

Performance on an episodic encoding task yields further insight into functional brain development

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To further characterize changes in functional brain development that are associated with the emergence of cognitive control, participants 14 to 28 years of age were scanned while performing an episodic encoding task with a levels-of-processing manipulation. Using data from the 12 youngest and oldest participants (endpoint groups), 18 regions were identified that showed group differences in task-related activity as a function of processing depth. One region, located in left inferior frontal gyrus, showed enhanced activity in deep relative to shallow encoding that was larger in magnitude for the older group. Seventeen regions showed enhanced activity in shallow relative to deep encoding that was larger in magnitude for the youngest group. These regions were distributed across a broad network that included both cortical and subcortical areas. Regression analyses using the entire sample showed that age made a significant contribution to the difference in beta weights between deep and shallow encoding for 17 of the 18 identified regions in the direction predicted by the endpoint analysis. We conclude that the patterns of brain activation associated with deep and shallow encoding differ between adolescents and young adults in a manner that is consistent with the interactive specialization account of functional brain development.

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Relatively little is known about the neural basis of cognition in typically developing children and adolescents. One of the most prominent views of functional brain development posits that cognitive abilities are enabled by the maturation of specific brain regions (Johnson, 2001, 2003). This maturational perspective is largely based on neuroanatomical evidence which suggests that maturation progresses sequentially in an inferior–superior and posterior–anterior direction. For example, gray matter density loss has been observed in frontal and parietal cortex between childhood and adolescence (Sowell et al., 1999a,b, 2003). During this age

range, gray matter density loss is greater in parietal regions compared with frontal regions. Interestingly, comparisons of adolescents and young adults have shown that this pattern reverses with age: gray matter density loss becomes localized to frontal cortex, with few reductions occurring in parietal cortex or other posterior brain regions (Sowell et al., 1999a,b, 2001). Such regional differences in brain development have been observed across a variety of other measures, including synaptic pruning (Huttenlocher and Dabholkar, 1997) and myelination (Yakovlev and Lecours, 1967).

The maturational perspective uses neuroanatomical evidence to predict when a given brain region will become functional. Given the direction in which brain development occurs, the maturational perspective predicts that posterior–inferior brain regions will become functional first and that anterior–superior brain regions will become functional thereafter. Some neuroimaging evidence is consistent with this prediction. For example, several studies have compared patterns of brain activation in children and young adults using tasks of cognitive control (e.g., tasks of inhibition and working memory). In some instances, children have failed to activate the same frontal brain regions as young adults while performing the tasks (Bunge et al., 2002). In other instances, children and young adults have activated similar frontal brain regions, but the magnitude of activation has been significantly greater (Booth et al., 2003; Casey et al., 1997; Durston et al., 2002; Tamm et al., 2002; Thomas et al., 1999) or lesser (Kwon et al., 2002; Tamm et al., 2002) in children. One interpretation of these findings is that the frontal circuitry of children is less mature than that of young adults and that it is the maturation of this circuitry which underlies the development of cognitive control.

Another perspective on functional brain development is that of interactive specialization (Johnson, 2000; Johnson et al., 2002). This perspective argues against the idea that cognitive abilities can be localized to specific areas of the brain. Rather, it posits that cognitive abilities emerge due to changes in activity across multiple brain regions. Initially, it is assumed that brain regions are partially activated and respond to a wide variety of stimuli. With experience, it is believed that some of the pathways connecting these brain regions are strengthened whereas other pathways are not. Consequently, brain regions that initially responded to a wide variety of stimuli become specialized for the processing of specific classes of

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stimuli. As a result of this specialization process, there is a change in the extent of brain activity that is associated with the presentation of a stimulus: a stimulus will engage multiple brain regions early in development; later in development, the same stimulus will engage progressively fewer brain regions.

Interactive specialization predicts that emerging cognitive abilities will be associated with activity across a widely distributed network and that this pattern of activity will progressively narrow with age. Furthermore, this perspective predicts that even when children activate the same brain regions as young adults they may do so to either a greater *or* lesser extent than their older counterparts. Recent work on the functional anatomy of language processing has provided evidence consistent with this view. A study by [Brown et al. \(2005\)](#) compared patterns of brain activation in participants 7–32 years of age while they performed three controlled lexical association tasks. Two patterns of activation were observed, differing in neuroanatomical location and the age at which the region became functionally “adult-like” (defined as 75% of the adult level of activation). Regions showing age-related increases in activation were localized to frontal and parietal cortex and were adult-like by 14.8 years of age. Regions showing age-related decreases in activation were distributed across a wider neuroanatomical network and included earlier processing areas such as occipital and temporal cortex. In addition, these regions had a more protracted course of development and were not adult-like until 16.5 years of age. These results are consistent with the interactive specialization framework, which predicts that age will be associated with changes in anterior–superior and posterior–inferior brain regions and that anterior–superior brain regions can be involved in tasks at an age earlier than expected.

The present study was undertaken in an effort to further characterize functional brain development associated with the emergence of cognitive control strategies. Specifically, we were interested in comparing patterns of brain activation in adolescents and young adults on an episodic encoding task that included a levels-of-processing manipulation. ‘Levels-of-processing’ refers to the fact that information is better remembered when it has been processed at a deep, semantic level compared to a shallow, non-semantic level ([Craik and Lockhart, 1972](#)). The rationale for using this task was fourfold. First, the use of semantically based strategies during episodic encoding is thought to be a critical aspect of effective learning that develops with age, as described further below. Second, previous studies have compared patterns of brain activation across development using tasks of inhibition and working memory. To our knowledge, only one study has used an episodic encoding task for this purpose ([Chiu et al., 2006](#)). In this study, the authors examined whether activation in the medial temporal lobes and left PFC during the performance of verb generation and story comprehension tasks predicted subsequent memory in younger and older children. Although there were no direct statistical comparisons between the younger and older children, the authors found some similarities and some differences in the regions that predicted subsequent memory in the younger and older age groups. We believed that an episodic encoding task with a levels-of-processing manipulation and direct statistical comparisons between age groups would provide additional information about the generalizability of results obtained from previous studies of episodic memory and other cognitive domains. Third, numerous lines of research suggest that episodic encoding is supported by both prefrontal and posterior brain regions (e.g., [Casasanto et al., 2002](#); [Fernandez et al., 1998](#); [Fletcher et al., 2003](#); [Fujii et al., 2002](#); [Heun et al., 1999](#); [Kirchhoff et al., 2000](#);

[McDermott et al., 1999](#)). Because of this, we believed that a levels-of-processing task would be well suited for studying functional brain development across a broad neuroanatomical network. Fourth, this episodic encoding task has been used extensively in neuroimaging studies of healthy young adults. As such, the patterns of brain activation associated with each kind of processing in healthy young adults are well understood: deep encoding has been associated with activity in left prefrontal cortex and left medial temporal lobe (e.g., [Buckner et al., 2000](#)); conversely, shallow encoding has been associated with activity in right prefrontal cortex as well as right caudate and putamen (e.g., [Fletcher et al., 2003](#)).

A number of studies have examined developmental trends in the spontaneous and prompted use of semantic elaboration strategies during episodic encoding tasks. Studies have shown that the spontaneous use of semantic elaboration strategies occurs relatively late in development. Children younger than 8 years of age do not organize their free recall semantically; however, this strategy begins to emerge between 9 and 12 years of age and becomes more widely used throughout adolescence ([Moely et al., 1969](#); [Neimark et al., 1971](#)). Interestingly, studies have also shown that children may avail themselves of semantic elaboration strategies when they are provided with a prompt. For example, [Owings and Baumeister \(1979\)](#) compared the performance of 2nd, 4th, and 6th grade students on an intentional encoding task in which words were processed at four different levels: a semantic level, in which children were asked to describe the meanings of the words; a phonemic level, in which children were asked to generate rhymes for the words; a surface level, in which children were asked to count the number of letters in the words; and a level in which children were simply instructed to remember the words to the best of their ability. [Owings and Baumeister](#) found a significant effect of encoding activity on subsequent memory performance. Overall, children had a superior remembrance of words that had been processed at the deep, semantic level, compared with the shallow, non-semantic levels. Other studies have found similar results using incidental paradigms (e.g., [Geis and Hall, 1976, 1978](#); [Ghatala et al., 1980](#)) in which children did not know they would receive a subsequent memory test. Although the spontaneous use of semantic elaboration emerges later in development, these results suggest that a levels-of-processing effect may be observed earlier in development when children are provided with a cue to use this strategy.

At present, it is unknown whether the patterns of brain activity associated with deep and shallow encoding in adolescents are the same as those observed in young adults. Our predictions in this regard were shaped by the differing perspectives of functional brain development described above. If the maturational perspective is correct, then adolescents and young adults should show similar patterns of activity in posterior–inferior brain regions but different patterns of activity in anterior–superior brain regions. Because deep encoding tasks are known to engage anterior–superior brain regions to a greater extent than shallow encoding tasks, deep encoding should elicit more age-related differences in functional brain activity. In contrast, if interactive specialization is correct, then adolescents should show a more diffuse pattern of activity than young adults on tasks in which they are less experienced. Consequently, one would expect age-related differences to be observed during either deep or shallow encoding, because adolescents may be less experienced than young adults with both semantic elaboration (deep) and judgments of alphabetical order (shallow).

Method

Participants

Seventy-two participants were recruited from the St. Louis community as a healthy control comparison group for a study of schizophrenia. Exclusion criteria included any of the following: (a) meeting *DSM-IV* criteria for an Axis I disorder (past or present) or any first-degree relative with a psychotic disorder; (b) meeting *DSM-IV* criteria for substance abuse (severe) or dependence (any type) at any time within the past 3 months; (c) the presence of any clinically unstable or severe medical disorder, or a medical disorder that would confound the assessment of psychiatric diagnosis or render research participation dangerous; (d) head injury (past or present) with documented neurological sequelae or resulting in loss of consciousness; and (e) meeting *DSM-IV* criteria for mental retardation (mild or greater in severity). The participants ranged in age from 14 to 28 years and included 44 females and 28 males. This age range permitted us to explore refinements in functional brain development that occur later than is typically studied. The upper age limit of 28 years was selected because brain maturation is completed by this time (e.g., Sowell et al., 2004). Handedness was ascertained using the Edinburgh Handedness Inventory (Oldfield, 1971). Using this measure, sixty-five participants were determined to be right-handed, 5 participants were determined to be left-handed, and 2 participants were determined to be ambidextrous. As described in detail below, we first identified brain regions showing functional differences across our age range using two endpoint groups. These groups consisted of the 12 youngest (range = 14 to 18 years, mean age = 15.6 years, F:M = 8:4) and 12 oldest (range = 25 to 28 years, mean age = 26.5, F:M = 7:5) participants. Handedness ($\chi^2(2, N=24)=2.00, p=0.37$) and gender ($\chi^2(1, N=24)=0.18, p=0.67$) did not vary across the endpoint groups. Brain regions identified in the endpoint groups were further interrogated in subsequent analyses using the entire sample.

Procedure

Participants were run in a battery of tasks at the Conte Center for the Neuroscience of Mental Disorders at Washington University. In the present study, we analyzed data from an incidental encoding task that represented a levels-of-processing manipulation. In our task, words were presented one at a time. In one run, deep encoding was promoted by asking participants to decide whether each word represented an abstract or a concrete entity. In a different run, shallow encoding was promoted by asking participants to decide whether the first or last letter of each word came first in the alphabet. Responses were made using a fiber-optic key press interfaced with the PsyScope Button Box. Participants were administered a recognition task approximately 10 min following the encoding tasks. During the recognition task, words were presented one at a time and participants were required to decide whether the word was old (i.e., presented during the encoding tasks) or new (i.e., not presented during the encoding tasks).

For the encoding tasks, stimuli consisted of two lists of 64 words. Each list contained 32 abstract words and 32 concrete words, with 16 in which the first letter came first in the alphabet and 16 in which the last letter came first in the alphabet. Administration of the encoding tasks was counterbalanced across participants, such that half performed the deep encoding task first and half performed the shallow

encoding task first. The lists used for the deep and shallow encoding tasks were also counterbalanced across participants. Analyses indicated that there was no effect of task order on the patterns of brain activation associated with deep versus shallow processing. For the recognition task, stimuli consisted of 64 words. Of these words, half were old and half were new. Of the old words, an equal number had been presented during the deep and shallow encoding tasks. For all words, average word length was 4.9 (range 3 to 7), the average Kucera–Francis written frequency was 146.3 (range 23 to 967), the average concreteness rating was 485.8 (range 296 to 637), the average imageability rating was 512.6 (range 285 to 635), and the average age of acquisition was 333.0 (range 144 to 600). There were no significant differences across word lists for any of these variables ($p>0.18$ for all analyses).

Participants performed the encoding tasks during two scanning runs lasting 4.25 min each. Each run included 4 task blocks of 16 trials each and 3 fixation blocks of 10 trials. During fixation trials, participants were instructed to look at a crosshair presented at the center of the screen. Task blocks and fixation blocks were interleaved in an alternating order (there were also four fixation trials at the beginning and end of each run). Task blocks lasted 40 s and fixation blocks lasted 25 s. During task blocks, each word was presented for 2 s followed by a 500-ms interstimulus interval (ISI). During fixation blocks, a cross hair appeared continuously and participants were instructed to fixate. Visual stimuli were generated by an Apple PowerMac computer and PsyScope software (Cohen et al., 1993) and were projected with a Sharp LCD projector onto a screen positioned at the head end of the bore. Participants viewed the screen through a mirror attached to the top of the MR head coil.

Imaging data acquisition and preprocessing

Structural and functional images were obtained from a 1.5 T Siemens VISION system at the Research Imaging Center of the Mallinckrodt Institute of Radiology at Washington University Medical School. Three-dimensional structural images were obtained using a coronal magnetization-prepared rapid gradient echo (MP-RAGE) T1-weighted sequence (TR = 9.7 ms, TE = 4 ms, flip = 10°; voxel size = 1 × 1 × 1.2 mm). Structural images were used for between subject registration and anatomic localization. Functional images were obtained using an asymmetric spin-echo echo-planar sequence sensitive to blood oxygenation level-dependent (BOLD) contrast (T2*) (TR = 2500 ms, TE = 50 ms, FOV = 24 cm, flip = 90°). During each functional run, 102 sets of axial images were obtained parallel to the anterior–posterior commissure plane (3.75 × 3.75 mm in plane resolution). Nineteen slices 7 mm thick were acquired in each functional image.

Preliminary processing was conducted to remove noise and artifacts, as described in an earlier manuscript by Bonner-Jackson et al. (2005). Preprocessing included: (1) compensation for slice-dependent time shifts; (2) elimination of odd/even slice intensity differences; (3) movement correction; (4) intensity normalization; and (5) spatial smoothing with an 8-mm full width half maximum (FWHM) Gaussian filter. Previous validation studies have shown that children as young as 7 years of age and young adults may be compared in a common stereotaxic space (Burgund et al., 2001; Kang et al., 2001). As such, functional data from all participants were transformed into standard stereotaxic space (Talairach and Tournoux, 1988) and were resampled to 3-mm cubic voxels using in-house software. Given the strong correlation between incremental movement and signal to noise ratios (Barch et al., 2001), our criteria

for excessive movement included no more than a mean of 0.075 mm (for the *X*, *Y* and *Z* dimensions) or 0.075 degrees (for the pitch, roll and yaw dimensions). Using these criteria, no participants were excluded from the current study for excessive movement.

Imaging data analysis

For each participant, the magnitude of task-related activation in each voxel was estimated using a general linear model (GLM) created using in-house software. More specifically, BOLD responses to the incidental encoding tasks and their control conditions were modeled as “boxcar” functions. These square wave functions were then convolved with a canonical hemodynamic response function to generate regressors for task and fixation for both deep and shallow encoding. The estimates were then analyzed using appropriately designed analysis of variance (ANOVA), with participants treated as a random factor. A multi-step approach was used to identify brain regions showing developmental changes in activation during deep and shallow encoding. This approach involved the application of multiple statistical tests, with each test set at a relatively low statistical threshold. We have used this approach in a number of previous studies (e.g., Barch et al., 2001; Braver et al., 2003) and believe that it optimizes the trade-off between false positive protection (type 1 error) and sensitivity/power (type 2 error). A brain region was considered to be “significant” in an analysis when every voxel within that region was statistically significant (defined as $p < 0.02$) in each test required for a given effect (described in detail below). Voxels meeting these criteria had an α level of at least 0.0004 for the inference that they demonstrated all of the required patterns. It should be noted that this α level of 0.0004 is likely an overestimate of the true α level because of non-independence in the error terms of the statistical contrasts. This multi-step approach does not change the significance level for any individual test (Nichols et al., 2005); however, it enhances the significance of the likelihood of all tests being significant simultaneously. In addition, a brain region was only considered to be “significant” in an analysis if it contained a cluster of 9 or more contiguous voxels. This cluster size requirement provides further protection against type 1 error rates (Forman et al., 1995; McAvoy et al., 2001) and was chosen based on Monte Carlo simulations.

In analyzing the fMRI data, we attempted to address two questions. First, we were interested in identifying brain regions that showed levels of processing effects across the youngest and oldest endpoint groups. To identify these brain regions, we required voxels to show a conjunction of the following two effects: (1) significant task-related activation in either deep or shallow encoding, using paired *t*-tests with all subjects and (2) significant differences in task-related activation for deep versus shallow encoding, using repeated measures ANOVAs with condition (task versus fixation) and task (deep versus shallow) as within subject factors. To confirm that any identified regions showed significant effects of processing depth in both the younger and older endpoint groups, we repeated the conjunction analysis separately for each endpoint group in ROI-based post hoc analyses.

Second, we were interested in identifying brain regions that showed significant differences in activation as a function of processing depth and age group. To ensure that any identified regions were ones that showed task responsivity in at least one endpoint group, we required voxels to show a conjunction of the following: (1) greater activity in task compared to fixation during deep or shallow encoding for either endpoint group, using paired *t*-tests

(e.g., showed activity in at least one of the encoding tasks in at least one of the groups); (2) greater task-related activity for either deep compared to shallow encoding or for shallow compared to deep encoding in either endpoint group, using repeated measures ANOVAs with condition (task versus fixation) and task (deep versus shallow) as within subject factors (e.g., showed a difference in levels-of-processing activity in at least one of the groups); and (3) significant group differences in task-related activity for processing depth, using repeated measures ANOVAs with condition (task versus fixation) and task (deep versus shallow) as within subjects factors (e.g., showed an age-related difference in the levels-of-processing effect). Regions that showed significant differences in activation as a function of processing depth and age group were further interrogated using regression-based analyses that included the entire sample. For each region of interest, linear regression was used to determine the contribution of age to the difference in beta weights between deep and shallow encoding. In doing so, we hoped to characterize how task-related activity as a function of processing depth changed across our age range.

Behavioral data analysis

In the first step of our behavioral analysis, data from the endpoint groups were analyzed. Accuracy was computed for deep and shallow encoding and subsequent recognition. Using trials on which correct responses were made, mean reaction time (RT) also was computed for deep and shallow encoding and subsequent recognition. Accuracy and mean RT were then entered into separate ANOVAs, using processing depth as a within-participants factor. In the second step of our behavioral analysis, regressions were used to evaluate the contribution of age to each of our dependent measures using data from the entire sample.

Lastly, we were interested in determining whether age was related to differences in performance across a wider variety of tasks. For 64 of our 72 participants, regressions were used to evaluate the contribution of age to each of the following raw score measures: Vocabulary and Matrix Reasoning subtests of the Wechsler Adult Intelligence Scale (WAIS-III; Wechsler, 1997a); free recall on trials 1 through 5 of the California Verbal Learning Test (CVLT-II; Delis et al., 2000); and the Logical Memory and Family Pictures subtests of the Wechsler Memory Scale (WMS-III; Wechsler, 1997b). In doing so, we hoped to better characterize the performance of participants across our age range.

Results

Behavioral results

Means and standard deviations are shown in Table 1. We used Levene’s tests for Homogeneity of Variance to compare variance across the endpoint groups for all measures. None of these tests were significant (all $ps > 0.20$). For encoding, repeated measures ANOVA using accuracy as a dependent measure showed a significant main effect of processing depth, $F(1,22)=45.77$, $MSe=0.005$, $p < 0.001$, $\eta^2=0.68$, with participants being more accurate in the shallow relative to deep encoding task. There was no significant processing depth \times endpoint group interaction ($p=0.40$, $\eta^2=0.03$). *T*-tests showed that the accuracy of the endpoint groups was comparable in the shallow encoding task ($t(22)=1.43$, $d=-0.58$, $p=0.17$) but that there was a trend for the youngest participants to be less accurate than the oldest participants in the deep encoding task ($t(22)=-1.77$,

Table 1
Means and standard deviations for endpoint groups as a function of experimental condition

	Endpoint group	
	Youngest	Oldest
<i>Encoding</i>		
Deep accuracy	0.77 (0.10)	0.83 (0.06)
Deep RT	1087.11 (147.75)	1029.22 (185.82)
Shallow accuracy	0.92 (0.05)	0.94 (0.04)
Shallow RT	1133.40 (162.63)	1099.79 (133.08)
<i>Recognition</i>		
Deep accuracy	0.91 (0.10)	0.90 (0.09)
Deep RT	1102.33 (170.43)	975.24 (177.11)
Shallow accuracy	0.54 (0.25)	0.65 (0.18)
Shallow RT	1258.39 (240.63)	1076.10 (228.99)

$d=-0.73$, $p=0.09$). Repeated measures ANOVA using RT as a dependent measure also showed a significant main effect of processing depth, $F(1,22)=5.96$, $MSe=6870.91$, $p=0.023$, $\eta^2=0.21$ with participants being faster in the deep relative to shallow encoding task. Again, there was no significant processing depth \times endpoint group interaction ($p=0.62$, $\eta^2=0.01$). *T*-tests showed that the youngest participants responded as quickly as the oldest participants in both the shallow ($t(22)=0.55$, $d=0.23$, $p=0.59$) and deep ($t(22)=0.85$, $d=0.34$, $p=0.41$) encoding tasks.

For recognition, repeated measures ANOVA using accuracy as a dependent measure showed a significant main effect of processing depth, $F(1,22)=45.77$, $MSe=0.005$, $p<0.001$, $\eta^2=0.73$. There was no significant processing depth \times endpoint group interaction ($p=0.13$, $\eta^2=0.10$). *T*-tests showed that the accuracy of the endpoint groups was comparable in both the shallow ($t(22)=-1.29$, $d=-.53$, $p=0.21$) and deep ($t(22)=0.37$, $d=0.15$, $p=0.72$) recognition tasks. Similarly, repeated measures ANOVA using RT as a dependent measure showed a significant main effect of processing depth, $F(1,22)=24.05$, $MSe=8234.88$, $p<0.001$, $\eta^2=0.52$. Participants identified words more accurately and more quickly when they had been processed at a deep rather than shallow level. Again, there was no significant processing depth \times endpoint group interaction ($p=0.30$, $\eta^2=0.05$). *T*-tests showed that there was a trend for the youngest participants to respond more slowly than the oldest participants in both the shallow ($t(22)=1.90$, $d=0.78$, $p=0.07$) and deep ($t(22)=1.79$, $d=0.73$, $p=0.09$) recognition tasks.

Regression analyses using the entire sample of participants failed to show a significant contribution of age to RT and accuracy in the shallow encoding task (RT: $R^2=0.00$, $p=0.93$; accuracy: $R^2=0.03$, $p=0.19$) or to RT in the deep encoding task ($R^2=0.01$, $p=0.44$), although there was a trend for age to show a contribution to deep encoding accuracy ($R^2=0.05$, $p=0.07$). Similarly, the contribution of age to recognition performance was not significant for words that had been encoded at the deep, semantic level (RT: $R^2=0.01$, $p=0.40$; accuracy: $R^2=0.01$, $p=0.32$) or the shallow, superficial level (RT: $R^2=0.01$, $p=0.37$; accuracy: $R^2=0.01$, $p=0.56$). Taken together, these results indicate that the performance of our youngest participants was comparable to the performance of our oldest participants for all indices other than deep encoding accuracy, which still only showed trend level differences. As such, obtained differences in the imaging data can be reasonably attributed to age group differences rather than differences in performance.

Regression analyses using other performance measures showed that age failed to make a significant contribution to immediate recall on Family Pictures ($R^2=0.01$, $p=0.51$) and delayed recall on Family Pictures ($R^2=0.02$, $p=0.30$). However, age did account for 8.9% of the variance in Vocabulary ($p=0.02$), 8.6% of the variance in free recall on trials 1–5 of the CVLT-II ($p=0.02$), 18.1% of the variance in immediate recall on Logical Memory ($p<0.001$), and 10.2% of the variance in delayed recall on Logical Memory ($p=0.01$). In addition, there was a trend for age to make a significant contribution to Matrix Reasoning ($R^2=0.05$, $p=0.08$). For each of these measures, performance improved as a function of age.

Imaging results

Collapsing across the endpoint groups, we identified 38 brain regions which showed significant levels-of-processing effects. These regions were classified according to their neuroanatomical locations and approximate Brodmann areas. Four of the regions showed greater activation in the deep relative to shallow encoding task (Table 2, Fig. 1). These regions were localized to left inferior frontal cortex (BA 47), left occipital cortex (BA 18), left cerebellum, and right brainstem. The other thirty-four regions showed greater activation in the shallow relative to deep encoding task (Table 3, Fig. 1). These regions were distributed across a wide neuroanatomical network, including bilateral inferior frontal gyrus (BA 44), bilateral precentral gyrus (BA 6), right postcentral gyrus (BA 2), right anterior cingulate (BA 24), bilateral posterior cingulate (BA 31), bilateral precuneus (BA 7), right middle temporal gyrus (BA 39), left temporal gyrus (BA 41), left parahippocampal gyrus (BA 36), right occipitotemporal gyrus (BA 37), bilateral middle occipital gyrus (BA 19), bilateral occipital gyrus (BA 18), bilateral cerebellum, bilateral thalamus, and left brainstem. Post hoc analyses with each endpoint group confirmed that these regions showed significant levels-of-processing effects for the youngest and oldest participants.

Using the two endpoint groups, we next identified 18 brain regions which showed significant group differences in the levels-of-processing effects. One region showed a greater difference between deep and shallow encoding activation in the oldest endpoint group compared with the youngest endpoint group. This region was located in left inferior frontal gyrus (BA 6/44; $X=-49$, $Y=2$, $Z=6$). In this region, older individuals showed enhanced activation in the deep (magnitude=0.31) compared to shallow encoding task (magnitude=-0.06), with younger individuals showing greater activation in the shallow (magnitude=0.25) compared to deep (magnitude=0.15) encoding task. In the other 17 regions, differences between deep and shallow encoding activation were greater in the youngest endpoint group compared with the oldest endpoint group (Table 4, Fig. 2). These regions were distributed across a broad neuroanatomical network, including left frontal polar cortex (BA 10), right middle frontal gyrus (BA 9), right inferior frontal gyrus (BA 44), bilateral precentral gyrus (BA 4, BA 6), right

Table 2
Regions showing greater activation in deep relative to shallow encoding for both endpoint groups

Region of interest	x	y	z	Volume	Brodmann area
Left inferior frontal gyrus	-45	31	-1	621	47
Left occipital cortex	-23	-101	7	351	18
Left cerebellum	-41	-57	-42	243	-
Right brainstem	17	-32	-38	432	-

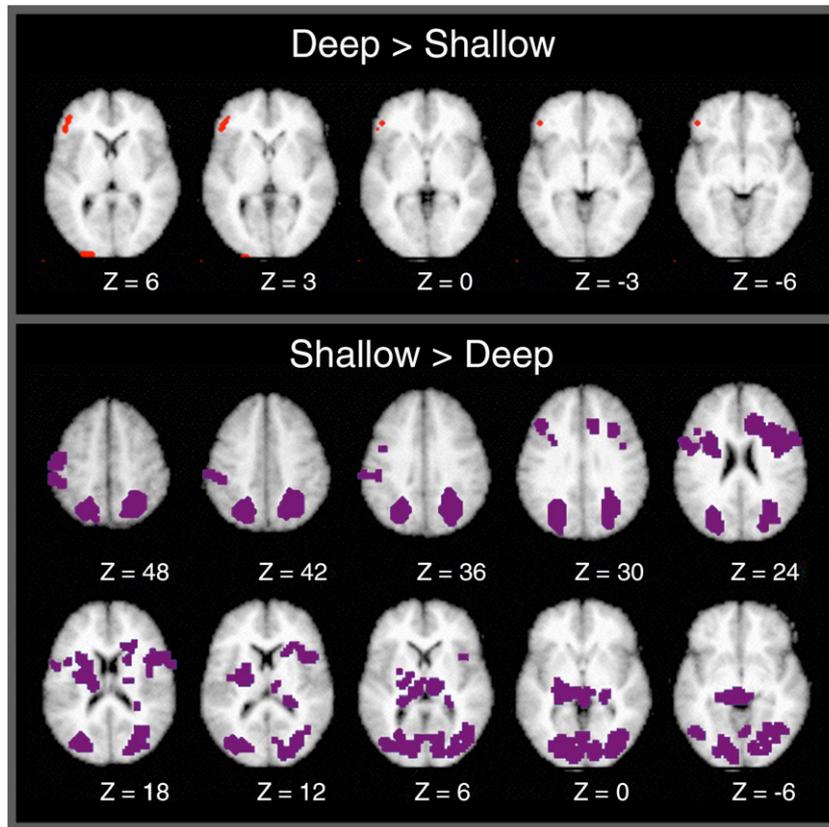


Fig. 1. Regions showing levels-of-processing effects for both endpoint groups. Top panel: regions in which activation was greater for deep compared with shallow encoding. Bottom panel: regions in which activation was greater for shallow compared with deep encoding.

anterior cingulate (BA 24), left posterior cingulate (BA 23), bilateral precuneus (BA 7), bilateral inferior parietal lobule (BA 40), right middle temporal gyrus (BA 21/22), bilateral middle occipital gyrus (BA 19), bilateral cerebellum, and right thalamus. In all of these regions, younger individuals showed greater task-related activity in the shallow as compared with the deep encoding task, whereas older individuals demonstrated either no significant differences between the tasks or equivalent effects in the opposite direction.

A concern could be raised that endpoint group differences in levels-of-processing effects were confounded by the somewhat worse performance of the youngest group in encoding performance. Even though endpoint group differences in encoding performance were not statistically significant, there was a trend for the youngest group to be less accurate than the oldest group in the deep encoding task. To address this concern, encoding performance was used as a covariate in regression analyses where brain activation was entered as the dependent variable, encoding performance was entered as an independent variable in the first step, and endpoint group was entered as an independent variable in the second step. Specifically, deep encoding RT and accuracy were used as covariates in a regression involving the 1 brain region in which the oldest endpoint group showed greater deep–shallow activation than the youngest endpoint group. Similarly, shallow encoding RT and accuracy were used as covariates in regressions involving the 17 brain regions in which the youngest endpoint group showed greater shallow–deep activation than the oldest endpoint group. The endpoint group differences in levels-of-processing effects remained significant even after controlling for possible group differences in encoding performance ($p < 0.01$ for all analyses).

An additional concern could be that endpoint group differences in levels-of-processing effects were confounded by the somewhat worse recognition performance of the youngest group. Although endpoint group differences in recognition performance were not statistically significant, there was a trend for the youngest group to be slower than the oldest group in recognizing words that had been encoded at both the deep and shallow levels. To address this concern, recognition performance was used as a covariate in regression analyses where brain activation was entered as the dependent variable, recognition accuracy and RT were entered as independent variables in the first step, and endpoint group was entered as an independent variable in the second step. Specifically, deep recognition RT and accuracy were used as covariates in a regression involving the 1 brain region in which the oldest endpoint group showed greater deep–shallow activation than the youngest endpoint group. Similarly, shallow recognition RT and accuracy were used as covariates for the 17 brain regions in which the youngest endpoint group showed greater shallow–deep activation than the oldest endpoint group. The endpoint group differences in levels-of-processing effects remained significant even after controlling for possible group differences in recognition performance ($p < 0.01$ for all analyses).

These 18 brain regions were further interrogated with regression analyses that included all participants across the entire age range. These regression analyses were used to evaluate the contribution of age to the difference in beta weights between the deep and shallow encoding tasks. For 17 of the 18 regions, age made a significant linear contribution to the difference in beta weights between deep and shallow encoding. Non-linear effects were not significant. Fig. 3 plots the relationship between age and: (1) deep encoding

Table 3
Regions showing greater activation in shallow relative to deep encoding for both endpoint groups

Region of interest	x	y	z	Volume	Brodman area
Left inferior frontal gyrus	-51	16	14	486	44
Left inferior frontal gyrus	-43	3	28	2565	44
Right precentral gyrus	47	0	16	4536	6
Right precentral gyrus	9	-1	70	702	6
Left precentral gyrus	-35	-20	65	999	6
Left postcentral gyrus	-55	-26	47	3591	2
Right anterior cingulate	22	14	23	5292	24
Right posterior cingulate	23	-59	23	3132	31
Right posterior cingulate	10	-66	9	1809	31
Left posterior cingulate	-12	-68	19	513	31
Right precuneus	19	-52	63	378	7
Right precuneus	24	-61	45	7992	7
Left precuneus	-21	-67	42	6453	7
Right middle temporal gyrus	40	-71	15	3699	39
Right temporal gyrus	27	-32	12	1377	41
Left parahippocampal gyrus	-22	-15	-22	351	36
Right occipitotemporal gyrus	60	-63	-12	537	37
Right middle occipital gyrus	19	-80	36	1863	19
Left middle occipital gyrus	-34	-73	19	6345	19
Left middle occipital gyrus	-17	-57	-9	1755	19
Left occipital gyrus	-16	-84	-4	8829	18
Right occipital gyrus	25	-85	3	6831	18
Cerebellum	0	-77	-21	7371	-
Right cerebellum	8	-24	-20	2079	-
Right cerebellum	19	-49	-17	4887	-
Right cerebellum	45	-56	-36	729	-
Right cerebellum	30	-65	-10	5886	-
Right cerebellum	2	-66	-46	513	-
Right cerebellum	26	-82	-22	1647	-
Left cerebellum	-38	-67	-19	5400	-
Left thalamus	-21	-7	18	4239	-
Left thalamus	-23	-31	6	2754	-
Right brainstem	2	-29	3	4914	-
Left brainstem	-18	-39	-31	729	-

magnitudes; (2) shallow encoding magnitudes; and (3) deep-shallow encoding magnitudes for each of the 17 regions. The nature of age-related differences in brain activation is readily apparent when one notes the location of the data points relative to zero. Points falling above zero indicate greater activation in the deep relative to shallow encoding task, whereas points falling below zero indicate greater activation in the shallow relative to deep encoding task. For the 1 brain region which had shown greater activation in the oldest endpoint group (Fig. 3, purple), more points fall above zero at older ages. This pattern suggests that age was positively associated with an increase in activation in the deep encoding task compared with the shallow encoding task. Conversely, for the 17 brain regions which had shown greater activation in the youngest endpoint group (Fig. 3, red), more points fall below zero at younger ages. This pattern of results suggests that age was negatively associated with an increase in activation in the shallow encoding task compared with the deep encoding task.

Of note, there was one brain region (BA 10) in which age did not make a significant linear contribution to the difference in beta weights between deep and shallow encoding. For this region, we used regression analysis with curve fitting to characterize the trend in brain activation across development. Results indicated that brain activation in this region was best characterized by a three parameter, single exponent rise-to-max function [$y=y_0+a(1-e^{-bx})$].

Discussion

The purpose of this study was to further characterize functional brain development associated with the emergence of cognitive control strategies. Specifically, we were interested in comparing patterns of brain activation in adolescents and young adults on an episodic encoding task that included a levels-of-processing manipulation. In regards to task performance, we found the expected levels-of-processing effect. That is, words were recognized more quickly and accurately when they had been processed at a deep, semantic level (i.e., living/non-living judgments) compared with a shallow, superficial level (i.e., first/last letter judgments). Interestingly, there were no significant age-related differences in either

Table 4
Regions showing greater differences between deep and shallow encoding activation in the youngest endpoint group

Region of interest	x	y	z	BA	Vol	Magnitude deep youngest	Magnitude shallow youngest	Effect size youngest	Magnitude deep oldest	Magnitude shallow oldest	Effect size oldest
Left frontal polar region	-29	45	25	10	432	-0.247	0.077	-1.157	0.092	0.037	0.199
Right middle frontal gyrus	28	37	32	9	945	-0.236	0.182	-1.203	0.088	-0.03	0.737
Right inferior frontal gyrus	42	14	10	44	1890	-0.108	0.184	-1.393	0.038	-0.006	0.248
Right precentral gyrus	12	1	52	6	4347	-0.079	0.194	-1.22	0.077	-0.041	0.518
Right precentral gyrus	35	-12	41	6	3645	-0.046	0.246	-1.192	0.115	0.01	0.58
Left precentral gyrus	-49	2	6	6	2349	-0.162	0.254	-1.224	0.076	-0.106	0.594
Left precentral gyrus	-21	-7	52	4	4131	-0.019	0.254	-1.101	0.112	0.047	0.367
Right anterior cingulate	0	8	30	24	702	-0.1	0.135	-0.948	0.05	-0.028	0.523
Left precuneus	-20	-43	52	7	6939	-0.186	0.056	-1.235	-0.072	-0.121	0.403
Right inferior parietal lobule	45	-46	37	40	9234	-0.159	0.21	-1.477	0.069	0.026	0.277
Left inferior parietal lobule	-49	-47	33	40	5373	-0.05	0.259	-1.393	0.066	0.004	0.401
Left middle temporal gyrus	-56	-41	-26	21/22	270	0.263	0.319	-0.53	-0.086	-1.563	0.919
Left middle occipital gyrus	-20	-70	33	19	2025	-0.127	0.268	-1.417	-0.012	0.023	-0.296
Right cerebellum	4	-64	-7	-	54	-0.198	0.105	-1.175	-0.106	-0.191	0.242
Left cerebellum	-20	-59	-42	-	486	-0.121	0.178	-1.299	0.022	-0.02	0.24
Left cerebellum	-12	-86	-15	-	297	0.416	0.876	-0.557	0.538	0.505	0.057
Right thalamus	22	-25	11	-	810	-0.107	0.102	-1.159	-0.018	-0.048	0.267

Effect size computed using $d' = (M_{Deep} - M_{Shallow}) / SD_{Group}$.

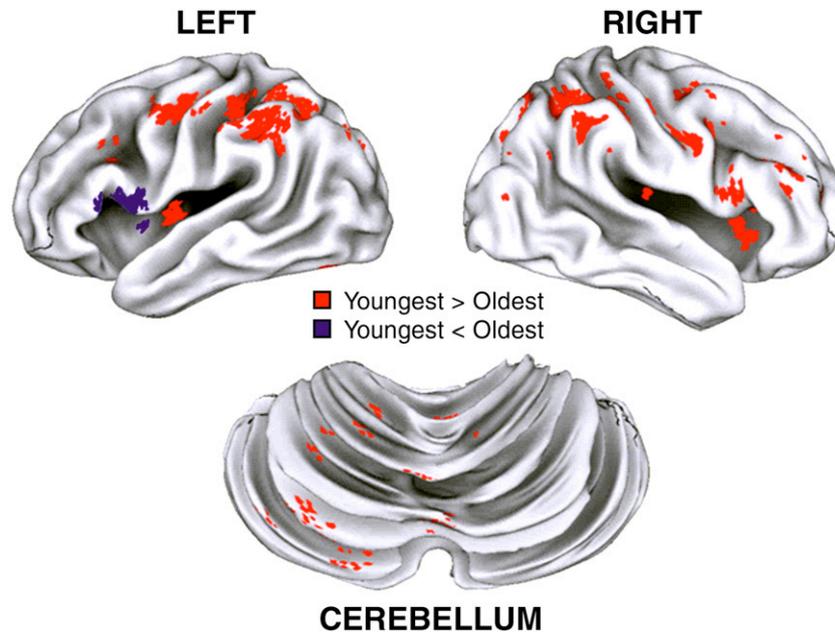


Fig. 2. Regions showing differences in activation as a function of processing depth and endpoint group. Purple represents the region which showed greater activity for the oldest endpoint group. Red represents the regions which showed greater activity for the youngest endpoint group.

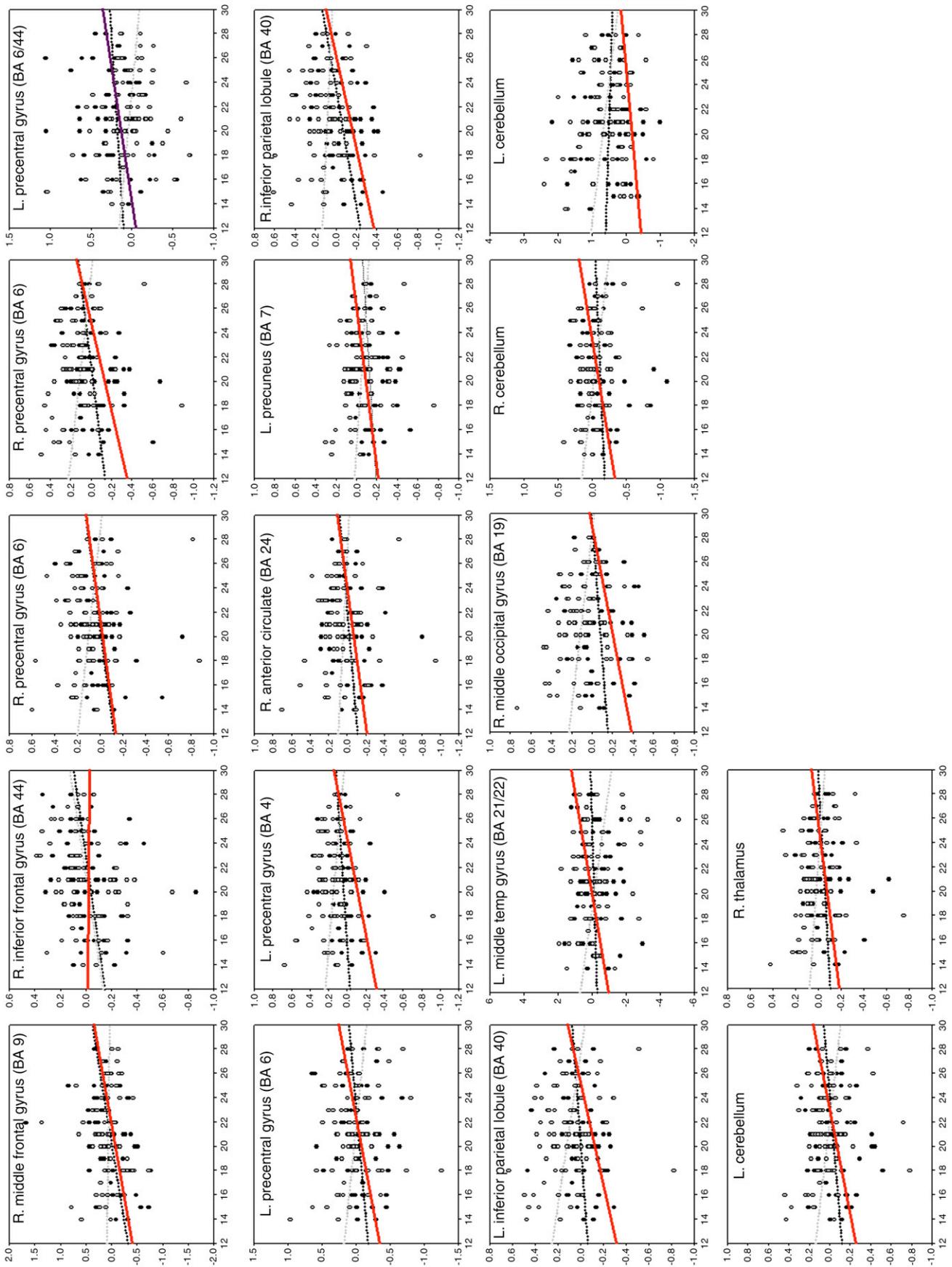
speed or accuracy during performance of the encoding and recognition tasks, although there was a tendency for adolescents to perform somewhat less accurately and more slowly than young adults. Nevertheless, performance across a battery of other neuropsychological tests administered outside of the scanner provided some evidence of improved episodic memory performance as a function of age. Age-related differences were not obtained on measures of fluid intelligence or episodic memory for spatial information. However, age-related differences were observed on measures of crystallized intelligence and episodic memory for verbal information. Performance on both of these measures improved as a function of age, with young adults demonstrating greater word knowledge and better recall of words and stories than adolescents. These findings suggest that there were behavioral differences across our age range, but that these differences emerged most clearly on measures of acquired language skills and highly demanding episodic memory tasks.

Overall, different patterns of brain activation were associated with performance of the deep and shallow encoding tasks. Deep encoding has been associated with greater activation in left inferior frontal cortex (for reviews, see Buckner et al., 2000; Cabeza and Nyberg, 2000) and, to a lesser extent, left medial temporal cortex (Fletcher et al., 2003, Fujii et al., 2002, McDermott et al., 1999). As expected, participants in our study showed greater activation of left inferior frontal cortex when information was processed at a deep, semantic level; however, greater activation of medial temporal

cortex was not observed (see also Chiu et al., 2006). Shallow encoding has been associated with greater activation in right prefrontal regions (e.g., Fletcher et al., 2003). However, participants in our study showed greater activation across a broad neuroanatomical network, including both the left and right hemispheres, when information was processed at a shallow, superficial level. The greater extent of brain activation observed in our study may reflect the younger age range of our participants. Given the predictions of the interactive specialization framework, one would expect brain activation to extend across more brain regions in younger compared with older participants. However, it is not clear why this effect was more apparent in the shallow encoding task. Because shallow encoding was more difficult than deep encoding for all participants, it is possible that age differences in brain activation were more apparent in the shallow encoding task because age interacted with task difficulty. A related possibility is that the adolescents were less practiced than the young adults on the alphabetization (shallow encoding) task compared with the semantic (deep encoding) task, though this suggestion is only speculative.

A question of interest is what the age-related differences in brain activation indicate about the cognitive processes engaged by adolescents and young adults during performance of the same task paradigm. Adolescents and young adults showed no differences in behavior and few differences in functional brain activity when they were required to process information at a deep, semantic level. This finding suggests that adolescents and young adults performed the

Fig. 3. X-axis represents age. Y-axis represents beta weights. Linear regressions show the contribution of age to brain activity in the deep (black) and shallow (gray) encoding tasks. Points above zero indicate greater activation in the deep relative to shallow encoding task, whereas points below zero indicate greater activation in the shallow relative to deep encoding task. A solid line (red or purple) represents the difference in beta weights between deep and shallow encoding. The red line represents regions in which brain activation was greater in the youngest endpoint group. For these regions, more points fall below zero at younger ages. This pattern indicates that age was negatively associated with an increase in activation in the shallow encoding compared with the deep encoding task. A purple line represents the region in which brain activation was greater in the oldest endpoint group. For this region, more points fall above zero at older ages. This pattern indicates that age was positively associated with an increase in activation in the deep encoding compared with the shallow encoding task.



deep encoding task in a similar way and with similar efficiency. Adolescents and young adults also showed no differences in behavior when they were required to process information at a shallow, superficial level. During performance of this task, however, widespread differences in functional brain activity were observed between the two groups. This finding may suggest that the phonological/orthographic processing required by participants in the shallow encoding task was less practiced in adolescents than in young adults. A possible outcome of this scenario is that the two groups executed different steps in order to make first/last letter judgments. For example, young adults may have processed letter position automatically whereas adolescents may have had to recite the letters of the alphabet. Alternatively, the two groups may have executed the same series of steps but with different levels of efficiency. For example, both groups of participants may have had to recite the alphabet in order to make judgments of letter position. Thus, despite executing the same series of steps, the demands placed on cognitive control may have been greater for adolescents compared with young adults. However, these are speculations that do not yet have empirical support and will require investigation in future research.

An additional possibility, potentially related to the discussion above, is that the age-related differences in task-related brain activity were influenced by age-related differences in either encoding performance or subsequent recognition performance. As noted above, we did not find any statistically significant differences in behavioral performance between the endpoint groups. Furthermore, regression analyses did not indicate any significant contributions of age to either accuracy or RT for any of the behavioral measures (although there were a few age effects that reached trend level). Nevertheless, adolescents were numerically slower than young adults across all performance measures. Although encoding accuracy was comparable for both groups in the shallow condition, adolescents were somewhat less accurate than young adults in the deep condition (5% less). Conversely, recognition accuracy was comparable for both groups for words that had been encoded at the deep, semantic level; however, adolescents were somewhat less accurate than young adults for words that had been encoded at the shallow, superficial level (11% less). Taken together, these findings suggest that the more widespread activation shown by adolescents in the shallow encoding condition may have reflected the fact that they experienced greater difficulty with successful encoding in this condition, even though their performance was comparable to that of the young adults from a statistical perspective. During performance of the shallow encoding task, young adults may have been more capable of carrying out effective encoding processes whereas adolescents may have been less able to divide attention or “dual-task.” Although this is only a speculative account, it is consistent with the fact that executive processes such as dual-task coordination continue to develop into adolescence.

These results have broader implications for our understanding of functional brain development. On the one hand, the maturational perspective predicts that adolescents and young adults will show similar patterns of activity in posterior–inferior brain regions but different patterns of activity in anterior–superior brain regions. Thus, on our episodic encoding task, one would expect to find fewer age-related differences in brain activation when information is processed at a shallow, non-semantic level, because this kind of processing is thought to rely more on posterior than anterior brain regions (for examples involving orthographic processing, see Joseph et al., 2003; Pernet et al., 2004; Polk et al., 2002; Tagamets et al., 2000). Rather,

one would expect to find age-related differences in brain activation when information is processed at a deep, semantic level, because this kind of processing tends to recruit anterior brain regions and is thought to place demands on cognitive control (e.g., Buckner et al., 2000). In addition to the predictions outlined above, interactive specialization predicts that adolescents may show a more diffuse pattern of brain activity than young adults on tasks in which they are less experienced. Thus, one would expect age to be associated with a narrowing of activation for less familiar kinds of processing and age-related differences could be observed during deep encoding, shallow encoding, or both if adolescents have less experience with these tasks than young adults.

We would argue that our results are more consistent with the interactive specialization framework. We did find that adolescents showed reduced activity in left inferior frontal cortex compared with young adults during the deep encoding task. However, much more dramatic and widespread age differences were found across a broad neuroanatomical network during the shallow encoding task. In all of these regions, adolescents showed enhanced activity compared with young adults, both in regions that were active in young adults (though to a lesser extent) as well as in regions that were not active in young adults. Consistent with the interactive specialization framework, these findings indicate that age-related change occurs across anterior–superior and posterior–inferior brain regions and that anterior–superior brain regions may show task involvement at an age earlier than expected. Consequently, we believe that the interactive specialization framework provides a more compelling account of changes in functional brain organization that occur across development.

This study is among the first to examine functional brain development using an episodic encoding task (see also Chiu et al., 2006). Previous studies have used other kinds of tasks to examine developmental changes in brain function associated with the emergence of cognitive control. For example, several imaging studies have examined developmental changes in response inhibition (e.g., Booth et al., 2003; Bunge et al., 2002; Casey et al., 1997; Tamm et al., 2002). In a study by Durston et al. (2002), patterns of brain activation were compared in children and young adults during performance of a go/no-go task. The task required participants to respond to all stimuli except a designated non-target which appeared on 25% of the trials. For both groups of participants, performance on the no-go trials was associated with greater activation in bilateral ventral prefrontal cortex, right dorsolateral prefrontal cortex, and right parietal cortex. However, the increases in magnitude were greater for children compared with young adults. The results of this study suggest that areas involved in response inhibition experience an age-related decrease in activation, a result that is similar to the pattern we observed in our episodic encoding task.

Other imaging studies have examined developmental changes in working memory (e.g., Casey et al., 1995; Schweinsburg et al., 2005; Thomas et al., 1999). For example, in one working memory study, Kwon et al. (2002) administered an *n*-back task to participants 7 to 22 years of age. The task required participants to determine whether the location of a stimulus on the present trial was the same as the location of a stimulus presented two trials back. Performance on this task was associated with age-related increases in brain activation in bilateral dorsolateral prefrontal cortex, left ventrolateral prefrontal cortex, left premotor cortex, and bilateral posterior parietal cortex. In another working memory study, Kleinberg et al. (2002) administered a span task to participants 9 to 18 years of age. The task required participants to decide whether the location of a probe matched the

locations of any stimuli that had been presented in a prior sequence. Performance on this task was associated with age-related increases in activation of bilateral superior frontal and intraparietal cortices. Taken together, the results of these studies provide compelling evidence that areas involved in working memory experience an age-related increase in activation.

Clearly, there are developmental differences in the patterns of brain activation associated with various kinds of cognitive control. It is important to note, however, that some brain regions may show either age-related increases in activation or age-related decreases in activation depending on the particular task that is used. For example, right dorsolateral prefrontal cortex shows an age-related decrease in activation during response inhibition (e.g., Durston et al., 2002) and an age-related increase in activation during working memory (e.g., Kwon et al., 2002). It may be the case that different kinds of cognitive control engage different areas within a region (e.g., subregions of dorsolateral prefrontal cortex) and that these areas show different patterns of activation as a function of development. Alternatively, it may be the case that different kinds of cognitive control engage the same brain regions. However, each kind of cognitive control may engage unique processes that elicit different patterns of activation as a function of development. This is an issue that warrants further clarification.

Future research should be aimed at observing changes that occur earlier in development, as the pattern of change that we observed in our study was likely limited by the older ages of our participants. In our study, 17 brain regions showed greater activation in adolescents compared with young adults. Of these regions, 53% were posteriorly located and 47% were anteriorly located. Furthermore, the relationship between age and activation in these regions was characterized by a linear function. However, other studies have shown that different brain regions mature at different rates and that activation in these regions may be characterized by non-linear functions. For example, Brown et al. (2005) found that anterior regions matured faster than posterior regions: the former were adult-like by 14.8 years of age, whereas the latter were adult-like at 16.5 years of age. Moreover, Brown et al. found that several areas of frontal cortex were best characterized by an exponential rise-to-max function. This suggests that increases in brain activation occur most rapidly early in development and that activation plateaus as development progresses. Consequently, our restricted age range might have precluded us from observing similar non-linear changes in more anterior regions of the brain.

This study makes an important contribution to our understanding of functional brain development by providing additional work in the domain of episodic memory. In order to relate changes in functional brain development to mnemonic processes that occur with other kinds of cognitive control, future research should include tasks in which participants are required to generate their own mnemonic strategies rather than having the strategies explicitly provided. We may see more dramatic age-related changes in the brain regions that support the spontaneous generation of strategy use, as this aspect of cognitive control appears to develop at a later point in time than the ability to use externally provided semantic elaboration strategies. List-learning and fluency tasks that require participants to self-select or self-organize strategies might be particularly well suited for this purpose.

In summary, the results of the current study join a growing literature suggesting that the pattern of neural development supporting cognitive development shows a more complicated pattern than a simple posterior–inferior and anterior–superior

maturational course, and that a more dynamic interplay between experience and functional specialization may characterize the development of the neural systems supporting a range of cognitive processes.

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