

A Developmental fMRI Study of the Stroop Color-Word Task

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We used fMRI to investigate developmental changes in brain activation during a Stroop color-word interference task. A positive correlation was observed between age and Stroop-related activation ($n = 30$) in the left lateral prefrontal cortex, the left anterior cingulate, and the left parietal and parieto-occipital cortices. No regions showed a negative correlation between activation and age. We further investigated age-related differences by stratifying the sample into three age groups: children (ages 7–11), adolescents (ages 12–16), and young adults (ages 18–22). Young adult subjects ($n = 11$) displayed significant activation in the inferior and middle frontal gyri bilaterally, the left anterior cingulate, and bilateral inferior and superior parietal lobules. Between-group comparisons revealed that young adults had significantly greater activation than adolescent subjects ($n = 11$) in the left middle frontal gyrus and that young adults showed significantly greater activation than children ($n = 8$) in the anterior cingulate and left parietal and parieto-occipital regions, as well as in the left middle frontal gyrus. Compared to children, both adult and adolescent subjects exhibited significantly greater activation in the parietal cortex. Adult and adolescent groups, however, did not differ in activation for this region. Together, these data suggest that Stroop task-related functional development of the parietal lobe occurs by adolescence. In contrast, prefrontal cortex function contributing to the Stroop interference task continues to develop into adulthood. This neuromaturation process may depend on increased ability to recruit focal neural resources with age. Findings from this study, the first developmental fMRI investigation of the Stroop interference task, provide a template with which normal development and neurodevelopmental disorders of prefrontal cortex function can be assessed. © 2002 Elsevier Science (USA)

(MacLeod, 1991). In this task, the subject is instructed to name the color of the ink of an incongruent word-color stimulus (i.e., RED printed in green ink). Because word reading is a more automatic cognitive process than color naming, subjects must resolve cognitive interference and inhibit the incorrect, but more facile, response in order to properly respond. This response competition commonly results in an increase in response time (RT) on incongruent trials as compared to congruent word-color pairs (i.e., RED printed in red ink) or neutral pairs (i.e., DOG printed in red ink, or XXX printed in red ink).

The cognitive processes underlying the Stroop task (i.e., response inhibition, interference resolution, and behavioral conflict resolution) are considered executive processes mediated by the frontal lobe. Patients with lateral prefrontal lobe lesions commit more errors on the Stroop task than do normal controls (Vendrell *et al.*, 1995). Perret (1974) proposed a left hemisphere frontal location for interference resolution in the Stroop task after studying patients with frontal lobe lesions. Because of its critical dependence on frontal lobe function, the Stroop task is an ideal tool for studying typical and atypical development of executive processes. Several studies have utilized the Stroop task (Dash and Dash, 1982) and modified Stroop tasks (Diamond and Taylor, 1996; Gerstadt *et al.*, 1994) to explore the maturation of executive processes, and have found that such processes develop with age.

In conjunction with the behavioral development of executive function, researchers have recently provided evidence for postadolescent maturation of the frontal lobes (Sowell *et al.*, 1999). Giedd *et al.* (1999) found that frontal gray matter increases during preadolescence, peaks during adolescence, and decreases during postadolescence. Although there has been evidence of structural frontal lobe maturation as well as behavioral maturation of executive processes during childhood, no functional imaging studies to date have used the Stroop task to investigate the relationship between frontal lobe function and cognition from a developmental standpoint.

INTRODUCTION

Since its introduction in 1935, the Stroop Color-Word task has been a classic measure of frontal lobe function

Although there have been no developmental imaging studies of the Stroop task to date, data from several Stroop task imaging studies have been reported in adults (Bench *et al.*, 1993; Carter *et al.*, 1995; Larrue *et al.*, 1994; Pardo *et al.*, 1990; Peterson *et al.*, 1999; Taylor *et al.*, 1997). However, considerable variability exists in the brain regions observed to be activated by the Stroop task. For example, utilizing a similar non-word control task as that used in the present study, Bench *et al.* (1993) reported Stroop task-related activation in right orbitofrontal cortex, right frontal polar cortex, and right anterior cingulate. Taylor *et al.* (1997), also employing a nonlexical control task, found activation in the right middle frontal gyrus (MFG), left inferior frontal gyrus (IFG), left parietal region, and left insula; no activation was observed in the anterior cingulate cortex (ACC). In summary, most investigations of the Stroop task have found activation in at least one of three main regions: the ACC (Carter *et al.*, 1995; Larrue *et al.*, 1994; Pardo *et al.*, 1990; Peterson *et al.*, 1999), parietal lobe (Bench *et al.*, 1993; Carter *et al.*, 1995; Peterson *et al.*, 1999; Taylor *et al.*, 1997), and lateral prefrontal cortex (Bench *et al.*, 1993; Carter *et al.*, 1995; Pardo *et al.*, 1990; Taylor *et al.*, 1997). The goal of the present study was to employ the classic Stroop interference task with functional magnetic resonance imaging (fMRI) to investigate neuromaturational processes underlying cognitive development in individuals ranging in age from early childhood to young adulthood. In accord with past Stroop task neuroimaging research, we hypothesized that development of executive processes involved in the Stroop interference process would be localized to these three regions.

In contrast to most functional imaging studies of cognitive development, which typically employ only two groups of subjects, children and adults (e.g., Thomas *et al.* (1999)), the present study utilized three developmental age groups (children, adolescents, and young adults), thus permitting a more fine-grained investigation of the trajectory of cognitive developmental changes. In particular, the inclusion of an adolescent group is a potentially significant addition as it is well known that the onset of puberty affects both development (Giedd *et al.*, 1999) and behavior (Buchanan *et al.*, 1992).

This study is a component of our laboratory's ongoing efforts to provide an initial template of neurofunctional maturation underlying key components of cognitive development during childhood. Broadening our knowledge base pertaining to the trajectory and variability of typical brain development in children will eventually permit a more precise interpretation of individual brain development and function in children with atypical cognitive development.

MATERIALS AND METHODS

Subjects

Subjects were recruited from the greater San Francisco Bay area. Two exclusion criteria were applied when screening for potential participants: (1) evidence of identifiable cognitive impairment or (2) the presence of a behavioral/psychological disorder. Cognitive functioning was assessed using the WISC-III (ages 7 through 16) or WAIS-III (ages 16 through 22). Persons who scored lower than 80 for full scale IQ were excluded from further participation. The presence of behavioral/psychological impairments was assessed using either the Symptom Checklist-90-R (SCL-90-R) (ages 13 through 22) (Derogatis and Savitz, 1999) or the Child Behavioral Checklist (CBCL) (ages 7 through 18) (Achenbach, 1991). Subjects with significant elevations (1 SD > population mean) on these instruments were excluded from the study.

Thirty healthy, right-handed, biologically independent subjects met these selection criteria and participated in the Stroop task fMRI study after giving written informed consent. The total sample included 10 males and 20 females ranging in age from 7 to 22 years (mean age: 15.42, SD = 4.24). Because of behavioral literature that suggests that by the age of seven children have developed their reading skills to the point that they experience semantic interference (Rosinski, 1977; Rosinski *et al.*, 1975) and that children under the age of seven do not show interference effects (Comalli *et al.*, 1962), we confined our subject pool to children aged seven and older.

Subjects were divided into three age groups with similar male to female proportions. The group of children consisted of 3 males and 5 females ($n = 8$) ranging in age from 7.66 to 11.96 years (mean = 10.16, SD = 1.66). The adolescent group included 4 males and 7 females ($n = 11$) ranging from 12.58 to 16.85 years of age (mean = 14.68, SD = 1.27). The young adult group consisted of 3 male and 8 female subjects ($n = 11$), ranging in age from 17.39 to 22.68 years (mean = 19.98, SD = 1.72).

Neuropsychological Stroop Test

Because of head movement that would result from fully vocalizing responses within the scanner, we used behavioral data acquired outside the scanner to investigate age-related changes in performance of the Stroop task. In the present study, a standard Stroop Color-Word task (Golden, 1978) was administered to every subject. The Stroop test includes 3 time-limited (45-s) subtests. First, subjects are asked to read a list of words printed in black ink that name colors (i.e., "red," "green," "blue"). Second, subjects are presented with a list of "XXXXX"s that differ in ink color. Subjects name the color of the ink for each "XXXXX." In the third

TABLE 1

Results of Multiple Regression Analysis Examining the Relationship between FSIQ, Age, and Stroop Subscores

Dependent variable	Predictor	Zero-order correlation	Partial correlation	Part correlation	R ² delta	Beta	Beta P value
Word raw score	FSIQ	0.191	-0.092	-0.067	0.037	-0.072	0.635
	AGE	0.685	0.674	0.661	0.437	0.712	<0.001
Color raw score	FSIQ	0.340	0.059	0.032	0.116	0.035	0.761
	AGE	0.837	0.814	0.765	0.585	0.824	<0.001
Color-word raw score	FSIQ	0.496	0.357	0.221	0.246	0.238	0.057
	AGE	0.786	0.747	0.649	0.421	0.698	<0.001
Interference raw score	FSIQ	0.514	0.434	0.401	0.246	0.432	0.019
	AGE	0.382	0.240	0.206	0.043	0.222	0.209

subtest, subjects are then presented with a list of the words “red,” “green,” and “blue;” in this presentation, however, the ink color of the words is discordant with the presented word (i.e., the word “red” printed in blue ink). Again, subjects are asked to say the color of the ink and ignore the word’s semantic meaning (i.e., respond “blue” instead of “red” in the previous example).

fMRI Stroop Task

The experiment presented in the scanner began with a 30-s rest epoch followed by 3 cycles of alternating 30-s epochs of experimental trials and control trials, a

30-s rest epoch, another 3 cycles of control and experimental epochs, and a final 30-s rest epoch. In each epoch, there were 15 stimuli, each presented for 1350 ms, with a total interstimulus interval (ISI) of 2000 ms. In order to highlight the complete network of brain regions involved in Stroop task-related cognitive components and their development, we employed a low-level nonlinguistic baseline as the control condition that only controlled for the process of color naming. The control stimuli consisted of a string of 3, 4, or 5 colored “X”s, presented in red, blue, or green. The subjects were asked to subvocalize the color of the “X”s

TABLE 2

Brain Areas That Showed Significant Activation in (1) Linear Correlation between Age and Activation; (2) Young Adult Group Average; (3) Adult versus Child Comparison; (4) Adult versus Adolescent Comparison; (5) Adolescent versus Child Comparison

Activated Region	No. of voxels	Cluster P (cor)	Z max primary peak	Primary peak location
Linear correlation between age and activation				
Left anterior cingulate cortex and lateral prefrontal regions (SFG/MFG)	6109	<0.001	4.57	-4, 14, 28 L ACC (BA 24/32)
Left inferior parietal lobe, parieto-occipital regions, cuneus, lingual gyrus, posterior cingulate cortex	1700	<0.001	3.67	-26, -62, 16 L PCC/cuneus (BA31/7)
Young adult group average				
Bilateral MFG, IFG, and anterior cingulate cortex	12030	<0.001	4.37	-34, 22, 34 L MFG (BA 8)
Right inferior parietal lobe, supramarginal gyrus, superior/medial occipital gyrus	1681	0.001	4.25	60, -46, 28 R IPL/supramarginal gyrus (BA 40)
Left inferior and superior parietal lobe	3474	<0.001	4.03	-28, -68, 52 L SPL (BA 7)
Adult-child				
Anterior cingulate cortex	827	0.049	4.12	-6, 26, 16 L ACC (BA 24)
Left MFG and SFG	2511	<0.001	3.92	-28, 14, 50 L MFG (BA 6)
Left parieto-occipital regions: lingual gyrus, precuneus, cuneus	937	0.025	3.58	-14, -66, -2 L lingual gyrus (BA 18/19)
Adult-adolescent				
Left MFG, ACC, SFG	1376	0.002	3.81	-28, 12, 52 L MFG (BA 6)
Adolescent-child				
Left cuneus, posterior cingulate gyrus, precuneus	1858	<0.001	4.11	-14, -74, 22 L cuneus (BA 17/18)

Note. For each cluster, the activated region(s), number of voxels activated, corrected *P* value, maximum *Z* score, and location of peak activation are shown. ACC, anterior cingulate cortex; MFG, middle frontal gyrus; SPL, superior parietal lobe; IPL, inferior parietal lobe; PCC, posterior cingulate cortex; IFG, inferior frontal gyrus; SFG, superior frontal gyrus.

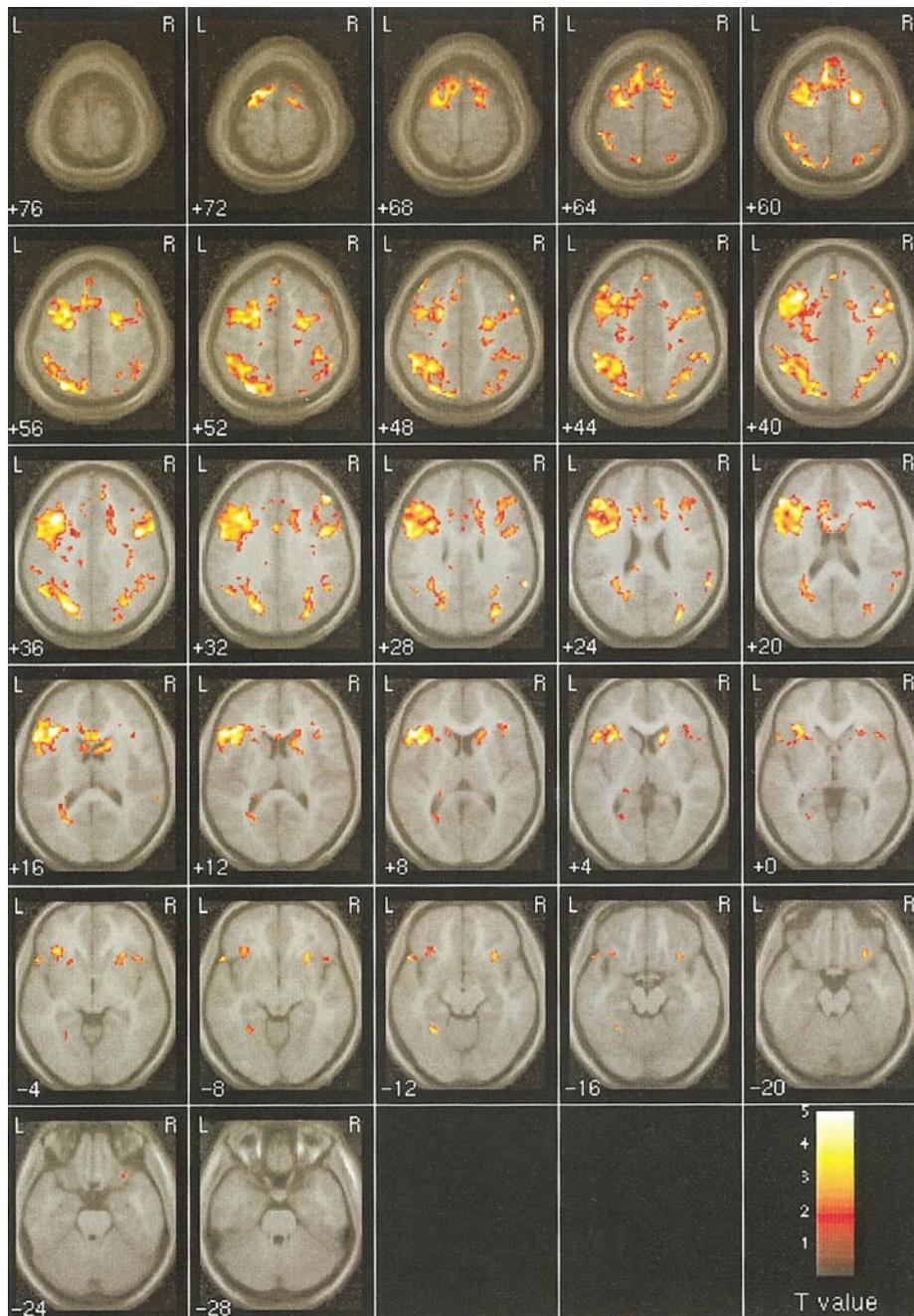


FIG. 1. Brain regions that showed significant ($P < 0.05$) Stroop task-related activation in the young adult group include the bilateral frontal regions and bilateral parietal and parieto-occipital regions. Activated regions include the middle frontal gyrus, inferior frontal gyrus, inferior parietal lobe, superior parietal lobe, and the superior/medial occipital gyrus. fMRI activation was superposed on the average of the 11 young adult subjects' individual T1-weighted images normalized to Talairach space.

quietly to themselves. The experimental stimuli were incongruent color-word pairs, in which the print of the ink did not match the color specified by the word (i.e., the word "red" printed in green). The subjects were asked to identify, and say quietly to themselves, the color of the ink in which the word was printed, and not to read the word itself (in our example, to say "green"). All subjects were trained on the task before scanning

until they showed and expressed both understanding and compliance.

fMRI Acquisition

Images were acquired on a 1.5T GE Signa scanner with Echospeed gradients using a custom-built whole head coil that provides a 50% advantage in signal to

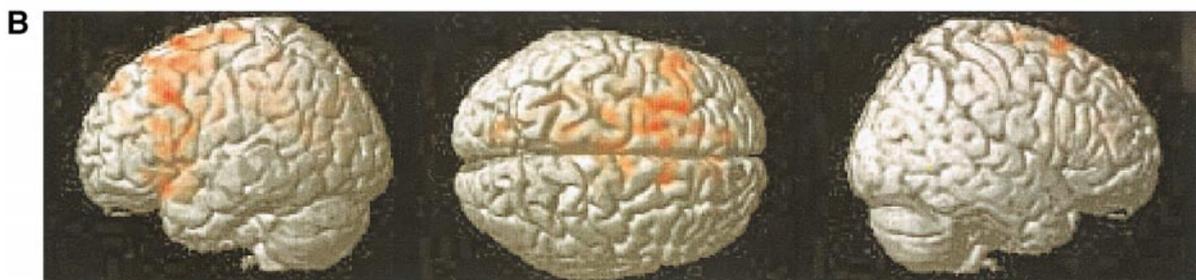
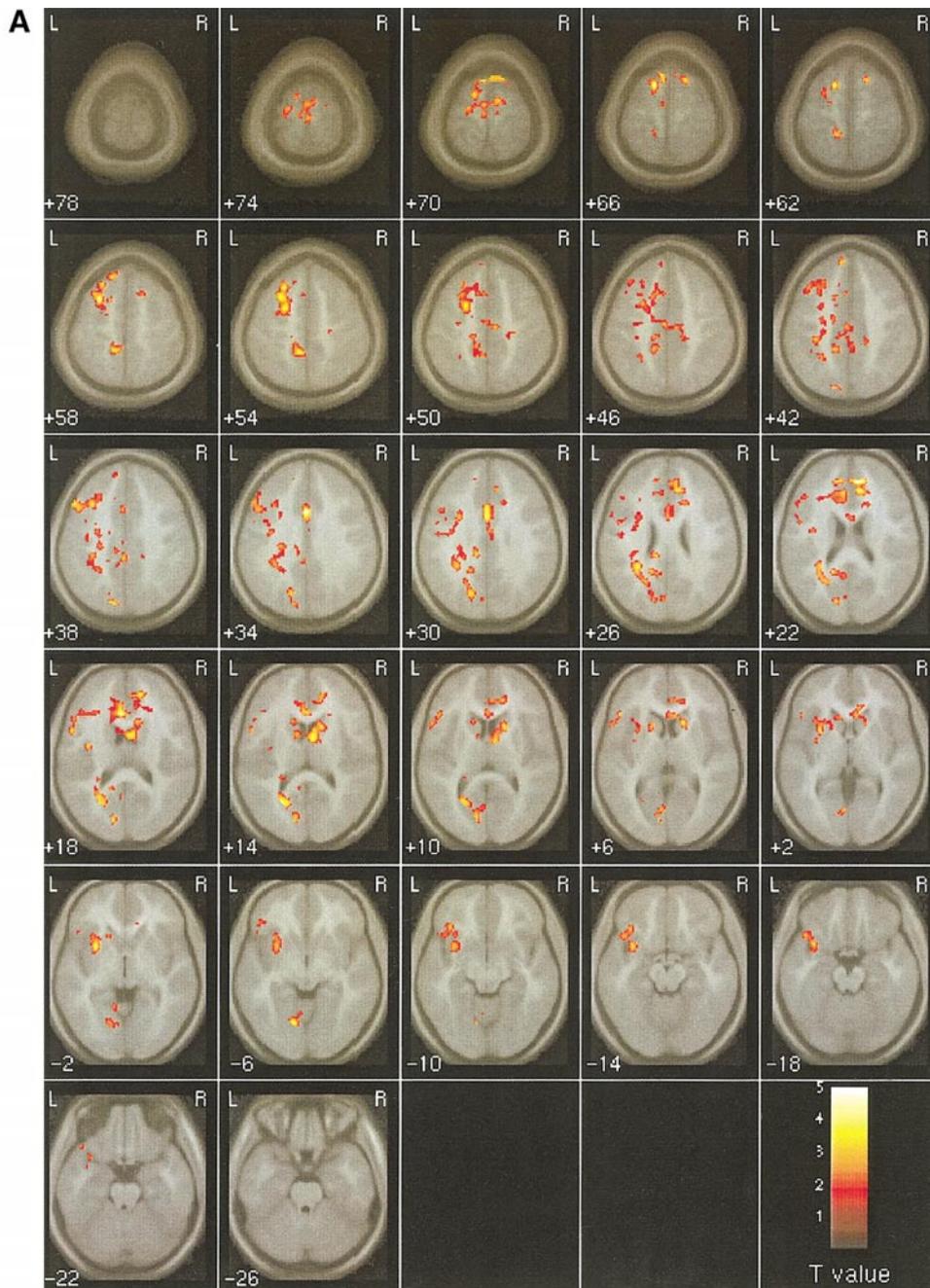


FIG. 2. Brain areas in which Stroop task-related activation was significantly ($P < 0.05$) correlated with age. (A) fMRI activation was superposed on the average of 29 individual T1-weighted images normalized to Talairach space. (B) Surface rendering of fMRI activation on a T1-weighted Montreal Neurological Institute (MNI) template image.

noise ratio over that of the standard GE coil (Hayes and Mathias, 1996). A custom-built head holder was used to prevent head movement. Eighteen axial slices (6 mm thick, 1 mm skip) parallel to the anterior and posterior commissure covering the whole brain were imaged with a temporal resolution of 2 s using a T2*-weighted gradient echo spiral pulse sequence (TR = 2000 ms, TE = 40 ms, flip angle = 89° and 1 interleave) (Glover and Lai, 1998). The field of view was 240 mm and the effective inplane spatial resolution was 3.75 mm. To aid in localization of functional data, a high resolution T1-weighted spoiled grass gradient recalled (SPGR) 3-D MRI sequence with the following parameters was used: TR = 24 ms; TE = 5 ms; flip angle = 40°; 124 slices in coronal plane; 256 × 192 matrix; acquired resolution = 1.5 × 0.9 × 1.2 mm. The images were reconstructed as a 124 × 256 × 256 matrix with a 1.5 × 0.9 × 0.9 mm spatial resolution. Structural image averages were made for the entire subject pool as well as for each age group. Because of excessive movement during one structural scan (an individual in the child group), only 29 subjects were included in the average structural image.

The task was programmed using Psyscope (Cohen *et al.*, 1993) on a Macintosh (Sunnyvale, CA) notebook computer. Initiation of scan and task was synchronized using a TTL pulse delivered to the scanner timing microprocessor board from a "CMU Button Box" microprocessor (<http://poppy.psy.cmu.edu/psyscope>) connected to the Macintosh. Stimuli were presented visually at the center of a screen using a custom-built magnet compatible projection system (Resonance Technology, CA).

Image Preprocessing

Images were reconstructed, by inverse Fourier transform, for each of the 225 time points into 64 × 64 × 18 image matrices (voxel size: 3.75 × 3.75 × 7 mm). fMRI data were preprocessed using SPM99b (<http://www.fil.ion.ucl.ac.uk/spm>). Images were corrected for movement using least square minimization without higher-order corrections for spin history and normalized to MNI coordinates. Images were then re-sampled every 2 mm using sinc interpolation and smoothed with a 4-mm Gaussian kernel to decrease spatial noise. MNI coordinates were transformed to Talairach (Tal) coordinates using a nonlinear transformation (Brett, 2000, <http://www.mrc-cbu.cam.ac.uk/Imaging/mnispace.html>).

Statistical Analysis

Behavioral data. Raw scores on the Stroop task were calculated by determining the number of items completed within the 45-s time interval on each of the three subtests (color, word, color-word). An interference score was derived from the prediction of perfor-

mance on the third task (based on performance on the first two tasks) minus the actual performance. Raw interference was calculated using the same equation the Stroop neuropsychological test provides for interference calculation.¹ For our experimental purposes, this calculation of an interference score was derived from the three subtest raw scores rather than from the age-corrected scores provided in the Stroop manual (which are described as "experimental" in the manual) (Golden, 1978). The benefits of using raw scores in cross-sectional studies of development have been discussed (Kraemer *et al.*, 2000) and have been used instead of age-standardized scores in similar investigations (Bettner *et al.*, 1971).

Multiple regression analyses were performed to assess the predictive value of age and full-scale IQ (FSIQ), as measured by the WISC-III or WAIS-III, on the Stroop performance measures.

fMRI data analysis. Statistical analysis was performed on individual and group data using the general linear model and the theory of Gaussian random fields as implemented in SPM99b (Friston *et al.*, 1995). This method corrects for temporal and spatial autocorrelations in the fMRI data (Worsley and Friston, 1995).

In the first step of analysis, a within-subject procedure was used to model all the effects of interest. The individual subject models were identical across subjects (i.e., a balanced design was used). Confounding effects of fluctuations in global mean were removed by proportional scaling where, for each time point, each voxel was scaled by the global mean at that time point. Low frequency noise was removed with a high pass filter (0.5 cycles/min) applied to the fMRI time series at each voxel. A temporal smoothing function (Gaussian kernel corresponding to dispersion of 8 s) was applied to the fMRI time series to enhance the temporal signal to noise ratio. The effects of interest for each subject were then defined with the relevant contrasts of the parameter estimates. For each of these contrasts, a corresponding contrast image was made. Voxel-wise *t* statistics were normalized to *Z* scores to provide a statistical measure of activation independent of sample size. Finally, in order to determine the presence of significant clusters of activation, the joint expected probability distribution of height and extent of *Z* scores (Poline *et al.*, 1997), with height ($Z > 1.67$; $P < 0.05$) and extent threshold ($P < 0.05$), was used in order to correct for spatial correlations in the data.

Activation analysis. Group analysis was performed using a random-effects model. The random-effects model estimates the error variance for each condition of interest across subjects, rather than across scans

¹ The equations employed were as follows: $(W * C) / (W + C) = CW$; $CW - CW = RAWINTF$. *W*, raw word score; *C*, raw color score; *CW*, raw color-word score.

(Holmes and Friston, 1998) and therefore provides a stronger generalization to the population. This analysis proceeded in two steps. In the first step, contrast images for each subject and each effect of interest were generated as described above. In the second step, these contrast images were used to examine the correlation between age and brain activation and between-group activation differences as described below. We initially analyzed data from young adult subjects to determine the consistency of our findings with those previously reported for adult samples.

Correlation between age and activation. Linear regression was used to determine voxels that showed either positive or negative age-related changes during the Stroop interference task (interference vs color naming condition contrast) across all subjects. Subject age was used as a covariate of interest and FSIQ was used as a nuisance covariate due to unexpected group differences for this measure. Voxel-wise t statistics were computed for the covariate of interest. The t statistics were then normalized to Z scores. Significant clusters of activation were determined using the joint expected probability distribution of height and extent of Z scores, with height ($Z > 1.67$; $P < 0.05$) and extent threshold ($P < 0.05$).

Group differences in Stroop task-related activation. In order to further delineate the trajectory of developmental changes, Stroop task-related activation differences between the three groups (children, adolescents, and young adults) were compared. Individual contrast images reflecting task-related activation were first created for each subject. Groups were compared using two-sample, two-tailed, t tests after covarying out differences in full scale IQ. The following group comparisons were made: (1) young adult versus child; (2) young adult versus adolescent; and (3) adolescent versus child.

RESULTS

IQ

Although age was not significantly correlated with verbal IQ ($r = 0.291$; $P = 0.118$) or performance IQ ($r = 0.297$; $P = 0.111$), linear regression indicated a significant correlation between age and full-scale IQ ($r = 0.37$; $P = 0.044$). This significant age-effect in IQ was related to a sampling bias in the young adult group due to the inclusion of undergraduates at Stanford University. Because of these age-related findings, we used full-scale IQ as a nuisance covariate in all analyses of group and age-related effects.

Stroop Task Performance

Multiple regression analyses (Table 1) showed that age explained a significant proportion of the variance in Stroop task subtest scores (word raw: $\beta = 0.712$,

$P < 0.001$; color raw: $\beta = 0.824$, $P < 0.001$; color-word raw: $\beta = 0.698$, $P < 0.001$). However, age was not significantly correlated with raw interference score ($P = 0.209$). In contrast, FSIQ did not account for a significant proportion of the variance in word raw ($P = 0.635$), color raw ($P = 0.761$), or color-word raw scores ($P = 0.057$), but was a significant predictor of raw interference score ($P = 0.019$).

Brain Activation

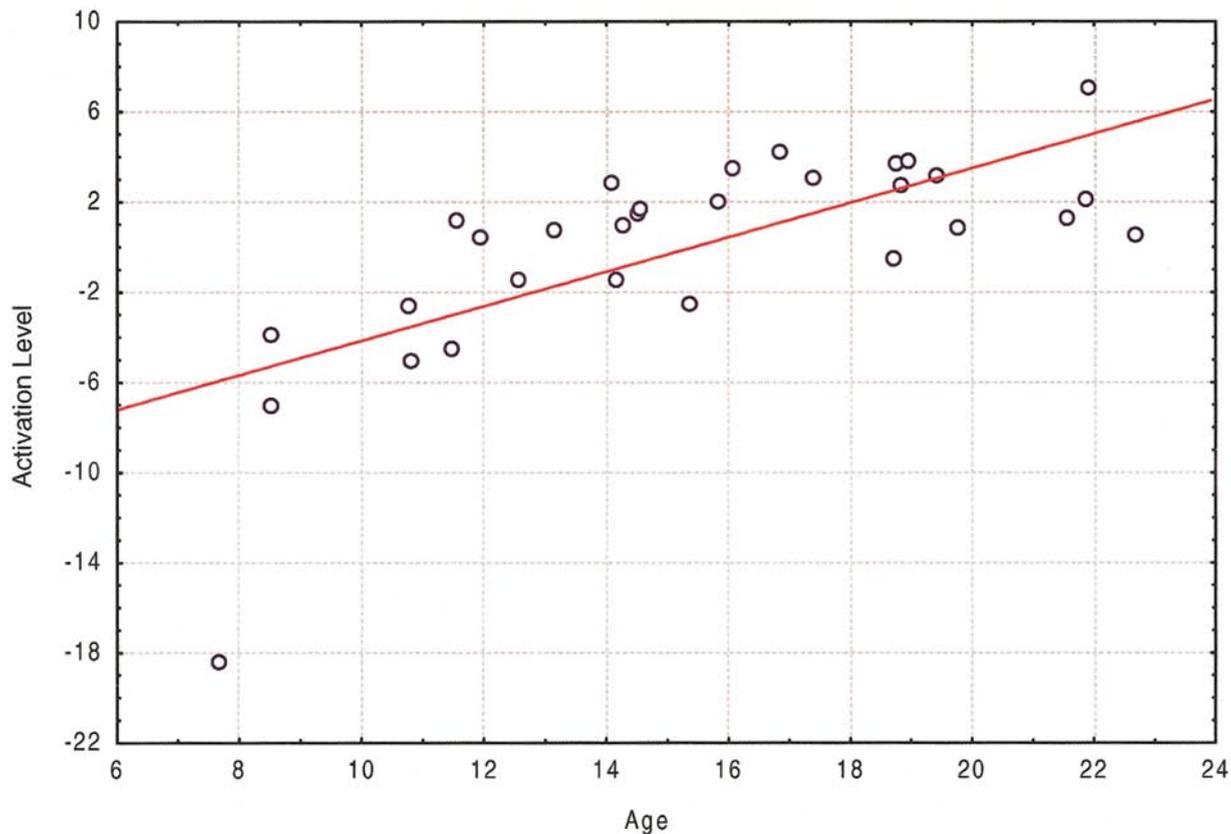
Young adult group activation. Young adults showed significant Stroop task-related activation bilaterally in the IFG, the MFG and the anterior cingulate (Z max = 4.37, $P < 0.001$), bilateral inferior parietal lobe/supramarginal gyrus (R side: Z max = 4.25, $P = 0.001$; L side: Z max = 4.03, $P < 0.001$), and the left superior parietal lobe (Z max = 4.03, $P < 0.001$; for summary of all activation see Table 2 and Fig. 1). Activation was also found to extend into the caudate (Tal $x, y, z = 16, 10, 6$ mm in Fig. 1).

Correlation between age and brain activation. After covarying for FSIQ, two clusters of brain activation were significantly correlated with age (Table 2; Fig. 2). The first cluster spanned the left anterior cingulate gyrus (BA 24/32) and prefrontal regions including the left superior frontal gyrus (SFG) (BA 6) and bilateral MFG (BA 9) (Z max = 4.57, $P < 0.001$). Activation from this cluster also was found to extend into bilateral caudate/putamen (Tal $x, y, z = 16, 10, 6$ mm in Fig. 2A). The second cluster spanned the left posterior cingulate gyrus and cuneus (BA 31/7), the left lingual gyrus (BA 18/19), and the left inferior parietal lobe (BA 40) (Z max = 3.67, $P < 0.001$).

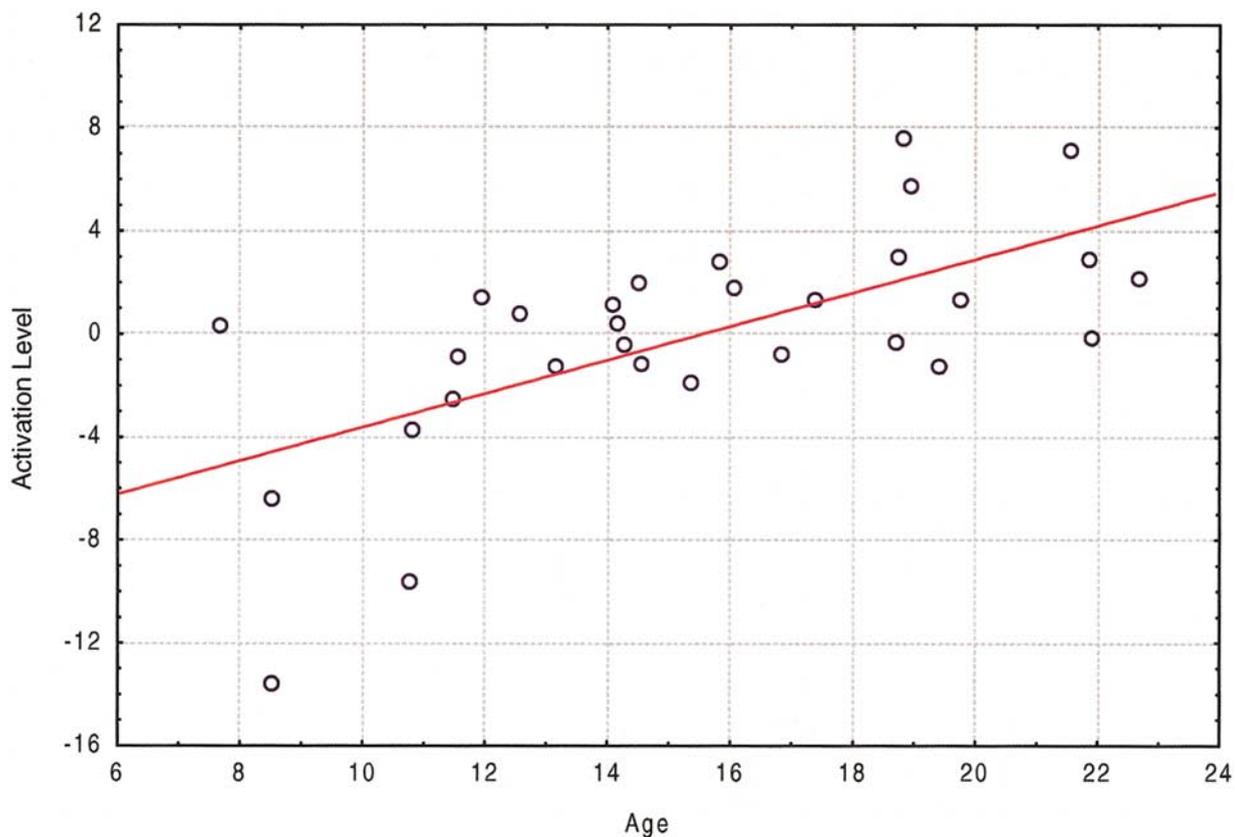
In order to further explore the relationship between age and focal activation in these two regions, a correlational analysis ($n = 30$) was run between age and activation level (arbitrary measure) in the foci maxima of the two regions. The foci maxima were located in (1) the left ACC (BA 24/32, Tal $x, y, z = -4, 14, 28$ mm), and (2) the left posterior cingulate cortex (PCC)/cuneus (BA 31/7, Tal $x, y, z = -26, -62, 16$ mm). The activation level in both of these foci was significantly correlated with subject age ($P < 0.0001$, see Figs. 3 and 4).

Young adults vs children. Young adults showed greater Stroop task-related activation, as compared to children, in the left and right anterior cingulate gyrus (BA 24/32) (Z max = 4.12, $P = 0.049$), the left MFG and SFG (BA 6/9/45) (Z max = 3.92, $P < 0.001$), and left occipitoparietal regions, including the lingual gyrus (BA 18/19), precuneus (BA 31/7), and the cuneus (BA 17) (Z max = 3.58, $P = 0.025$; for summary of all activation see Table 2 and Fig. 5). Children did not show significantly greater Stroop task-related activation than young adults in any brain region.

Young adults vs adolescents. Young adults had significantly greater activation during the Stroop task, as



3



4

FIG. 3. Correlation ($n = 30$) between age and activation level (arbitrary scale) in the peak voxel of activation in the left anterior cingulate cortex (BA 24/32, Tal $x, y, z = -4, 14, 28$ mm, $P < 0.0001$).

FIG. 4. Correlation ($n = 30$) between age and activation level (arbitrary scale) in the peak voxel of activation in the left posterior cingulate cortex/cuneus (BA 31/7, Tal $x, y, z = -26, -62, 16$ mm, $P < 0.0001$).

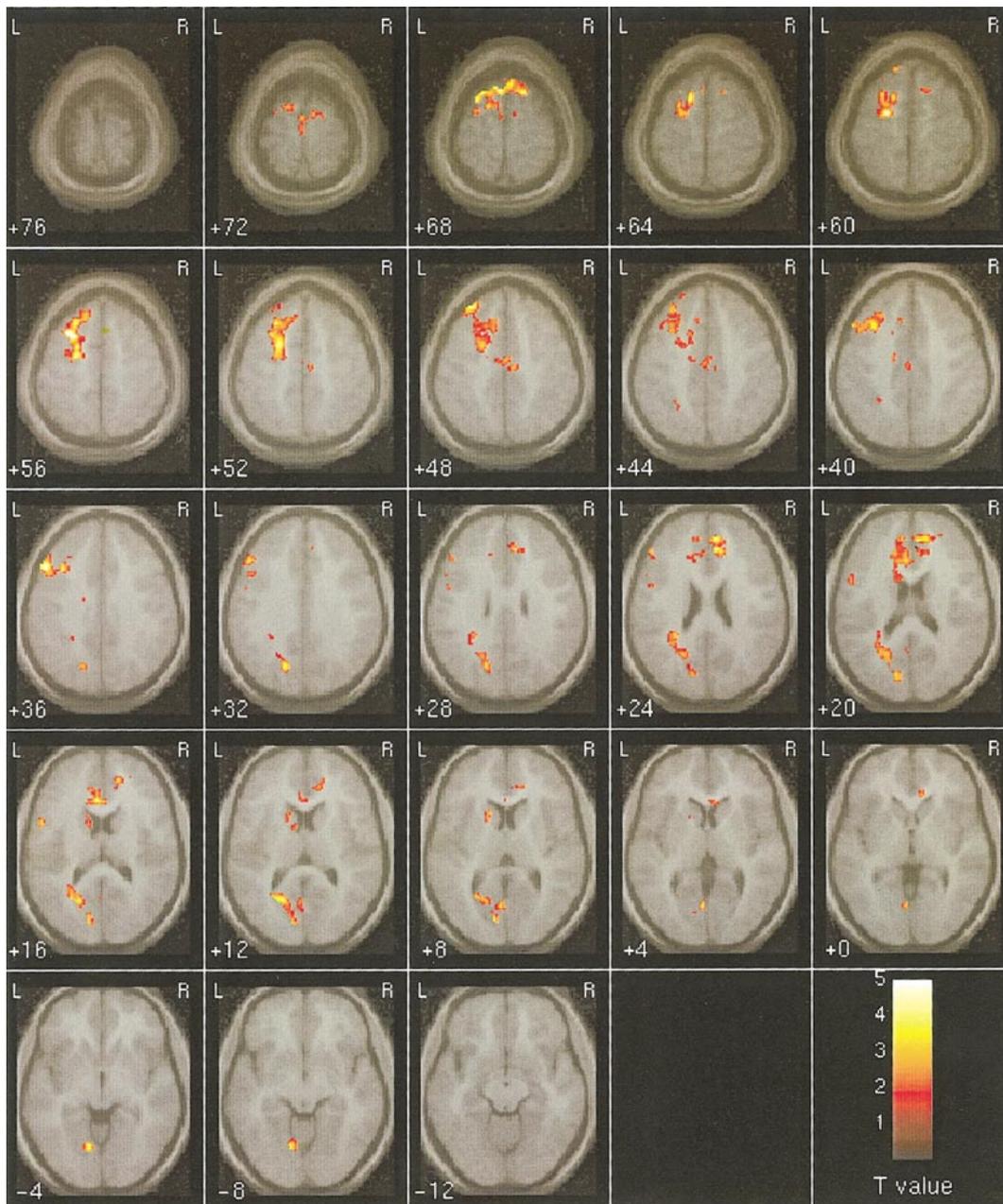


FIG. 5. Brain areas showing significantly greater Stroop task-related activation in the young adults, compared to the children, included the anterior cingulate bilaterally, the left MFG, the lingual gyrus, precuneus, and cuneus. Other details as described in the legend of Fig. 2.

compared to adolescents, in the left middle frontal gyrus (BA 6/8/9) (Z max = 3.81, P = 0.002; for summary of all activation see Table 2, Fig. 6). Adolescents did not show significantly greater Stroop task-related activation than young adults in any brain region.

Adolescents vs children. Adolescents exhibited significantly greater activation than children in the left cuneus (BA 17/18) and the posterior cingulate gyrus/precuneus (BA 31) (Z max = 4.11, P < 0.001; for summary of all activation see Table 2, Fig. 7). Children showed greater activation than adolescents in two sig-

nificant clusters: the first included the right cerebellum, right hippocampus, and midbrain; the second cluster was localized in the right superior temporal gyrus (STG) (BA 22/42).

DISCUSSION

Improved understanding of the dynamic and variable nature of brain development and function throughout the human lifespan is of the highest scientific priority. In particular, elucidating typical develop-

mental processes during childhood and adolescence will enhance our ability to recognize and treat atypical development and disease processes in the future.

The present study is the first to describe the relationship between Stroop task-related brain activation and age, as well as the first to provide evidence for ongoing developmental changes in Stroop-processing brain networks that correspond to improvements in behavioral task performance. A major strength of the present study was the voxel-by-voxel correlation analysis using a random effects model (Holmes and Friston, 1998). We examined both positive and negative age-related changes in brain activation during performance of the Stroop task. This allowed us to examine whether there is an increase in activation with age corresponding to an ability to recruit appropriate resources for task performance or a decrease in activation corresponding to better optimization and decreased task difficulty with age.

There are three major processes involved in performance of the Stroop Color-Word task: word reading, color naming, and interference resolution. In order to fully characterize the development of brain activity during Stroop task performance, we used a control task involving color naming. Using this nonlexical control task (colored "XXXXX"s) allowed us to examine the development of interference resolution in the context of word reading.

Activation in Young Adults

Young adults showed significant Stroop task-related activation bilaterally in the IFG, MFG, inferior parietal lobe/supramarginal gyrus, superior parietal lobe, and the left anterior cingulate. This pattern of brain activation in adults is consistent with Stroop task activation revealed in other adult neuroimaging studies (Pardo *et al.*, 1990; Larrue *et al.*, 1994; Carter *et al.*, 1995; Peterson *et al.*, 1999; Bench *et al.*, 1993). These data, combined with those of the literature, provided a template against which developmental-related differences in activation could be assessed in the two younger age groups.

Linear Changes with Age

Both behavioral performance and patterns of brain activation showed age-related changes. Raw word, color, and color-word scores showed linear increases with age, reflecting cognitive maturation in several major processes associated with the Stroop task (reading, color identification, and resolution of cognitive interference). The behavioral results of this study are consistent with previous behavioral studies that have reported improvement in word reading skill with age. Basic reading skills, as measured by the Woodcock-Johnson III, are shown to markedly increase between

the ages of 5 and 25 years (McGrew and Woodcock, 2001). Analyses from the behavioral Stroop task in the present study, also show a significant relationship between age and word reading skill, which develops over the course of childhood and adolescence.

A positive correlation also was observed between age and activation in the left lateral prefrontal cortex, the left anterior cingulate, and the left parietal and parieto-occipital cortices. This linear correlation was most significant in the left lateral prefrontal cortex and left parieto-occipital regions. The left lateral prefrontal cluster consisted of a much larger cluster of voxels (No. of voxels = 6109) than the left parieto-occipital cluster (No. of voxels = 1700). No regions showed decreased activation with age. These results suggest that the developmental trajectory of cognitive processing needed for the Stroop task is characterized by increasing ability to recruit additional neural resources.

Several recent developmental imaging studies of frontal lobe function have shown increased, more diffuse, activation in children as compared to adults (Casey *et al.*, 1997; Gaillard *et al.*, 2000; Thomas *et al.*, 1999). At first glance, these results may seem to contradict our findings of increased Stroop task-related activation with age. These differences may arise partly from methodological differences. Previous studies have used broadly defined regions of interest (ROIs); for example, in a developmental study of the gonogo, Casey *et al.* (1997) examined activation in the entire ACC, SFG, MFG, and IFG. In contrast, the present study used a voxel-by-voxel regression analysis to examine the precise voxels in which Stroop task-related activation changes with age. Thus, it is possible that there are focal increases in activation that are not captured using broadly defined ROIs. It is also possible that there is more diffuse activation in children, which becomes more focal with age in very specific brain regions.

Subjects showed increases in behavioral performance in conjunction with increases in regional activation. The increase in activation with age may be correlated with simultaneous improvements in behavioral performance. Rubia *et al.* (2000) studied normal adolescents and adults performing a motor timing task and found that better delay-task performance in adults paralleled increased activation in a brain network including prefrontal and parietal cortical regions and the putamen. Below, we further discuss age-related changes in activation during performance of the Stroop task by specific brain region (lateral prefrontal cortex, parieto-occipital cortex, and anterior cingulate cortex). We discuss these results with regard to both linear age-related changes as well as differences between stratified age groups (young adult, adolescent, and child).

Lateral Prefrontal Cortex

Data from the present study provide evidence for functional development in lateral prefrontal cortex related to the Stroop task. Prefrontal regions in which activation was significantly correlated with age included bilateral MFG (BA 9) and left SFG (BA 6). Left MFG and SFG also showed significant differences in activation in both the adult-child comparison, and the adult-adolescent comparison, suggesting that the neural processes associated with prefrontal cortex activation develop throughout childhood, adolescence, and into young adulthood.

Age-related differences in prefrontal activation were specifically localized to the left hemisphere. Left hemisphere differences in activation are consistent with the verbal nature of the Stroop task. Due to the low-level baseline control task, some of the age-related changes in functional activation may reflect increasing word reading proficiency. In the present study, no age-related activation changes were seen in the right prefrontal cortex. In particular, we did not see increased right-sided activation in young children as compared to adolescents and young adults.

Previous lesion and imaging studies have implicated lateral prefrontal regions in both interference processing/response inhibition (Casey *et al.*, 1997; Pujol *et al.*, 2000) and word reading/production (Cabeza and Nyberg, 2000). Pujol *et al.* (2000), in a study of demyelinating lesions in patients with multiple sclerosis, reported that 45% of the variance in Stroop interference time was accounted for by a combination of frontal and parietal lesions. Prefrontal cortex lesions also produce deficits in response inhibition tasks (Grant and Berg, 1948; Malloy *et al.*, 1993; Perret, 1974). Casey *et al.* (1997) reported that ventral and dorsal prefrontal regions were activated in both children and adults during a Go/No-Go response inhibition task, although children activated more in these regions and performed more poorly than adults. Response inhibition is an important component of the Stroop task, as subjects must inhibit an inappropriate response (i.e., reading the word) in order to correctly respond (i.e., naming the color).

Another important cognitive process involved in Stroop task performance is word reading and production. Activation in prefrontal regions described in this study also have been observed in tasks that require vocal word reading (Bookheimer *et al.*, 1995; Hirano *et al.*, 1996) as well as silent word reading (Bookheimer *et al.*, 1995; Hirano *et al.*, 1996; Petersen *et al.*, 1990). This is an intriguing finding considering the positive correlation between age and word reading raw score on the behavioral Stroop task. Word reading and production play an important role in Stroop interference resolution and functional development in the prefrontal

cortex may influence both reading skills and interference resolution skills.

Parietal and Parieto-occipital Cortex

There was a significant linear correlation between activation in left inferior parietal/parieto-occipital regions and age. In the between-group analysis, significant differences were confined to the adult-child and adolescent-child comparisons. No differences in parietal cortex activation, however, were evident in the adult-adolescent comparison. This finding suggests that Stroop task-related processes of the parietal lobe are mostly developed by adolescence.

Activation in the parietal lobe during the Stroop task was observed bilaterally in the inferior parietal lobule in agreement with previous results (Carter *et al.*, 1995), as well as in parieto-occipital regions. Our findings also are in accord with those of Bench *et al.* (1993) and Peterson *et al.* (1999) who found Stroop task-related inferior parietal activation. These authors suggest that the parietal cortex plays a role in maintaining sustained attention during the Stroop task. In the present study, parietal cortex activation also may reflect sustained attention to an important stimulus feature in the face of more salient and misleading stimulus features. A number of studies have shown that parietal regions are activated during sustained attention, attention shifts, and when attention is reflexively drawn to prominent features of a stimulus (see Chelazzi and Corbetta (2000) for a review). For example, Menon *et al.* (1997) found both fMRI and EEG evidence that the inferior parietal cortex plays an important role in allocation of directed attention to an unexpected event.

In addition to playing a role in sustained attention, parieto-occipital activity may be associated with word reading (Brunswick *et al.*, 1999; Buchel *et al.*, 1998; Shaywitz *et al.*, 1998) and visual attention processes (Carpenter *et al.*, 2000). In a recent review of PET studies, Posner *et al.* (1999) reported that letter strings activate prestriate and parietal areas in the right hemisphere, but only word-like stimuli activate these regions in the left hemisphere. In the present study, the presence of words in the experimental, but not the control condition could explain the left prestriate and parietal region activation evident in Stroop task performance. In addition, previous studies suggest that extrastriate occipital regions, which were active in the adult-child comparison, may be involved in visual word form analysis (Petersen *et al.*, 1988; Pugh *et al.*, 1996). As cognitive development occurs and subjects become more familiar with words and reading, it appears that they exhibit more activation in these parietal areas. Reading skill may be a factor in the activation levels seen in the parietal and parieto-occipital regions during performance of the Stroop task.

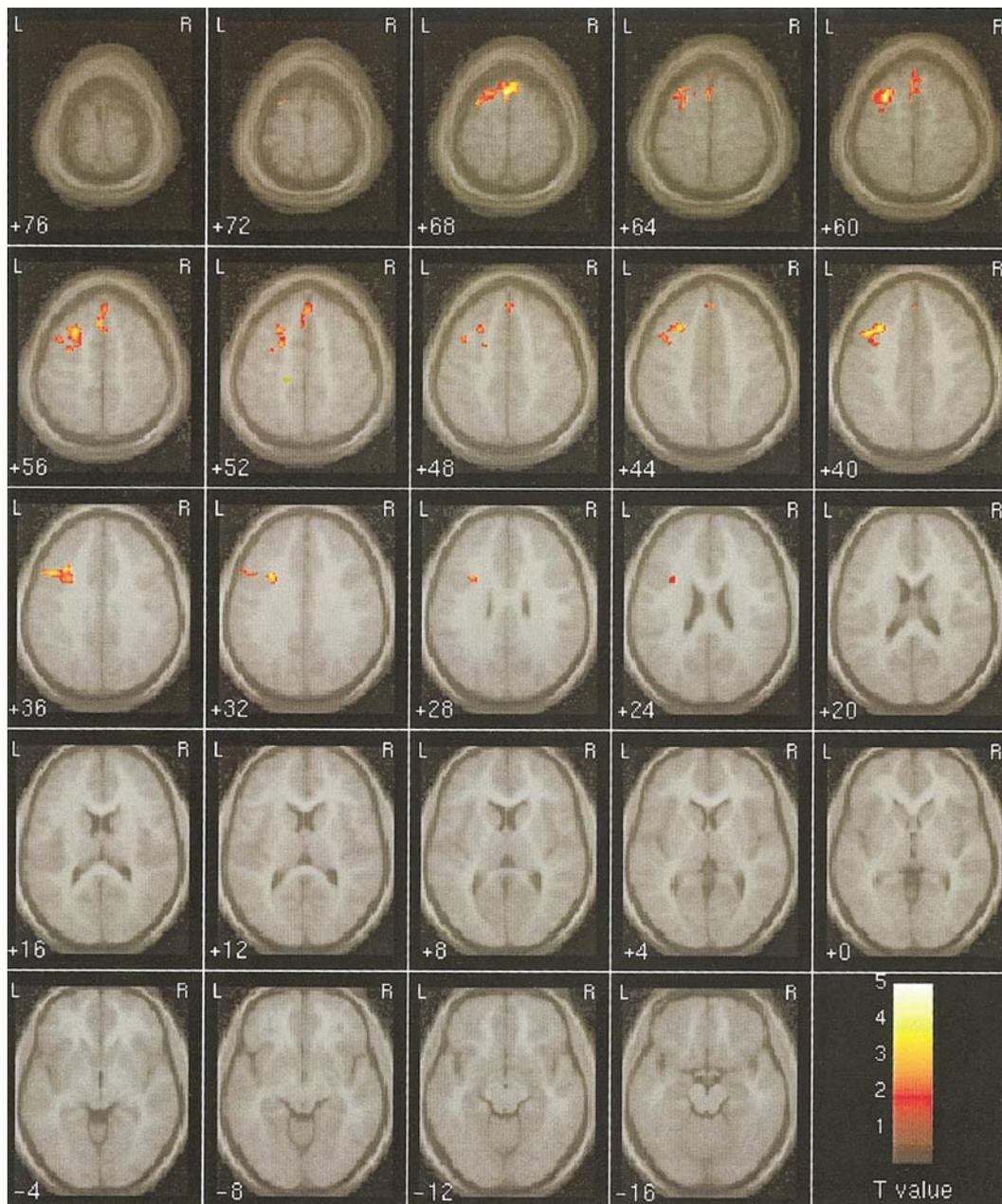


FIG. 6. Only the left middle frontal gyrus and anterior cingulate cortex showed significantly greater Stroop task-related activation in the young adults, compared to the adolescents. There were no differences in the parietal lobe. Other details as described in the legend of Fig. 2.

Anterior Cingulate Cortex

The present study provides evidence for Stroop task-related functional development in the left anterior cingulate cortex. There was a significant positive linear correlation between activation in the left ACC and age. Greater activation in this region also was evident in the adult-adolescent and adult-child comparisons. These differences suggest that functional development in the left ACC continues throughout childhood, adolescence, and into young adulthood.

Stroop task-related activation in the ACC is in agreement with several studies of interference resolution (Bench *et al.*, 1993; Bush *et al.*, 1998; Carter *et al.*, 1995; Pardo *et al.*, 1990). However, compared to Stroop task-related activation in the lateral prefrontal cortex, activation in the anterior cingulate cortex has been observed less consistently. A PET study conducted by Pardo *et al.* (1990) showed that the most robust activation during a Stroop task was in the ACC. Taylor *et al.* (1997) observed that the ACC was active in one of two different Stroop conditions: the Stroop compared to

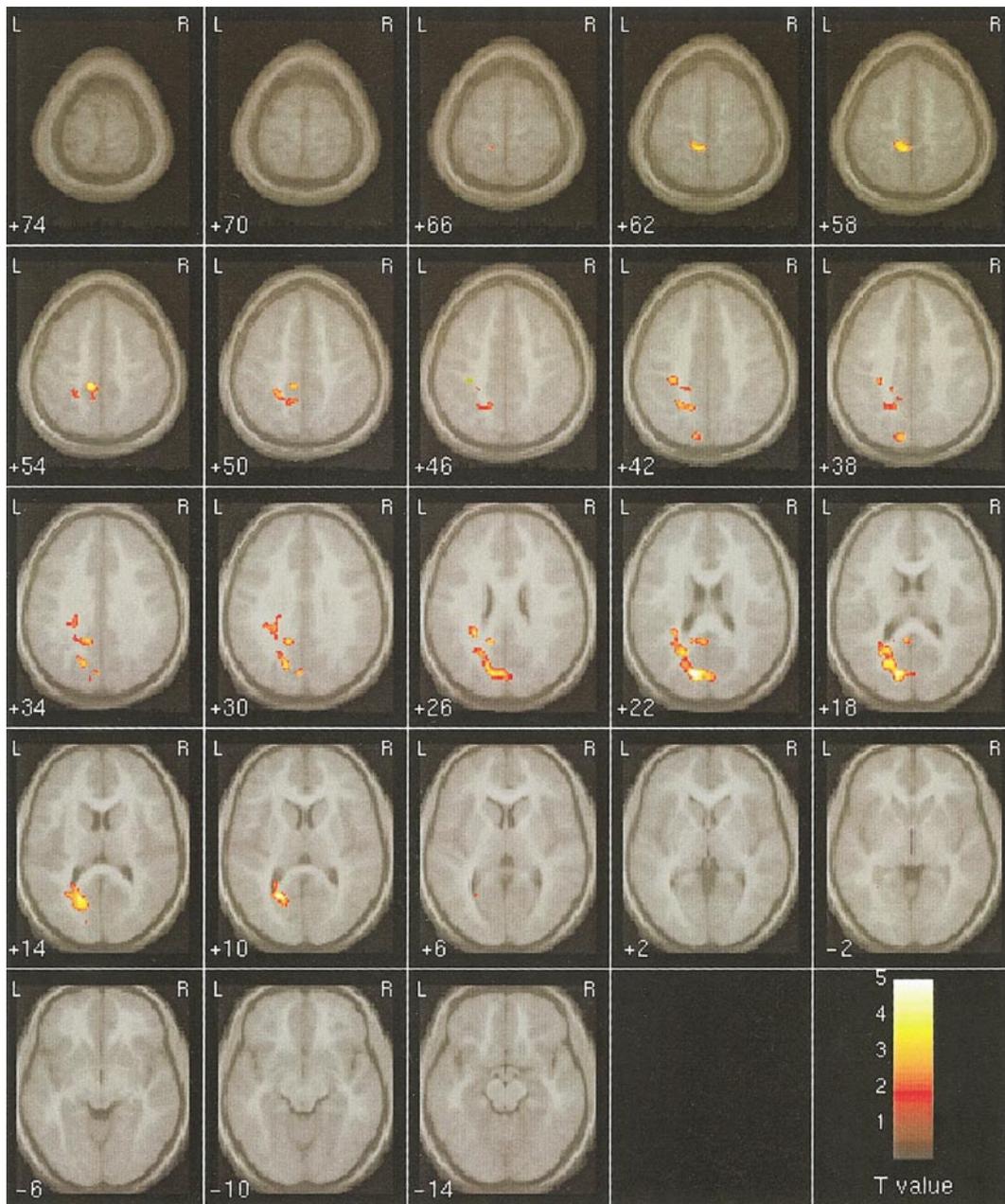


FIG. 7. Brain areas showing significantly greater Stroop task-related activation in the adolescents, compared to the children, included the left parietal and parieto-occipital regions such as the cuneus and posterior cingulate/precuneus. Other details as described in the legend of Fig. 2.

neutral word contrast, but not in the Stroop compared to false font comparison. Bench *et al.* (1993) found activation in the ACC in a Stroop versus colored crosses comparison. However, they did not find a significant correlation between reaction times and regional cerebral blood flow in the ACC and therefore, concluded that activation in the ACC alone could not explain Stroop interference. Activation in the ACC also has been observed during the Go/No-Go response inhibition task in adults (Menon *et al.*, 2001) as well as in

children (Casey *et al.*, 1997). An event-related Go/No-Go task, however, did not yield ACC activation (Garavan *et al.*, 1999).

Neuroimaging studies have suggested that the ACC may be involved in executive control processes such as inhibition of inappropriate responses (Paus *et al.*, 1993), selective attention (Pardo *et al.*, 1990), and monitoring of response conflict (Barch, 1999). The ACC has been shown to be active when subjects are instructed to produce a less practiced response instead of a more

automatic, prepotent response (Barch *et al.*, 2000). These executive control processes are important in the Stroop task. In order to perform the Stroop task, subjects must inhibit the inappropriate response of word reading, pay selective attention to color, and monitor the response conflict between the possible responses of color naming and word reading.

Conclusions

The results of the present study indicate that increased activation occurs with age in a number of brain regions thought to be important in performance of the Stroop task, including the left lateral prefrontal cortex, left parietal/parieto-occipital cortex, and left anterior cingulate cortex. Specifically, activity in the left lateral prefrontal cortex and the anterior cingulate increases linearly with age, suggesting an increase in focal resource recruitment during maturation. This age-related increase in activation occurs in conjunction with better behavioral performance on some measures of the Stroop task.

The present study is the first developmental fMRI study of the color-word Stroop test. As such, the results are preliminary and warrant further investigation. In order to minimize head movement during the scan, we asked the subjects to silently respond to the Stroop task presented within the scanner. Consequently, a limitation of the study is that task compliance and behavioral performance during the scan could not be measured. Future studies should attempt to record verbal responses during fMRI acquisition. More importantly, the differentiation between verbal and nonverbal components involved in the development of interference processing remains to be elucidated. The present study suggests that brain regions involved in word reading and interference resolution processes co-evolve with development. Future studies should attempt to isolate interference processing from word reading in a developmental paradigm.

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