientific studies that suggest that maintenance and manipulation are dissociable components of working memory (12–14). Under the process-specific account of working memory development, manipulation has a prolonged developmental time course relative to maintenance because it relies on additional brain regions that mature more slowly than the brain network that underlies pure maintenance. The goal of this study was to use functional MRI (fMRI) methods to test these competing accounts of working memory development.

Brain imaging studies focusing on working memory in adults suggest that different parts of lateral prefrontal cortex (PFC) are involved in maintenance and manipulation (12–14, but also see ref. 15). These studies associate ventrolateral (VL) PFC with the online maintenance of information, and generally show that mid-dorsolateral (DL) PFC is additionally recruited when manipulation is required (12–14, 16, 17). Interestingly, although DL PFC is most commonly considered to be important for manipulation, a meta-analysis by Wager and Smith (18) reveals that superior parietal cortex is the region most consistently implicated in tasks involving manipulation. It has been hypothesized that representations of magnitude (19) or space (20) in parietal cortex serve as the substrate for the organization and manipulation of items in working memory.

On the basis of the adult neuroimaging data, it is possible to make specific predictions regarding the two alternative accounts of working memory development outlined above. Under the process-specific account of working memory development, we predict that children (aged 8–12), who have difficulty with manipulation but perform relatively well on pure maintenance tasks, should fail to appropriately recruit DL PFC and superior parietal cortex for manipulation but should exhibit similar patterns of VL PFC activation relative to adolescents and adults. Under the unitary account of working memory development, we predict age-related increases in the recruitment of the working memory network, including VL PFC, DL PFC, and parietal cortex, for both maintenance and manipulation.

Structural brain imaging studies of development indicate cortical gray matter loss and white matter increases during late childhood and adolescence, associated with pruning of excessive neurons and increased structural connectivity between brain regions (21). Longitudinal measurements of cortical gray matter volume indicate that VL PFC is structurally mature at an earlier age than DL PFC (22), lending support to our prediction regarding the order of functional maturation of these regions.

There have been several functional brain imaging studies of working memory involving children (23–26), although none of these studies have focused on the neural substrates of manipulation. Event-related studies of spatial working memory indicate that PFC and parietal cortex activation is stronger in adults than in 8- to 12-year-old children when higher maintenance demands are required, suggesting that the working memory network is still being strengthened in this age range (25, 26). However, prior developmental imaging studies of working memory have used tasks that required maintenance of information (e.g., ref. 25) or both maintenance and manipulation (e.g., ref. 24). To our knowledge, this study is the first study to isolate manipulation requirements by

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Abbreviations: DL, dorsolateral; fMRI, functional MRI; PFC, prefrontal cortex; ROI, region-of-interest; VL, ventrolateral.

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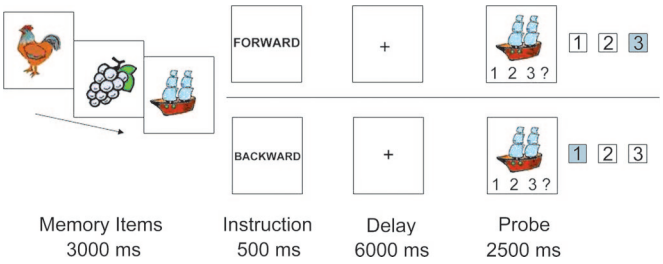

Fig. 1. Each trial started with a 250-ms fixation cross, followed by three nameable objects that were presented for 750 ms each, interleaved with 250-ms fixation crosses. After the last object, the instruction ''forward'' or ''backward'' was presented for 500 ms. Participants were instructed to mentally rehearse or reorder the names of the three objects during the 6,000-ms delay, and then to indicate with a button press whether the probe object was the first, second, or third object in the forward or backward sequence. Correct answers are shaded in blue for illustrative purposes.

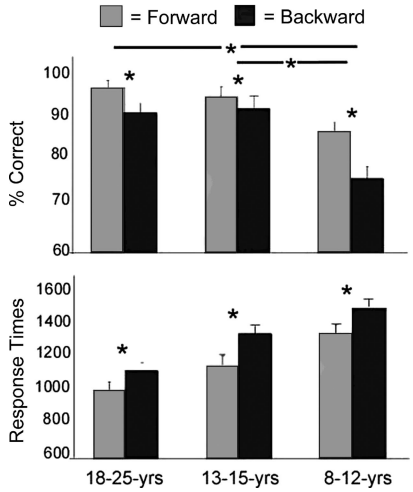

Fig. 2. Accuracy and response times associated with task performance during fMRI data acquisition. Age × condition interactions between 8- to 12-year-olds and the two other groups are denoted by horizontal lines with asterisks. $P<0.05$.

comparing a maintenance + manipulation condition with a pure maintenance condition.

In this study, a low working memory load (three nameable objects) was chosen to enable us to focus on developmental changes in manipulation. Indeed, with higher ("supraspan") working memory loads, there is the possibility that participants will use chunking strategies to maintain the large amount of information, and chunking, in and of itself, could be considered a manipulation process. Indeed, Rypma and colleagues (27) have argued that DL PFC activation on high-load maintenance tasks is related to chunking, rather than to maintenance *per se*. As such, we selected a load of three items to avoid contaminating our maintenance condition with manipulation demands.

In this study, we acquired event-related fMRI data while healthy right-handed participants performed a working memory task with both maintenance and manipulation conditions. Prior work indicates that large changes in working memory performance take place in late childhood, and that mature levels are generally reached in adolescence (28). Thus, in the present study, we included participants of three age groups: children, aged 8–12 ($n = 14$); adolescents, aged 13–17 ($n = 12$); and young adults, aged 18–25 ($n = 18$). In the working memory task, three nameable objects were presented sequentially (Fig. 1). During a 6-s delay period, participants were instructed to repeat the objects in a forward order (the maintenance task) or to reverse the order of the objects (the manipulation task). After the delay, participants were prompted with one of the objects and indicated with a button press whether this target object occurred first, second, or third in the forward or backward sequence.

Results

Performance. Compared with maintenance trials, responses to manipulation trials were associated with more errors [$F(1, 41) = 28.82$, $P < 0.001$] and slower response times [$F(1, 41) = 55.59$, $P < 0.001$] across participants. Eight- to twelve-year-old children made more errors than adolescents and adults on maintenance trials [$F(2, 41) = 6.31$, $P < 0.05$]. However, as expected, there was a more dramatic difference between 8- to 12-year-olds and older participants in terms of accuracy on manipulation trials [age group × condition interaction; $F(2, 41) = 3.42$, $P < 0.05$, Fig. 2]. Response times and accuracy were not affected by the position of items in the list of object (first, second, or third); in all instances, $F < 1$.

Whole-Brain Analyses. Whole-brain contrasts focused on the delay period of correctly performed maintenance and manipulation trials. In adults, regions that were recruited more strongly on manipulation than maintenance trials included left VL PFC, bilateral DL PFC, and bilateral inferior and superior parietal cortex. At the same statistical threshold ($P < 0.001$, uncorrected for multiple comparisons), children and adolescents did not activate additional brain areas. Brain regions that were active for this contrast are reported in Table 1, which is published as supporting information on the PNAS web site.

VL PFC Versus DL PFC. We conducted region-of-interest (ROI) analyses to examine the delay-period activation profiles of VL PFC and DL PFC in each age group. For each ROI, activation levels relative to a fixation baseline were extracted for each condition and subject, and submitted to ANOVAs. To test our predictions regarding VL PFC and DL PFC activation, we tested for an age group (children, adolescents, or adults) × condition (maintenance or manipulation) × ROI (left VL PFC or right DL PFC) interaction, and we found that this interaction was highly significant [$F(2, 41) = 13.23$, $P < 0.001$]. As predicted, the right DL PFC activation profile differed significantly between the three age groups [$F(2, 41) = 3.69$, $P < 0.05$], whereas the VL PFC profile did not ($F < 1$; Fig. 3). Adults and adolescents recruited right DL PFC more strongly during the delay period for manipulation than maintenance [$F(1, 17) = 29.01$, $P < 0.001$ and $F(1, 11) = 30.31$, $P < 0.001$], whereas 8- to 12-year-olds did not ($F < 1$). Left DL PFC was also more active for manipulation than maintenance trials [$F(1, 41) = 19.28$, $P < 0.001$], but this region did not differ significantly between age groups ($F < 1$).

Superior Parietal Cortex. In addition to DL PFC, superior parietal cortex is consistently implicated in tasks involving manipulation (18, 20). In this study, left and right superior parietal cortex exhibited a similar pattern to right DL PFC ($F < 1$ for all interactions with DL PFC), in that children (unlike adolescents and adults) failed to recruit this region more strongly for manipulation than maintenance during the delay period (Fig. 4). When comparing maintenance versus manipulation trials in superior parietal cortex, there were significant age × condition interactions for left superior parietal cortex [$F(2, 41) = 4.25$, $P < 0.01$] and right superior parietal cortex [$F(2, 41) = 4.62$, $P < 0.05$], and there were no differences in activation profiles for left and right superior parietal cortex [age group × region (left versus right) × condition; $F(2, 41) = 1.67$, $P = 0.20$].

Performance-Matched Analyses. We conducted two analyses to test whether the observed differences in brain activation were related to true age differences, rather than being related specifically to

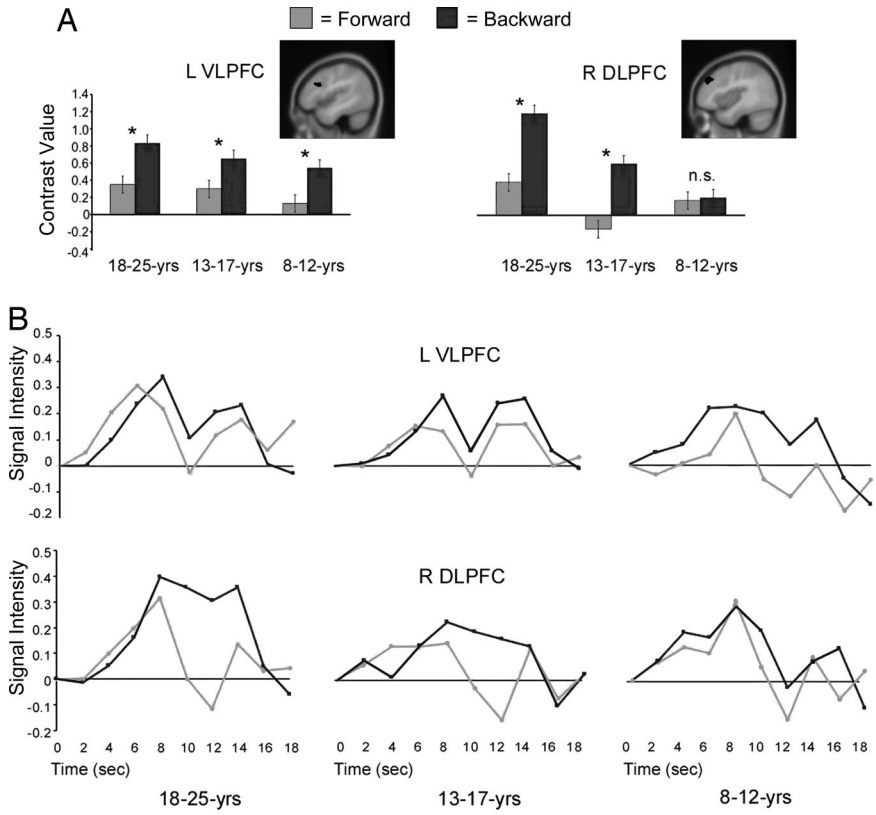

Fig. 3. Contrast values and time courses for ROIs in left VL PFC and right DL PFC for children, adolescents, and adults. (*A*) Average contrast values for delay-period activation of ROIs in left VL PFC (−45, 18, 28; BA 44) and right DL PFC (41, 39, 35; BA 9). The ROIs were functionally defined on the basis of delay-period activation across conditions and participants. Unlike adolescents and adults, children aged 8–12 failed to recruit DL PFC more strongly on manipulation trials relative to maintenance trials during the delay period. (*B*) Group-averaged time courses of VL PFC and DL PFC activation on forward and backward trials are presented for each age group. The group-averaged time courses illustrate the finding that adults and adolescents, but not children aged 8–12, showed clear sustained DL PFC activity during the delay period.

differences in performance (29, 30). First, we performed a median split analysis on the adult group and selected the 12 adults who were least accurate on the task. These worse-performing adults were still more accurate and faster than the children [F (1, 23) = 6.48, $P < 0.05$ and F (1, 23) = 18.24, $P < 0.001$], but, critically, there was no age group × condition interaction either in terms of accuracy or response times (both $F < 1$). As before, a significant age × region × condition interaction was observed for right DL PFC versus left VL PFC [F (1, 24) = 18.15, $P < 0.001$]. This interaction revealed a nonsignificant age × condition interaction for left VL PFC and a significant interaction for right DL PFC [F (1, 24) = 4.46; $P < 0.05$]. A significant age × condition interaction was also observed for bilateral superior parietal cortex [left, F (1, 24) = 7.00, $P < 0.05$; right, F (1, 24) = 5.62, $P < 0.05$], such that adults, but not children, engaged this region more strongly on manipulation trials relative to maintenance trials (Fig. 5). In summary, the age × condition interactions observed in terms of DL PFC and parietal activation remained significant in the subgroup analysis, despite the fact that the age × condition interactions for accuracy, and reaction times were not significant for this subset of the participants. Thus, these findings show that the developmental changes in neural activation associated with manipulation could not simply have resulted from the pattern of behavioral results.

Second, we equated the average number of correct forward and backward trials included in the fMRI analyses for 8- to 12-year-olds and adults. Children had fewer correct trials than adults on average (7% and 15% fewer correct forward and backward trials, respectively), and therefore it is possible that differences between children and adults could be associated with fewer data points. For this reason, we performed an additional fMRI analysis in which we selected a subset of trials for adults. For each adult, 7% of the correct trials in the forward condition and 15% of the correct trials in the backward condition, selected at random, were modeled as a covariate of no interest that also included all of the incorrect trials.

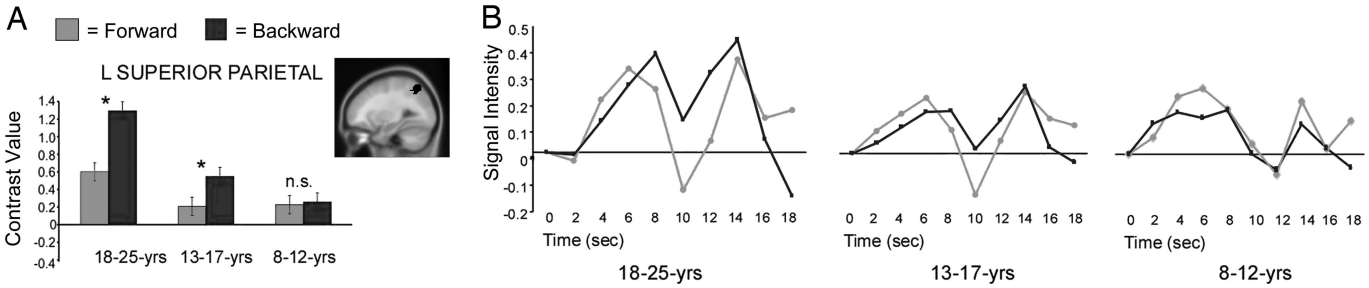

Fig. 4. Contrast values and time courses for ROI in left superior parietal cortex for children, adolescents, and adults. (*A*) A ROI for left superior parietal cortex (−28, −65, 52; BA 7) was functionally defined based on delay-period activation across conditions in all participants. The contrast values are presented for each age group separately. (*B*) Storage and manipulation time courses are presented for each age group for left superior parietal cortex. The time courses were based on a model with the onset of the cue event only. The time courses confirm that adults (18–25 years) and adolescents (13–17 years) show superior parietal cortex activity during the delay period, whereas this is not observed for the children (8–12 years).

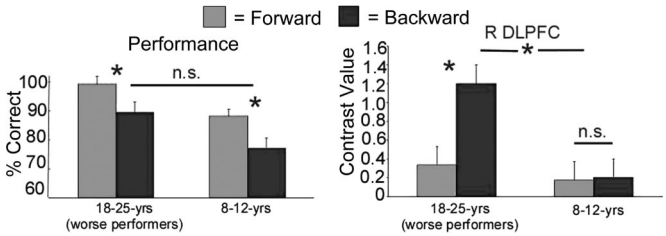

Fig. 5. Performance and DL PFC activation for all 14 8- to 12-year-old children and the 12 worst-performing adults. The ROI for DL PFC is the same as in Fig. 3.

All effects reported earlier remained significant [age group × condition interactions for right DL PFC, $F(1, 30) = 4.80$, $P < 0.05$; left superior parietal cortex, $F(1, 30) = 6.88$, $P < 0.05$; right superior parietal cortex, $F(1, 30) = 6.90$, $P < 0.05$; and a nonsignificant interaction for left VL PFC, $F(1, 30) = 0.09$, $P < 0.76$]. Taken together, these two analyses demonstrate that the group differences in right DL PFC and bilateral superior parietal cortex activation do not result from different patterns of behavioral results or from different numbers of correct trials being submitted to the fMRI analyses.

Brain-Behavior Correlations. We tested whether there were significant correlations between level of activation during the delay period in these ROIs and performance on the maintenance and manipulation tasks. As predicted, greater activation in right DL PFC and left and right superior parietal cortex was associated with higher accuracy in the manipulation condition across the whole sample ($r = 0.37$, $P < 0.05$; $r = 0.41$, $P < 0.005$; and $r = 0.42$, $P < 0.005$, respectively). In contrast, left VL PFC and left DL PFC activations were not correlated with accuracy in the manipulation condition ($r = 0.18$, $P = 0.24$ and $r = 0.19$, $P = 0.20$). When controlling for age, the brain-behavior correlations were still significant for right DL PFC ($r = 0.38$, $P < 0.05$), left superior parietal cortex ($r = 0.39$, $P < 0.01$), and right superior parietal cortex ($r = 0.40$, $P < 0.01$). Thus, in school-aged children and adolescents, as well as in adults, the ability to manipulate information is associated with the strength of recruitment of regions in DL PFC and bilateral superior parietal cortex.

With respect to maintenance, brain-behavior correlations were observed in all of the ROIs: left VL PFC ($r = 0.30$), left DL PFC ($r = 0.33$), right DL PFC ($r = 0.36$), left superior parietal cortex ($r = 0.43$), and right superior parietal cortex ($r = 0.36$); all P's < 0.05. As above, these correlations remained significant when we controlled for age.

Testing the Specificity of Group Differences Observed During the Delay Period. To test whether the age differences noted above were specific to the delay period, we extracted cue-period and probe-period activation for each of the ROIs. These analyses confirmed that the observed group differences were specific to the delay period (age × condition interactions for cue and probe period activation in right DL PFC, left VL PFC, and bilateral superior parietal cortex; all P's > 0.20. Thus, specifically during the period in which participants were required to reorganize information in working memory, children failed to engage the brain regions that have been most closely associated with manipulation in adults.

Discussion

To our knowledge, this study constitutes the first fMRI study to dissociate manipulation from maintenance across development. As expected, children aged 8–12 made more errors than adults on the trials requiring pure maintenance but had disproportionately greater difficulty with manipulation than older participants. This performance decrement was observed, despite the fact that the experimenters verified that children understood the task instructions and were able to reverse items in working memory when asked to do so aloud.

During the delay period, adults and adolescents aged 13–17 recruited DL PFC and superior parietal cortex for manipulation relative to maintenance trials. In contrast, children aged 8–12 failed to recruit these regions during the delay period, despite the fact that they did recruit them during other parts of the trial. Delay-period activation on manipulation trials was correlated with behavior: Across all participants, strong recruitment of right DL PFC and bilateral superior parietal cortex, but not VL PFC, was associated with better manipulation ability. These correlations were still significant when the effect of age was accounted for, indicating that level of engagement of these regions in and of itself impacts performance. Unlike the older age groups, 8- to 12-year-olds did not recruit additional regions for manipulation above and beyond what they would use for pure maintenance; this reliance on maintenance circuitry was associated with suboptimal manipulation ability.

Subgroup analyses indicated that the difference in delay-period activation profiles in right DL PFC and bilateral superior parietal cortex for children relative to the older participants does not merely reflect group differences in profiles of task performance (see also ref. 31). However, differences in experience could have contributed to the observed age differences, because children are likely to have much less experience than adults at mentally manipulating information. Prior studies have shown that DL PFC and parietal activation in adults can increase with practice (32). Similarly, children might begin to recruit these regions for manipulation if given extensive training.

Although the performance differences across age groups were more pronounced for manipulation than maintenance trials, it is nonetheless the case that 8- to 12-year-olds performed the pure maintenance task less well than the older participants. This performance difference was not rooted in differential recruitment of VL PFC across age groups. It is possible that children have weaker working memory representations in posterior cortical regions. Future experiments could test this hypothesis explicitly by varying pure maintenance demands, either by varying the delay period duration or the perceptual difficulty of the memory judgement.

In this study, children aged 8–12 exhibited a similar VL PFC profile to adolescents and adults, whereas prior developmental studies have observed immature VL PFC activation in this age range on tasks requiring inhibitory control (30, 33). Even within this study, age differences were observed in DL PFC during maintenance but not during the cue or probe periods. These findings suggest that age differences in brain activation can be task-specific; it is plausible that a brain region and its connections to other brain regions could be sufficiently mature to participate in one cognitive function but not in another. This study, like some other developmental neuroimaging studies, shows a pattern of enhanced recruitment of some brain regions in adults relative to children (e.g., 25, 29, 30, 34), although, in this study focusing on working memory manipulation, children did not activate any regions more strongly than adults. Also, unlike some studies, the current results are not well described by a developmental shift from diffuse to focal brain activation (e.g., ref. 35), although it is possible that this pattern would be evident with a larger number of child participants.

In summary, this study supports a process-specific explanation for the behavioral finding that the ability to manipulate items in working memory develops more slowly than the ability to simply keep items in mind. Similar patterns of maintenance-related activation were observed in the prefrontal and parietal ROIs in 8- to 12-year-olds, 13- to 17-year-olds, and adults. In contrast, at the precise time points when manipulation was required, 8- to 12-year-olds failed to recruit the regions that adolescents and adults rely on to manipulate information. These findings point to slower developmental changes in the neural substrates of manipulation rather

than maintenance. In particular, the data reveal that children aged 8–12 recruit VL PFC for working memory similarly to adolescents and adults but fail to additionally recruit right DL PFC and superior parietal cortex for manipulation during the delay. The various analyses reported here strongly suggest that children have difficulty with manipulation because they fail to recruit these regions appropriately during the delay period. Consistent with these developmental data, working memory deficits in older adults are associated with reduced recruitment of right DL PFC (36).

Although differences in brain activation between children and adults have been observed in a variety of cognitive tasks (10, 37, 38), few other developmental brain imaging studies have attempted to isolate distinct cognitive processes and their underlying neural substrates. A longitudinal study would extend the current cross-sectional findings by tracking within-subject changes in VL PFC, DL PFC, and superior parietal activation, and their association with changes in behavioral performance.

Methods

Participants. Fifty volunteers, ranging in age from 8–25, were recruited through local advertisements and from the University of California at Davis. Participants' consent was obtained according to the Declaration of Helsinki, and the study was approved by the Internal Review Board at the University of California at Davis. One adult participant was excluded because of equipment malfunction, and five children aged 8–12 were excluded because of excessive movement (>3 mm). Forty-four healthy, right-handed, native English speaking, volunteers were included in the study. Participants were subdivided in three age groups, including 14 8- to 12-year-olds (mean age, 10.5; eight males), 12 13- to 17-year-olds (mean age, 15.3; five males), and 18 18- to 25-year-olds ($n = 18$; mean age, 19.7; seven males). A χ^2 analysis confirmed that the gender distribution was equal between age groups.

Behavioral Assessment. Children and adults participated in a separate behavioral testing session before scanning. Cognitive functioning was assessed by using the Raven Standard Progressive Matrices (R-SPM) test. Estimated mean Intelligence Quotients (IQs) were 123 for the 8- to 12-year-olds, 118 for the 13- to 17-year-olds, and 122 for the 18- to 25-year-olds. IQ scores did not differ across age groups [$F\ (2, 39) = 1.90, P = 0.17$]. Children and adults practiced the behavioral tasks in a quiet laboratory. Children were also trained to lie still in a mock scanner, which simulated the environment and sounds of an actual MRI scanner. Parents filled out the behavioral questionnaires in this session. Participants were screened for psychiatric conditions by using the child behavior checklist (39) for children 8–17, or the symptom checklist–revised (SCL-R) for 18- to 25-year-olds. All participants had scores within 1 SD of the mean of a normative standardized sample.

Tasks. The experimental task involved an object-working memory task. To minimize age differences in verbalization, all images depicted objects that were nameable by the youngest children. The visual stimuli consisted of 90 simple objects selected from Microsoft ClipArt. Each image appeared twice during the task. Before practicing the computer task, the participant was asked to name all of the objects that were printed on sheets of paper. On these sheets, each object appeared twice in a prerandomized order. The participants were instructed to name each object in a way that they thought was easiest and were told that there were no right or wrong answers. The experimenter checked whether all of the names were compatible with the objects and whether the participants were consistent in their labeling of a given object over the two presentations. Indeed, all participants consistently named all of the objects correctly. On the occasion that a participant could not come up with a name quickly, the experimenter went back to that object at the end of the naming session, to confirm that this object was named quickly.

After naming the objects, participants were extensively trained on the experimental task to make sure that they understood the task instructions. On each 12-s trial, a "fixation cue" was presented for 250 ms, followed by a set of 3 "memory items" (750-ms presentation per item and 250 ms between items; total duration: 2,750 ms). Next, a 500-ms "instruction cue" ("forward" or "backward") appeared on the screen, followed by a "memory delay" of 6,000 ms during which participants either maintained (forward) or reversed (backward) the order of the three objects. Finally, a "memory probe," with one of the target images and the number 1, 2, or 3 below it, was presented on the screen for 2,500 ms. At this time, participants pressed one of three buttons with their left hand, to indicate whether the probe corresponded to the first, second, or third item in the remembered order.

During the practice session, participants were instructed to first name the objects out loud in the forward order and then to reverse the objects out loud if necessary. This way, we verified that children understood the instructions and were able to reverse the items. Participants practiced a block with ten forward items, a block with ten backward items, and a block with 30 mixed items (15 forward and 15 backward), before performing the task in the scanner. Before each experimental block in the scanner, the experimenter reminded the participants of the task requirements. The participants were instructed to do the naming quietly to reduce movement effects. Once they came out of the scanner, the experimenter asked the participants how they had performed the forward trials and how they performed the backward trials. All participants reported that they had performed the tasks in the same way as in the practice session.

During scanning, forward and backward trials were presented in a pseudorandomized order. The order of trial types within each scan was determined by using an optimal sequencing program designed to maximize the efficiency of recovery of the blood oxygenation level-dependent (BOLD) response (40). Periods of fixation lasting between 2 and 8 s, jittered in increments of 2 s, were interleaved with the experimental trials as determined by the optimization program.

Data Acquisition. Trials were presented in two scans of 8 min each, with 15 trials for each of the condition (forward and backward) in each scan, for a total of 30 forward and 30 backward trials. There were an equal number of trials of each type requiring index, middle, or ring finger responses.

Scanning was performed with a standard whole-head coil on a 1.5 Tesla General Electric scanner at the University of California at Davis Imaging Research Center. Functional data were acquired by using a gradient-echo echo-planar pulse sequence (TR = 2 s, TE = 40 ms, 24 axial slices, 3.44 × 3.44 × 5 mm, 0-mm interslice gap, 235 volumes per run). Before each scan, four volumes were discarded to allow for T1-equilibration effects. High-resolution T1-weighted anatomical images were collected. Head motion was restricted by using a pillow and foam inserts that surrounded the head. Visual stimuli were projected onto a screen that was viewed through a mirror.

fMRI Data Analysis. Data were preprocessed by using SPM2 (Wellcome Department of Cognitive Neurology, London). Images were corrected for differences in timing of slice acquisition, followed by rigid body motion correction. For all participants, head movement was 3 mm or less across the entire scan session. There were no significant differences in movement parameters between age groups [$F\ (2, 10) = 1.4, P = 0.29$]. Structural and functional volumes were spatially normalized to T1 and echo planar imaging (EPI) templates, respectively. The normalization algorithm used a 12-parameter affine transformation together with a nonlinear transformation involving cosine basis functions. During normalization, the volumes were resampled to 3-mm cubic voxels. Templates were based on the MNI305 stereotaxic space (41), an approximation of

Talairach space (42). These procedures have been validated for use in children (e.g., 43, 44). Functional volumes were spatially smoothed with an 8-mm full width at half maximum isotropic Gaussian kernel.

Statistical analyses were performed on individual participants' data by using the general linear model in SPM2. The fMRI time series data were modeled by a series of events convolved with a canonical hemodynamic response function. The three phases of each correct fMRI trial were modeled separately: The cue period (which included the presentation of the three memory items followed by the instruction) was modeled as an event; the delay period was modeled as a 6-s epoch; and the target/response period was modeled as an event (45). These events and epochs were convolved with a canonical hemodynamic response function in SPM2. Error trials were modeled separately and were excluded from the analyses. The correct trial functions were used as covariates in a general linear model, along with a basic set of cosine functions that high-pass filtered the data and a covariate for session effects. The least-squares parameter estimates of height of the best-fitting canonical hemodynamic response function (HRF) for each condition were used in pairwise contrasts. The resulting contrast images, computed on a subject-by-subject basis, were submitted to group analyses. At the group level, contrasts between conditions were computed by performing one-tailed *t* tests on these images, treating subjects as a random effect. Task-related responses were considered significant if they consisted of at least ten contiguous voxels that exceeded an uncorrected threshold of $P<0.001$. Clusters that survived correction for multiple comparisons are indicated in Table 1.

ROI analyses were performed for DL PFC, VL PFC, and superior parietal cortex with the MARSBAR toolbox for use with SPM2 (46). ROIs consisted of all active voxels for a general contrast (delay-period activation for all correct trials > fixation, across all participants) within a specific MARSBAR anatomical ROI. The ROI for right superior parietal cortex was derived from the contrast all correct delay trials > fixation based on adults only, because this region could not be derived from the contrast for all participants. For ROI analyses, effects were considered significant at an alpha of 0.05. The center of mass of each ROI is reported.

Blood oxygenation level-dependent (BOLD) activity time series, averaged across all voxels in an ROI, were extracted for each experimental session by using MARSBAR. Mean time courses for each condition were then constructed by averaging together appropriate trial time courses, which were defined as 18-s windows of activity after each trial onset. These condition-averaged time courses were then averaged across sessions and across subjects.

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