

## ORIGINAL ARTICLE

# Preparatory Engagement of Cognitive Control Networks Increases Late in Childhood

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## Abstract

The ability to engage task control flexibly, especially in anticipation of task demands, is beneficial when juggling different tasks. We investigated whether children in late childhood or early adolescence engaged preparatory task control similar to adults in a trial-wise cued task-switching paradigm. Twenty-eight children (aged 9–15 years) and 30 adults (aged 21–30 years) participated in an fMRI study in which the Cue (preparatory) period across 2 tasks was analyzed separately from the execution of the tasks (the Target period). Children performed more slowly and less accurately than adults, and showed behavioral improvement within the child group age range of 9–15 years. Children exhibited weaker Cue period activation than adults within a number of putative cognitive control regions. In contrast, children exhibited greater activity than adults in several regions, including sensorimotor areas, during the Target period. Children who activated cognitive control-related regions more during the Cue period tended to activate the Target signal age-related regions less, and this correlated with improved accuracy and reaction time on the task, as well as age. The results endorse previous findings that preparatory cognitive control systems are still developing in late childhood, but add new evidence of age-related shifts in activity at the trial level.

**Key words:** adolescence, development, fMRI, fronto-parietal, task-switching

## Introduction

Each of us has to adjust to changing circumstances; it is this capacity that is critical to success in an ever-shifting environment. It has been proposed by our group and by others that there are multiple networks of brain regions involved in this type of task control, that they are anatomically separate from the moment-to-moment processing regions (e.g., primary sensory and motor cortex), and that the control signals they exhibit may operate over different time scales (Posner and Petersen 1990; Corbetta et al. 2000; Braver 2012; Petersen and Posner

2012; Wilk et al. 2012; Miller and Buschman 2013; Botvinick and Braver 2015). This multiple-network model, including a cingulo-opercular task-maintenance network, fronto-parietal adaptive control network, salience network, and dorsal and ventral visual attention networks, has been supported by both task-based and resting-state fMRI research (Dosenbach et al. 2007, 2010; Church, Wenger, et al. 2009; Shulman et al. 2010; Yeo et al. 2011; Bullmore and Sporns 2012; Petersen and Posner 2012; Buckner et al. 2013; Jost et al. 2013; Power and Petersen 2013; Mišić et al. 2014). However, examining the engagement

of these networks within a control-demanding compound trial has not been explored in children.

Developmentally, it is well established that children do not perform at adult levels on a variety of task-control measures (Ridderinkhof and van der Stelt 2000; Bedard et al. 2002; De Luca et al. 2003; Crone et al. 2004; Luna et al. 2004; Diamond et al. 2005; Bunge and Wright 2007; Van Leijenhorst et al. 2007; Chatham et al. 2009; Blackwell and Munakata 2013). Children are slower, show greater perseveration in the face of rule changes, and are less flexible during multitasking or switching, demonstrating greater switch costs. These performance differences are thought to be driven by delayed maturation or delayed implementation of frontal-parietal adaptive systems for cognitive control (e.g., Bunge et al. 2002; Gogtay et al. 2004; Luna et al. 2004; Konrad et al. 2005; Crone, Donohue, et al. 2006; Rubia et al. 2007; Velanova et al. 2008; Wendelken et al. 2011; Wilk and Morton 2012; Rubia 2013).

One possible reason children do poorly on tasks demanding cognitive flexibility, at least in part, is that they fail to prepare adequately for the task at hand. This inadequate preparation could be due to ineffective loading of task parameters (e.g., loading response mappings relevant to that trial's cue) within the given timeframe (Logan and Gordon 2001), in turn requiring greater reliance on moment-to-moment processing. This framing of children's poorer task-control performance (i.e., relatively ineffective task-level control and relatively greater burden on moment-to-moment processing), conceptually similar to the proactive/reactive task-control construct (e.g., Braver 2012; Munakata et al. 2012), has yet to be examined at the subtrial level of functional brain activity in children (though it has been examined with eye-tracking, e.g., Chatham et al. 2009; Chevalier et al. 2010). Thus, the present study focuses on the development of appropriate preparatory period (i.e., in response to a Cue) task control using a Cue-Only catch-trial fMRI design not previously implemented in children [note that Geier et al. (2010) used a similar design in adolescents to study reward components]. Briefly, this incisive task design allowed us to separately characterize blood oxygenation level-dependent (BOLD) signaling associated with processing of the preparatory Cue from that associated with task execution (Target). Cue-Target pairs are intermixed with about 20% Cue-Only catch trials. Participants did not know, and could not anticipate, when a given cue would be followed by a target. Thus, our "Cue-Only" catch trials capture brain activity related to cue processing and allow estimation of cue-specific and target-specific activity from the Cue-Target pairs (Ollinger, Shulman, et al. 2001).

We predicted that, compared with adults, children would have different (i.e., immature) preparatory cognitive control during the Cue period. Specifically, we predicted that the fronto-parietal adaptive task-control network would be particularly affected, given its purported role in fast-acting, flexible control. Finally, we hypothesized that if children were indeed less effective in instantiating preparatory control processes during the Cue period, then additional processing of the Target could be necessary for successful task performance. As our child age range was relatively broad, we were able to test the hypothesis that older children in our sample would exhibit more adult-like performance levels and brain activity.

## Materials and Methods

### Subjects

Thirty adults (12 females) aged 21–30 years (average = 25.6 years) participated in the experiment, and all 30 datasets met

postprocessing eligibility criteria (see details below). Subjects were recruited from the Washington University graduate or medical student population, and from the surrounding St. Louis area. Individuals with contraindications for MRI were excluded. Individuals were also screened for a history of developmental delay, neurologic or psychiatric diagnoses, or the use of psychotropic medications. Each adult was scanned once. Neuropsychological tests were administered for approximately 30 min prior to or immediately following the scanning session (tests described below).

Fifty typically developing children participated in the experiment. All minors were screened as described above for adults. Children and their parents were brought in for a visit prior to the scanning session to undergo consenting, neuropsychological testing, and a mock scanning session. Eight subjects did not continue after the mock visit (due to claustrophobia, extensive dental work, or scheduling difficulties), leaving 42 who were scanned at least once. Twenty-eight child participants (16 males) between ages 9 and 15 years (average = 12.6 years) met postprocessing eligibility criteria (28/42 = 66% scan success). As part of a larger study of adaptive control in developmental disorders, these typically developing children were scanned twice, using nonoverlapping stimuli, with scan dates approximately 2 months apart. Twenty-six of the 28 subjects had 2 days of data that each met eligibility criteria, and were combined as one large set for this analysis to provide the greatest amount of data and power possible per person. All of the group differences reported below remained significant at least at a  $P < 0.05$  level using each day of data separately from the child group. Behavior within the child group revealed faster response times (RTs) at the second session ( $P < 0.001$ ) but no significant difference in accuracy (ACC;  $P = 0.17$ ).

All adult subjects gave informed consent prior to participation. For all minor subjects, verbal assent and parental informed consent to the testing and scanning were acquired. All subjects were compensated for their participation. All aspects of the study were carried out in accordance with the guidelines and approval of the Washington University Human Studies Committee.

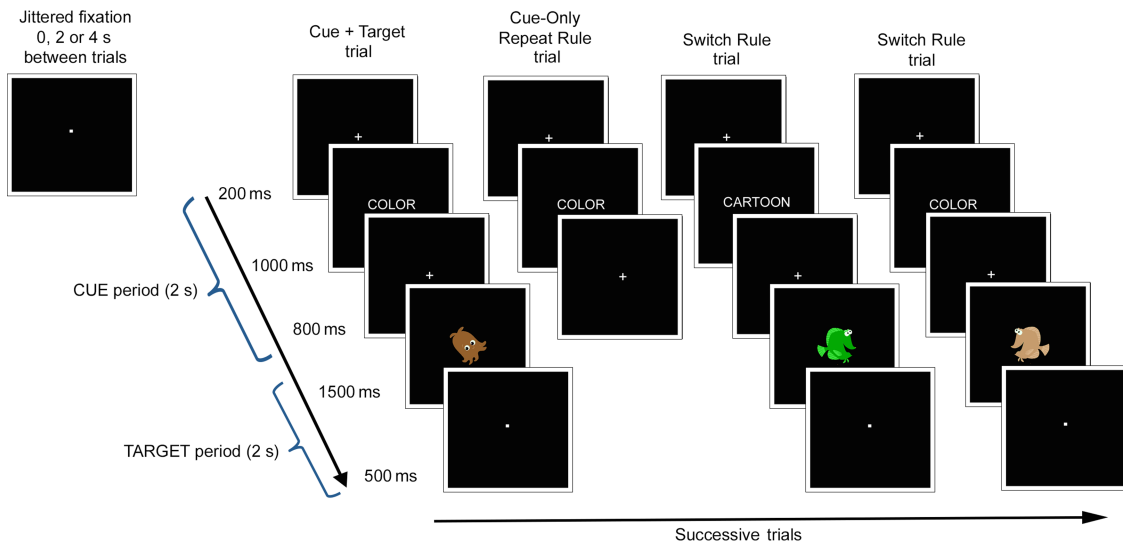
### Neuropsychological Testing

All subjects were tested with the following neuropsychological battery: the two-test WASI estimate of IQ (Vocabulary and Matrix-Reasoning; Wechsler 1999); the Digit Span (forward and backward) and Coding task from the WISC-IV (child) or WAIS-III (adult; Wechsler 1997, 2003); the Woodcock-Johnson III Cross-Out task (Schrack and Wendling 2009); the Stroop Color and Word task (Golden and Golden 2002); and adult and child versions of Trails A and B. These data were collected as part of a larger study, and we report the IQ estimate results here.

### Task and Experimental Design

Subjects performed 6 sets of a cue-switching task displaying 1 of 2 visual, lexical cues ("COLOR" or "CARTOON") followed by a single target picture. The 6 task sets were grouped into 3 sets of 2. For each task run pair, subjects learned two-button choice mappings for 2 colors and 2 cartoon characters adapted from the Disney/Pixar film "Finding Nemo" (e.g., to press the left button in response to the color orange or the cartoon character "Dory," and to press the right button in response to the color purple or the cartoon character "Peach"). The color and orientation of these stimuli were manipulated in Adobe Photoshop CS3.

Subjects were taught the relevant stimulus-response (S–R) mappings for the 2 tasks prior to each pair of scan runs within



**Figure 1.** The task design. Participants saw a dot fixation point when not engaging in a trial. A plus sign indicated a trial beginning, and a word cue was presented on screen for 1000 ms in all capital letters. This was followed by another plus sign, and either the presentation of a target stimulus for 1500 ms containing both task features (COLOR and CARTOON) or the plus sign returned to a dot to indicate the end of the trial (Cue-Only catch trial). Cue-Only trials allowed us to estimate the Cue signal separate from the Target signal. See text for details.

the scanner environment, but while the scanner was offline. Each participant had to verbally repeat the rules aloud and complete a brief practice run offline before starting the first fMRI acquisition of the stimulus pair, and repeat the rules aloud again prior to the second run of the pair.

The task design was highly similar to Baym et al. (2008), but included 21% Cue-Only trials. Forty-seven trials were presented per run (1 first trial, 36 Cue + Target paired trials and 10 Cue-Only trials). Cue-Target paired trials lasted 4 s, whereas Cue-Only trials lasted 2 s (Fig. 1). The Cue-Only trials were combined with the other Cue frames to estimate the Cue signals (Cue + Cue-Only) separate from the Target signals in a manner consistent with Ollinger, Corbetta, et al. (2001).

Color and Cartoon-cued trials were pseudorandomly ordered throughout the scan with 0, 1, or 2 frames (0, 2, or 4 s) of fixation interspersed between them. The order of trial presentation and jittered fixation was determined using the in-house software (bestDesign, Fran Miezin) to allow for maximal efficiency in deconvolving trials from each condition and baseline.

### fMRI Data Collection

Data were acquired using a Siemens MAGNETOM TIM Trio 3.0 T scanner with a Siemens 12-channel Head Matrix Coil (Erlangen, Germany). Head movement was restricted using a thermoplastic mask on the upper face that was created afresh for each entry into the scanner, and which subjects were allowed to keep afterward. A  $T_1$ -weighted sagittal magnetization-prepared rapid gradient-echo (MP-RAGE) structural image was obtained [time echo (TE) = 3.06 ms, time repetition (TR) partition = 2.4 s,  $T_1$  = 1000 ms, flip angle =  $8^\circ$ , 176 slices with  $1 \times 1 \times 1$  mm voxels]. A  $T_2$ -weighted (turbo spin echo structural image (TE = 84 ms, TR = 6.8 s, 32 slices with  $2 \times 1 \times 4$  mm voxels) was collected in the same anatomical plane as the BOLD images.

Functional images were collected using a BOLD contrast-sensitive, gradient-echo, echo-planar sequence (volume TR = 2.0 s, TE = 27 ms, flip angle =  $90^\circ$ , in-plane resolution =  $4 \times 4$  mm, 32 contiguous interleaved 4-mm axial slices). Each task run lasted 144 volumes (4 min 48 sec), and the first 4 frames were dropped at the beginning to allow for signal intensity acclimation.

### fMRI Preprocessing

Functional MRI images were preprocessed to reduce artifacts (Miezin et al. 2000). Preprocessing steps included: (1) correction of odd versus even slice intensity differences attributable to interleaved acquisition without gaps, (2) correction for head movement within and across runs, and (3) within run intensity normalization to a whole-brain mode value (across TRs and voxels) of 1000. All data for each individual were transformed to a common atlas using the high-resolution MP-RAGE scan. The atlas target was a combined adult-child atlas of 12 adults and twelve 7- to 8-year-old children (Mazziotta et al. 1995). All coordinates and images reported here were subsequently transformed to the MNI-152 coordinate space.

### Motion Censoring and Performance Criteria

The motion censoring procedure was based on frame-wise displacement (FD; Van Dijk et al. 2012; Siegel et al. 2013; Power et al. 2014). All volumes whose FD exceeded 0.7 mm were flagged to form a temporal mask for the general linear model [GLM; see Siegel et al. (2013) for additional details]. The model used for analysis ignored all flagged volumes during parameter estimation, equivalent to single-frame regressors.

Our eligibility criteria for any subject, regardless of whether that subject contributed 1 or 2 days of data, were that at least 500 frames of data survived scrubbing with a postscrubbed rms variance of  $<0.8$  mm, and overall task ACC of at least 80%. The postscrubbing rms group data are summarized in Table 1; the prescrubbing mean rms was 0.18 mm (adults) and 0.40 mm (children). An average of 3% of frames was scrubbed for the adult group, and 7.5% for the child group. By combining data from 2 sessions in 26 of 28 children, the child group (average 1435 frames postcensoring) contributed significantly more data to the analysis than the adult group (average 838 frames postcensoring).

### Behavior

Behavior was recorded using a two-button box in the scanner. Behavioral data were analyzed separately for ACC and RT effects

Table 1 Subject groups and matched subgroups

	N	M/F	Age	ACC	RT	MVMT	IQ
All subjects							
Adults	30	18/12	25.55 (2.4)	0.97 (0.03)	703 (147)	0.18 (0.09)	128.1 (7.2)
Children	28	16/12	12.64 (1.8)	0.91 (0.04)	874 (130)	0.36 (0.17)	112.1 (10.6)
t-test (P)				<0.0001	<0.0001	<0.0001	<0.0001
ACC match							
Adults	14	10/4	25.81 (2.8)	0.95 (0.03)	738 (159)	0.19 (0.11)	127.2 (8.2)
Children	14	8/6	13.34 (1.5)	0.94 (0.01)	843 (145)	0.30 (0.16)	113.7 (9.8)
t-test (P)				0.213	0.079	0.048	0.00053
RT match							
Adults	19	10/9	25.65 (2.3)	0.97 (0.03)	788 (112)	0.18 (0.08)	128.7 (7.4)
Children	19	11/8	13.19 (1.7)	0.92 (0.03)	816 (111)	0.35 (0.18)	113.1 (10.3)
t-test (P)				<0.0001	0.43	0.0007	<0.0001
MVMT match							
Adults	18	12/6	25.50 (2.4)	0.97 (0.02)	711 (137)	0.22 (0.09)	128.1 (6.1)
Children	18	10/8	13.00 (1.7)	0.92 (0.04)	856 (144)	0.26 (0.11)	113.4 (10.4)
t-test (P)				<0.0001	0.0039	0.2938	<0.0001
IQ match							
Adults	16	9/7	25.87 (2.6)	0.96 (0.03)	671 (134)	0.19 (0.09)	122.6 (4.3)
Children	16	9/7	12.68 (1.9)	0.91 (0.04)	832 (124)	0.36 (0.19)	119.4 (6.4)
t-test (P)				0.0004	0.0014	0.0048	0.11

ACC: accuracy (% correct); RT: response time (ms); MVMT: postcensoring rms variance (mm); IQ: IQ estimate from two-test WASI. Light gray shading indicates a subgroup that was considered “matched” on that variable.

using 2 within-group factors (Task, Switch) and 1 between-group factor (Age) in a GLM with repeated measures in SPSS Inc. (2007).

## fMRI Analyses

Statistical analyses of the BOLD data used the GLM as previously described (Miezin et al. 2000; Schlaggar et al. 2002; Brown et al. 2005). Temporal masks (movement censoring) were incorporated into the model estimation. Subjects with multiple scan sessions were analyzed as one long day of data, after preprocessing of each day separately (aligning all data to the subject’s best MP-RAGE—most often collected during the first scanning session). Analyses did not assume a shape of the hemodynamic response, and were conducted using the in-house software programmed using Interactive Data Language (IDL) (ITT Visual Information Solutions, Boulder, CO, USA) and C (Miezin et al. 2000; Ollinger, Corbetta, et al. 2001). GLMs also included baseline terms and linear drift terms.

Compound Cue + Target trials were modeled separately for Cues and Targets, with Target onsets offset by 2 s from the Cue onsets, and each regressor lasting 18 s (9 TRs). Correct trials were modeled separately from error trials. Error trials were modeled as a single event type, starting at the Cue onset of an incorrect response (lasting 20 s, 10 TRs).

For each type of signal (Cue and Target), an ANOVA was created with age (adult/child) as a two-level between-group factor, and Task (cartoon/color) and Switching (task repeat/switch), as two within-group factors (a 2 x 2 x 2 repeated-measures ANOVA for Cue and for Target).

In-house peak-finding software was run on the ANOVA images (peak\_4dfp, Abraham Snyder) to extract regional timecourses, corrected for multiple comparison correction using Monte Carlo simulation and a score of  $z > 3.5$ , with a cluster size of 24 voxels (Forman et al. 1995; McAvoy et al. 2001). Visualization of timecourses was important to reveal the direction of effects. Because the statistics from those regions are biased toward the effect observed, only timecourses and timecourse peak

magnitudes are shown; no statistics are derived from non-a priori regions of interest (ROIs).

## Cue-Target Signal Interactions in Children

Because we hypothesized that preparation during the Cue period would aid success on the task, we wished to explore whether children who most engaged Cue-related brain regions were the same children who had less engagement of Target-related, potentially compensatory, brain regions. Twenty-five frontal and parietal regions that had a significant age effect during the Cue period were clustered together and the average % BOLD signal peak activity (average of TR 4 and 5) from that cluster was examined for each child. These 25 frontal and parietal regions all showed positive activity that was significantly greater in adults than in children (Table 2, green highlighted regions).

Seventeen regions that had a significant effect of age (larger in children) during the Target period were clustered together, and the average peak % BOLD signal change in Target activity from that cluster was also examined for each child (orange and white regions of Table 3).

The correlations between peak Cue activity in the Cue cluster and peak Target activity in the Target cluster were examined across individuals in each age group, as well as the correlations between peak activity and age, RT, or ACC.

## Secondary fMRI Analyses

**Applied ROI Analyses.** Resting-state functional connectivity (RSFC) MRI has been used to study intrinsic functional networks of the human brain (Fox and Raichle 2007; Power et al. 2011; Cole et al. 2014). We overlaid one version of resting-state-derived brain communities (functional area borders) (Power et al. 2011) with the main effect of Cue and main effect of Target. The RSFC area borders and MNI space data from this experiment were overlaid in the same CARET brain space: the Conte69 midthickness atlas in 164k (Van Essen 2012; Van Essen et al. 2012).

Furthermore, the original 18 fronto-parietal and cingulo-opercular ROIs reported in a meta-analysis of task fMRI studies

Table 2 Regions showing a significant group effect during the Cue period

X	Y	Z	Voxels	Location	Direction	Activity
-50	0	50	117	Left precentral Cx	Adult > child	POS
-43	-3	59	84	Left superior frontal Cx	Adult > child	POS
-42	35	31	53	Left DLPFC	Adult > child	POS
-25	1	58	274	Left superior frontal Cx	Adult > child	POS
-7	9	57	319	Medial superior frontal Cx	Adult > child	POS
4	18	49	188	Medial superior frontal Cx	Adult > child	POS
29	5	56	341	Right superior frontal Cx	Adult > child	POS
30	43	18	122	Right anterior frontal Cx	Adult > child	POS
31	28	-3	161	Right IFG/insula	Adult > child	POS
37	33	38	69	Right DLPFC	Adult > child	POS
44	2	54	143	Right superior frontal Cx	Adult > child	POS
53	11	17	98	Right IFG/insula	Adult > child	POS
-56	-3	37	195	Left frontal Cx	Adult > child	POS
41	4	41	47	Right frontal Cx	Adult > child	POS
-41	-41	42	296	Left inferior parietal Cx	Adult > child	POS
-39	-46	54	152	Left superior parietal Cx	Adult > child	POS
-29	-46	45	140	Left inferior parietal Cx	Adult > child	POS
-28	-52	55	169	Left superior parietal Cx	Adult > child	POS
-28	-73	34	75	Left inferior parietal Cx	Adult > child	POS
-20	-65	59	81	Left superior parietal Cx	Adult > child	POS
8	-64	48	134	Medial superior parietal	Adult > child	POS
31	-45	46	326	Right inferior parietal Cx	Adult > child	POS
44	-44	54	239	Right superior parietal Cx	Adult > child	POS
55	-39	39	210	Right inferior parietal Cx	Adult > child	POS
57	-43	27	245	Right supramarginal gyrus	Adult > child	POS
-49	-70	-13	62	Left occipital/temporal Cx	Adult > child	POS
-35	-49	-16	72	Left occipital/temporal Cx	Adult > child	POS
-18	-88	-7	238	Left occipital Cx	Adult > child	POS
-13	-97	14	118	Left occipital Cx	Adult > child	POS
-6	-92	6	124	Medial occipital Cx	Adult > child	POS
-3	-78	-14	156	Medial occipital/cerebellum	Adult > child	POS
1	-79	10	216	Medial occipital Cx	Adult > child	POS
10	-86	5	207	Medial occipital Cx	Adult > child	POS
20	-77	-7	151	Right occipital Cx	Adult > child	POS
22	-91	4	193	Right occipital Cx	Adult > child	POS
-46	-68	-1	346	Left temporal Cx	Adult > child	POS
60	-47	14	205	Right superior temporal sulcus	Adult > child	POS
61	-41	4	227	Right temporal Cx	Adult > child	POS
51	-61	0	264	Right temporal Cx	Adult > child	POS
-21	-1	12	212	Left caudate	Adult > child	POS
-10	5	6	192	Left putamen	Adult > child	POS
-20	8	-1	209	Left putamen	Adult > child	POS
2	-18	14	225	Medial thalamus	Adult > child	POS
7	-7	10	180	Right thalamus	Adult > child	POS
20	0	18	148	Right caudate	Adult > child	POS
14	6	6	267	Right putamen	Adult > child	POS
29	7	-4	198	Right putamen	Adult > child	POS
-30	-58	-27	342	Left cerebellum	Adult > child	POS
-12	-75	-22	305	Left cerebellum	Adult > child	POS
10	-73	-24	100	Right cerebellum	Adult > child	POS
32	-54	-25	251	Right cerebellum	Adult > child	POS
-55	-32	47	107	Left inferior parietal Cx	Adult +, child -	MIX
-28	-24	1	170	Left lentiform	Adult +, child -	MIX
26	-14	1	162	Right lentiform	Adult +, child -	MIX
34	-45	-11	73	Right occipital lobe	Adult +, child -	MIX
29	-67	-11	202	Right extrastriate/temporal	Adult +, child -	MIX
52	-15	25	43	Right postcentral gyrus	Adult +, child -	MIX
-47	28	-9	65	Left inferior frontal gyrus	Adult > child	NEG
-16	40	44	42	Left anterior frontal Cx	Adult > child	NEG
-15	30	51	173	Left anterior frontal Cx	Adult > child	NEG
19	26	51	112	Right anterior frontal Cx	Adult > child	NEG
4	52	32	108	Medial frontal Cx	Adult > child	NEG
-3	52	21	201	Medial frontal Cx	Adult > child	NEG
1	16	27	151	<b>Medial frontal Cx</b>	<b>Child &gt; adult</b>	<b>NEG</b>
-6	-45	37	104	Precuneus	Adult > child	NEG
8	-50	33	82	Precuneus	Adult > child	NEG
14	-45	47	200	<b>Precuneus</b>	<b>Child &gt; adult</b>	<b>NEG</b>
-22	-50	-4	41	<b>Left parahippocampal gyrus</b>	<b>Child &gt; adult</b>	<b>NEG</b>
-46	-62	43	136	Left angular gyrus	Adult > child	NEG
-47	-71	35	124	Left angular gyrus	Adult > child	NEG
49	-59	38	135	Right angular gyrus	Adult > child	NEG

Note: Coordinates are in the MNI space. Three regions exhibited greater activity in children (in bold). Green highlighted regions formed the Cue cluster for the Cue-Target interaction analysis (see text for details).

**Table 3** Regions showing a significant Age effect during the Target period

X	Y	Z	Voxels	Location	Direction
-44	-2	29	126	Left frontal Cx	Child > adult
-33	2	31	164	Left frontal Cx	Child > adult
-27	-18	69	32	Left frontal Cx	Child > adult
-21	-13	48	50	Left frontal Cx	Child > adult
5	-10	66	78	Midline frontal Cx	Child > adult
7	-10	55	157	Midline Frontal Cx	Child > adult
14	1	38	145	Right frontal Cx	Child > adult
41	-3	32	48	Right frontal Cx	Child > adult
-34	-93	-3	48	Left occipital Cx	Child > adult
-23	-100	-3	70	Left occipital Cx	Child > adult
26	-100	-2	39	Right occipital Cx	Child > adult
38	-89	2	126	Right occipital Cx	Child > adult
-36	-30	64	48	Left parietal Cx	Child > adult
34	-71	-26	142	Right cerebellum	Child > adult
-1	-28	19	191	Subcortical	Child > adult
24	-3	17	32	Subcortical	Child > adult
-25	-5	62	34	Left frontal Cx	Adult before child peak
61	-14	34	28	Right frontal Cx	Adult > child
-19	-85	-6	155	Left occipital Cx	Adult > child
14	-97	2	30	Right occipital Cx	Adult > child
-62	-14	33	44	Left parietal Cx	Adult > child
18	-47	69	90	Right parietal Cx	Adult > child
52	-29	57	43	Right parietal Cx	Adult > child
55	-39	22	105	Right parietal Cx	Adult > child
35	-45	-18	51	Right temporal Cx	Adult > child

Note: Coordinates are in the MNI space. Sixteen regions exhibiting greater activity in children (peach color) and one ambiguous region (white) were used in the Target cluster for the Cue-Target interaction analysis (see text for details).

(Dosenbach et al. 2006) were examined for age differences in the Cue and Target periods separately. Timecourse  $\times$  Age interactions within those regions were coded at a sphericity-corrected  $P < 0.05$  and  $P < 0.001$  level.

**Subgroup Analyses.** The 2 age groups differed on numerous factors besides age, including IQ and RT (see Results; [Supplementary Material](#)). For ROI analysis from significant ANOVA interactions, the peak activity in each region was compared visually with the peak activity within 4 subgroups matched on individual behavioral factors [RT, ACC, Intelligence Quotient estimate from the two-subtest WASI (IQ), and remaining movement postcensoring (MVMT); Table 1]. Matching was determined for subgroups if they were no longer significantly different on that factor, had numerically similar group averages for the factor of interest, and their group average age had not become more than a year different from the full group. It was not possible to create a single subset that matched between groups on all variables of interest. Instead, each variable of interest was addressed separately. For each subgroup, individuals most distant from the central tendency were removed, one at a time, until the groups were no longer different. This approach allowed for retention of the maximum number of individuals for each variable of interest.

A region was determined to be robust to these particular factors (e.g., not driven by RT or IQ) if the pattern of peaks of timecourses across the 5 groupings (whole group and 4 subgroups) was consistent and highly similar. These results are reported in [Supplementary Figures 2 and 3](#).

A separate GLM was created for each individual that regressed out RT using a single, mean-centered regressor across all event

types for each run, in addition to the above modeled events. Event files were coded using the individual RT for each correct Target trial. Because error trials were coded in a way that combined Cue and Target aspects together, only correct trial RTs were included in the model. The main effect of the RT regressor and the RT interaction with age were examined at a whole-brain level (see [Supplementary Fig. 4](#)).

## Results

### Behavior

The subject group and matched subgroup characteristics are presented in Table 1. Consistent with the task-switching literature and our predictions, adults were significantly faster and more accurate than children (RT  $P < 0.0001$ ; ACC  $P < 0.0001$ ; Adult 703 ms, 97%; Child group 874 ms, 91%). The age groups also differed on IQ estimates and postcensoring movement variance estimates. Four subgroups were created that were “matched” (i.e., not statistically different, and with similar means) on each of the differing factors (Table 1; see [Supplementary Material](#)).

Behavior is shown in Figure 2A. There was a main effect of Switching/Repeating tasks, such that subjects were faster and more accurate when the rule was the same as on the previous trial than when the rule switched (RT  $P < 0.0001$ ; ACC  $P < 0.0001$ ; Repeat 774 ms, 95%; Switch 816 ms, 92%). See [Supplementary Material](#) for an examination of Task effects.

Beyond the main effect of Group, there were no significant interactions of Group with any of the within factors for RT ( $P > 0.05$ ). There was a significant interaction of Group  $\times$  Switching ( $P < 0.001$ ) for ACC, with adults having higher ACC than children in all cases. There was a significant correlation of Age within the child group for overall RT ( $r = -0.44$ ,  $P < 0.05$ ) and ACC ( $r = 0.43$ ,  $P < 0.05$ ), but not within the adult group (RT  $r = 0.15$ ,  $P = 0.42$ , ACC  $r = 0.09$ ,  $P = 0.64$ ; Fig. 2B).

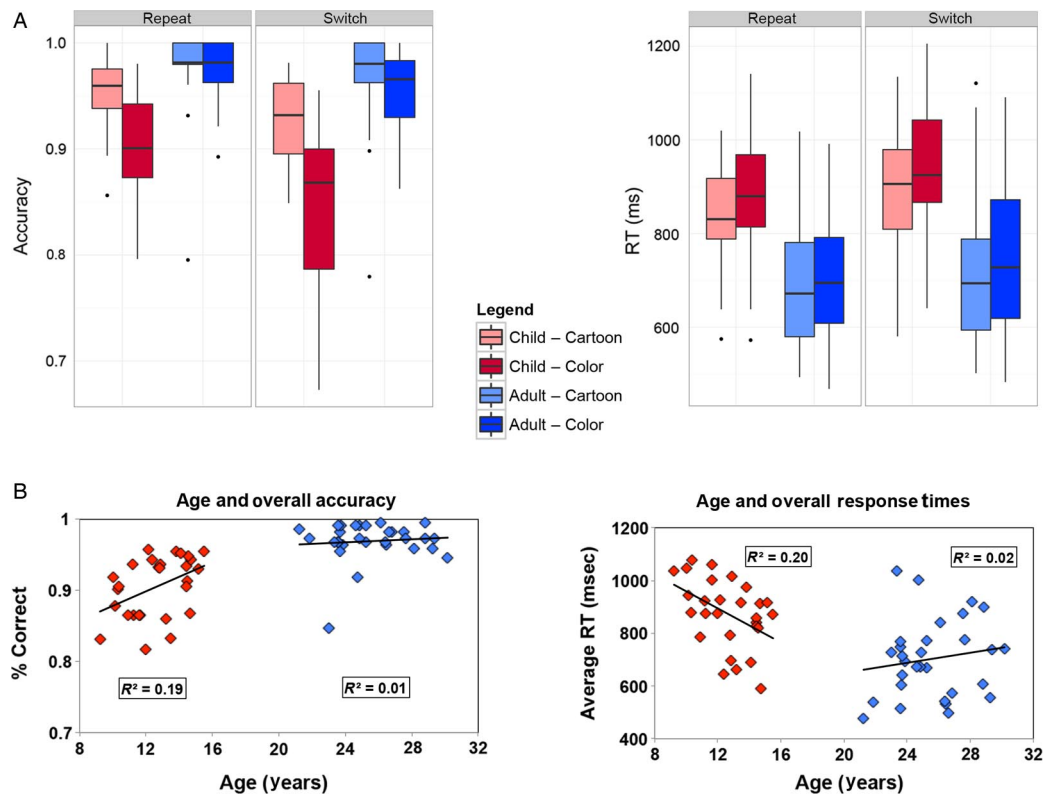
There was no significant behavioral effect of interspersing Cue-Only trials. When RT and ACC were sorted depending on whether the current trial followed a compound Cue + Target trial or followed a Cue-Only trial, there were no significant differences (RT  $P = 0.89$  and ACC  $P = 0.61$ ).

### Imaging: Cue Period

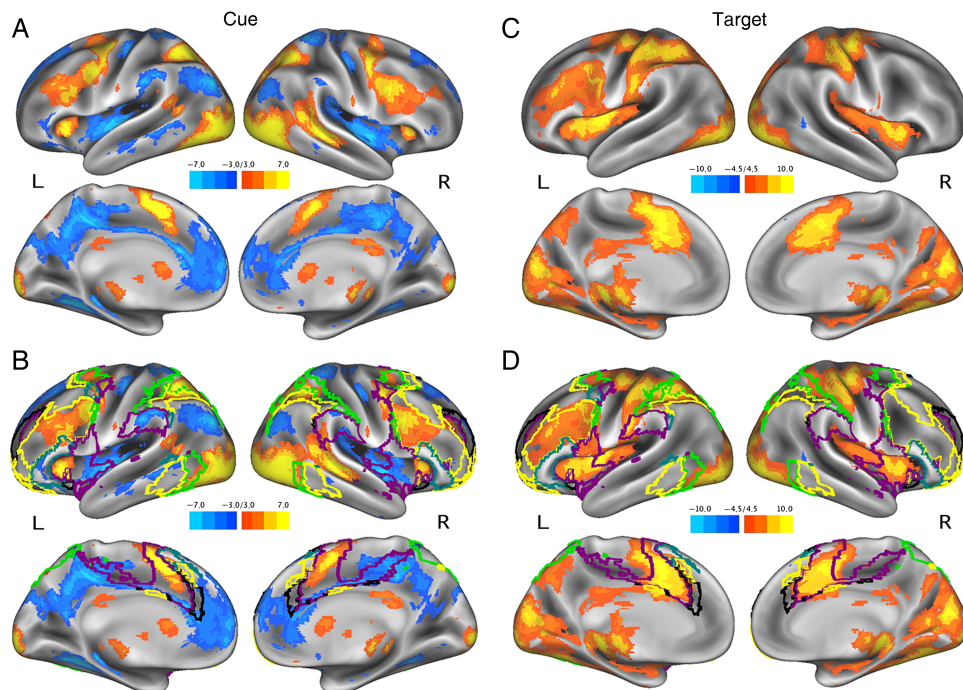
We hypothesized that fronto-parietal control regions would be particularly engaged during the Cue period. The main effect of Cue image across all subjects was very robust (Fig. 3A), and many regions hypothesized to be important in task control were observed, including activity in dorsal frontal and parietal areas, bilateral temporo-parietal junction, medial frontal gyrus, and inferior frontal gyrus. Extensive bilateral occipital activity was also observed, as well as significant negative activation in default-mode regions.

When the RSFC areas derived from previous adult data (Power et al. 2011) were overlaid on the main effect of Cue results, it appeared that many putative control systems were engaged, including fronto-parietal (yellow), dorsal attention (green), and cingulo-opercular (purple) systems (Fig. 3B). Thus, we did not see our predicted targeting of the fronto-parietal network, but rather observed engagement of multiple control networks. Many peaks of activity fit well within the FC-defined area borders. Motor activity was minimal in the Cue image, as was expected, given the lack of motor response during the Cue period.

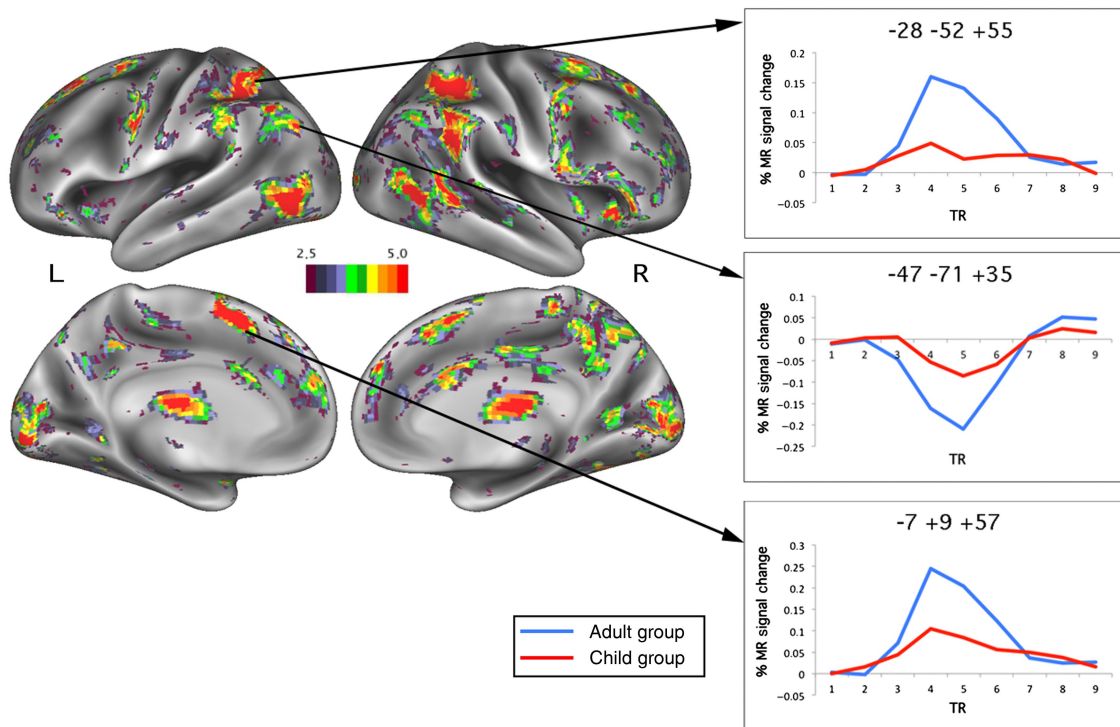
Consistent with our hypothesis that children would fail to engage in cue processing in the same way as adults, there were a great number of group differences during the Cue period (Fig. 4



**Figure 2.** The behavioral results. (A) Box plots: The children were slower and less accurate than adults, especially for the COLOR task (darker colors) and for switch trials (right halves of the graphs). (B) Correlations: While adults did not show significant change over age (blue; 21–30 years), ACC and RTs improved over age within the child group (red; 9–15 years).



**Figure 3.** The main effect of Cue and Target. (A) The main effect of the Cue period across all participants. Yellow regions have timecourse peaks greater than zero, while blue regions have negative peaks. (B) The main effect of Cue overlaid with putative control-related RSFC functional area borders from Power et al. (2011). (C) The main effect of the Target period across all participants. (D) The main effect of Target overlaid with putative control-related RSFC functional area borders from Power et al. (2011). L: left; R: right; the color bar is scaled by Monte Carlo corrected z-score. RSFC-derived border colors: yellow: fronto-parietal; purple: cingulo-opercular; bright green: dorsal attention; sea green: ventral attention; black: salience network.



**Figure 4.** Significant age effects during the Cue period. The vast majority of significant age regions was more active in adults (but see 3 regions in Table 3 that were more negative in children). Exemplar timecourses are shown from a parietal region (fronto-parietal control network), the left angular gyrus (default network), and medial frontal/anterior cingulate (cingulo-opercular control network). In general, the regional age effects were robust to matching on individual factors and involved numerous task-control networks. The color bar indicates Monte Carlo corrected z-score thresholds.

and Table 2). These differences were not limited to the fronto-parietal network, but were rather widespread: Regions of difference included members of putative dorsal attention, fronto-parietal, cingulo-opercular, and default networks among others. In all but 3 cases, adults exhibited greater Cue activity (larger in either positive or negative directions from a flat baseline) than children. In the 3 regions with greater BOLD activity in children, the activity was negative (see bolded regions in Table 2). The pattern of greater activity in adults was robust to subgroup matching on movement, estimated IQ, ACC, and RT (see [Supplementary Fig. 2](#)).

### Imaging: Target Period

The Target period potentially captured both control and response processing. The main effect of Target image across all participants was highly reliable. Many regions important for execution of the task (i.e., bilateral occipital cortex and finger motor cortex) were active (Fig. 3C). Task-control-related activity was also present, particularly in the left frontal part of the frontal-parietal network; activity in putative control regions was less extensive than in the Cue period. When the RSFC borders were applied, there was overlap of engagement with left dorsal attention (green) and fronto-parietal (yellow) networks, as well as the medial frontal cortex of the cingulo-opercular (purple) network (Fig. 3D). There was a notable lack of negative activity, including in the default network.

We predicted that the child group, failing to engage in Cue processing sufficiently, might have additional Target period activity relative to adults. The Target timecourse  $\times$  Age group interaction image had fewer regions of significant difference than the Cue period, but many regions had greater activity in the children than in the adults (Fig. 5 and Table 3, orange regions). These

differences appeared to persist despite subgroup matching for 4 behavioral factors (see [Supplementary Fig. 3](#)). Regions with significantly greater activity in children included medial supplementary motor cortex, left frontal cortex, “finger” motor cortex, and occipital cortex. Adults had greater activity than children in the Target period primarily in occipital cortex and right inferior parietal cortex (Table 3, green regions).

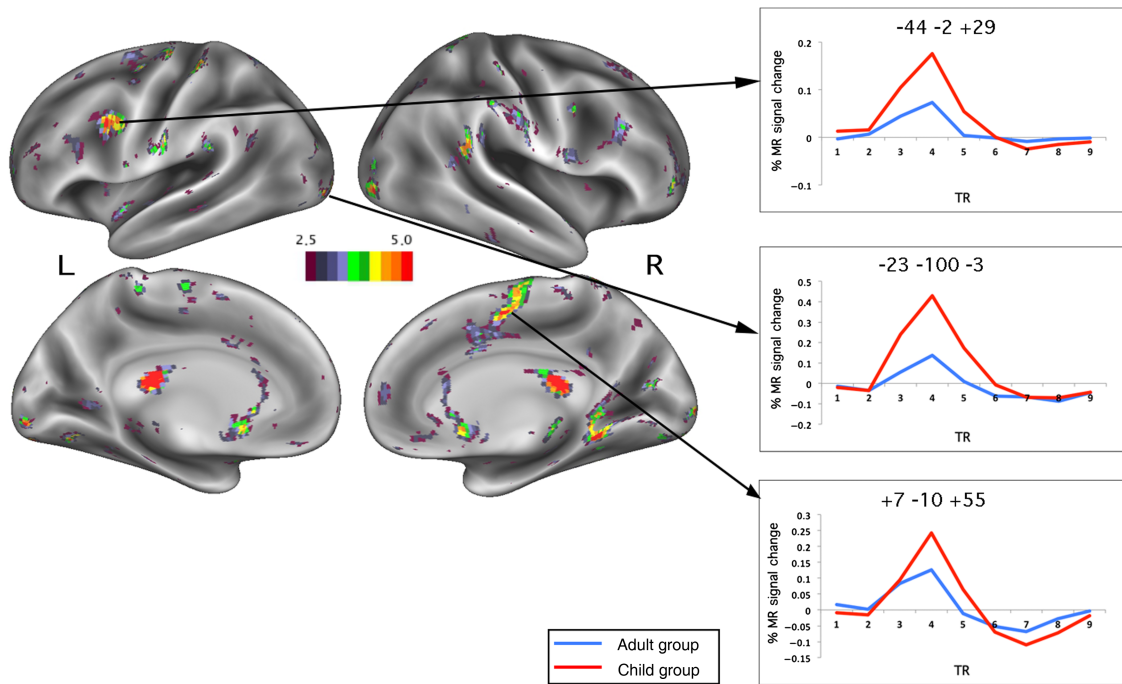
### Imaging: Effects of Switching

We hypothesized that age differences would extend to switch costs during the tasks, but we saw highly similar switch activity in our 2 age groups. There was a strong main effect of switching (a trial that repeats the same task as the previous trial vs. switching to a new task) for both the Cue and Target signals (Fig. 6).

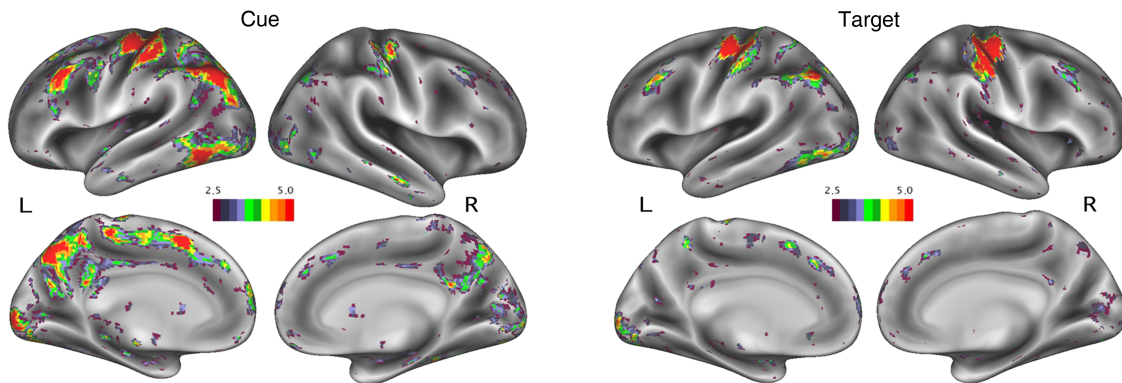
In the Cue analysis, the results were markedly lateralized, with many of the positive and negative regions occurring in the left hemisphere. An examination of the timecourses from these regions revealed that many of the results were driven by Switch trials having a larger peak than Repeat trials, but also by Repeat trials having a sustained positive tail compared with Switch trials (data not shown). There were numerous regions within the default-mode network that showed a more negative peak for Repeat trials compared with Switch trials, but still had a larger late positive sustained tail.

There was only one significant Switch  $\times$  Age interaction, in the right frontal cortex, where adults had a Repeat  $>$  Switch effect, but children did not (data not shown).

In the Target analysis, bilateral finger motor cortex had the strongest effect, where the tails of the switching timecourses were more sustained than the repeat timecourses.



**Figure 5.** Significant age effects during the Target period. The majority of these regions was significantly larger in the child group than in the adult group. Exemplar timecourses are shown for a left frontal region (fronto-parietal control network), an occipital region, and a paramotor region. In general, the regional age effects were robust to matching on individual factors. The color bar indicates Monte Carlo corrected z-score thresholds.



**Figure 6.** Effects of switching between tasks. Regions during the Cue period (left) and the Target period (right) that showed a significant difference between consecutive trials of the same task and trials that switched between tasks. Note the left lateralized results of the Cue-switching effect, which is consistent with previous switch trial investigations (e.g., Bunge et al. 2003). L: left; R: right. The color bar indicates Monte Carlo corrected z-score thresholds.

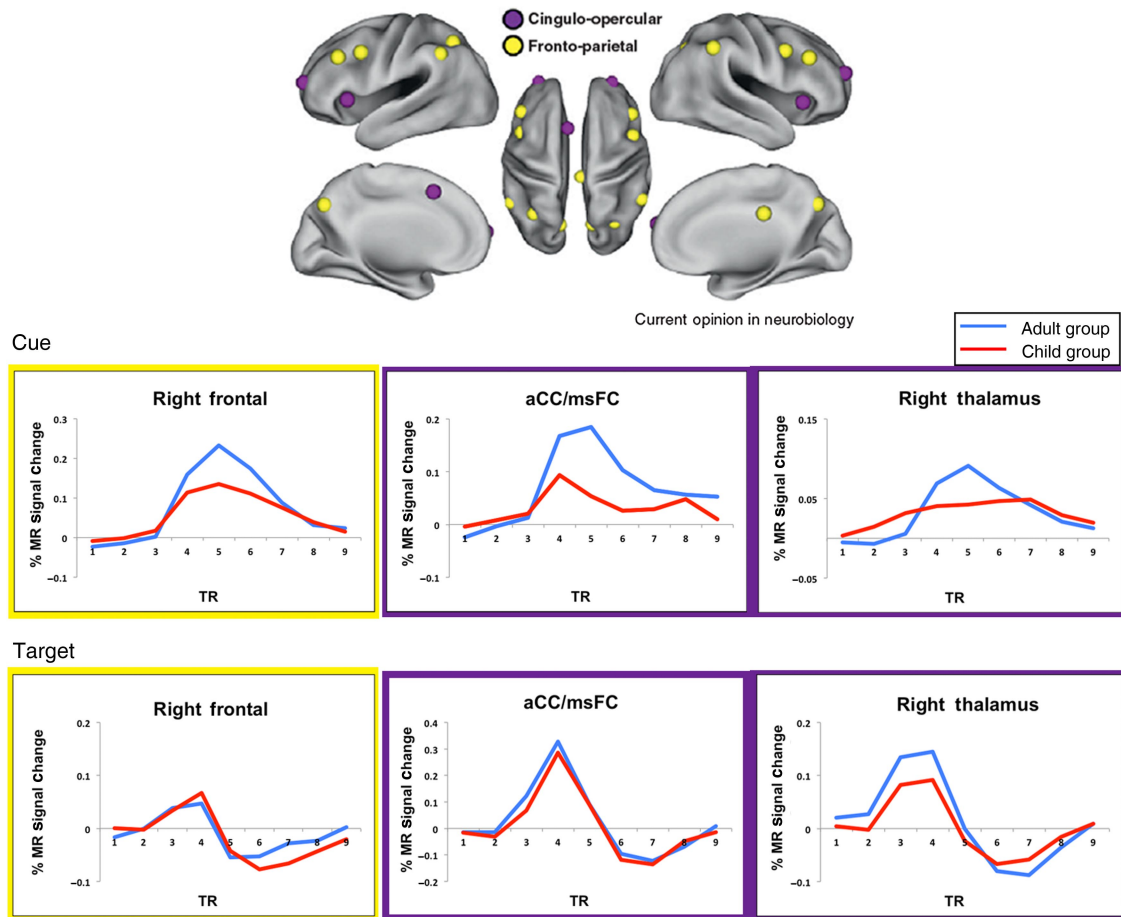
There were no significant interactions with Age and Switching in the Target period.

### Imaging: Application of Control Network ROIs

Eighteen ROIs previously found to be important in networks of task control were applied to this dataset to examine age effects within fronto-parietal network activity more specifically (Fig. 7; Dosenbach et al. 2007). However, numerous members of both the fronto-parietal and cingulo-opercular network were significantly different over age during the Cue period (4 fronto-parietal and 3 cingulo-opercular ROIs at the  $P < 0.05$  level, with 3 additional fronto-parietal and 2 cingulo-opercular ROIs at the  $P < 0.001$  level), whereas only one, the right thalamus, was significantly different over age group during the Target period ( $P < 0.05$ ). In all cases, adults had greater activity than children.

### Imaging: Interactions Between Cue and Target Activity

Because our child group covered a large age range, we wished to study whether there were differences within the child group (e.g., older children or higher-performing children) in terms of the amount of control activity observed during the Cue or Target periods. All frontal and parietal regions with significantly greater activity in adults than in children during the Cue period were averaged into a single cluster to examine individual activity correlations within the child group (green regions, Table 2). A similar cluster was made of regions with significantly greater activity in the children during the Target period (orange and white regions, Table 3). The hypothesis was that the children who were “more adult-like” would engage the Cue cluster more and the Target cluster less, supporting the idea that the extra Target activity observed in children is



**Figure 7.** Study of applied control network ROIs. Eighteen regions from the fronto-parietal adaptive control network (yellow) and cingulo-opercular task-maintenance network (purple) were applied to the current dataset (Dosenbach et al. 2007). The 18 regions are shown on the brain adapted from Power and Petersen (2013). There was significantly greater activity for adults in many of these regions during the Cue period (see Results). Timecourses are shown for 3 of the regions that were different over age group for the Cue period ( $P < 0.001$  for right frontal and dACC/MSFC ROIs,  $P < 0.05$  for right thalamus). Only the right thalamus ROI had different age group activity during the Target period ( $P < 0.05$ ). dACC/MSFC: dorsal anterior cingulate cortex/medial superior frontal cortex.

related to compensatory processing due to failure to engage the Cue properly.

Within the child group, there was a strong negative correlation between engagement during the Cue period in the Cue cluster, and during the Target period in the Target cluster ( $r = -0.66$ ,  $P < 0.001$ ; Fig. 8). Children who engaged frontal or parietal regions more than their peers during the Cue period tended to engage potential compensatory Target regions (in occipital and frontal cortex) less. There was a strong relationship with age for both signal types, such that engagement of the Cue cluster increased over age within the child group ( $r = 0.52$ ,  $P < 0.005$ ) and engagement of the Target cluster decreased over age ( $r = -0.45$ ,  $P < 0.05$ ; Fig. 8). These Cue–Target engagement relationships were not present within the adult group:  $r = -0.12$  for the correlation of Cue activity with Target activity and  $r = -0.04$  and  $0.06$  for Cue and Target activity, respectively, correlated with age in the adult group.

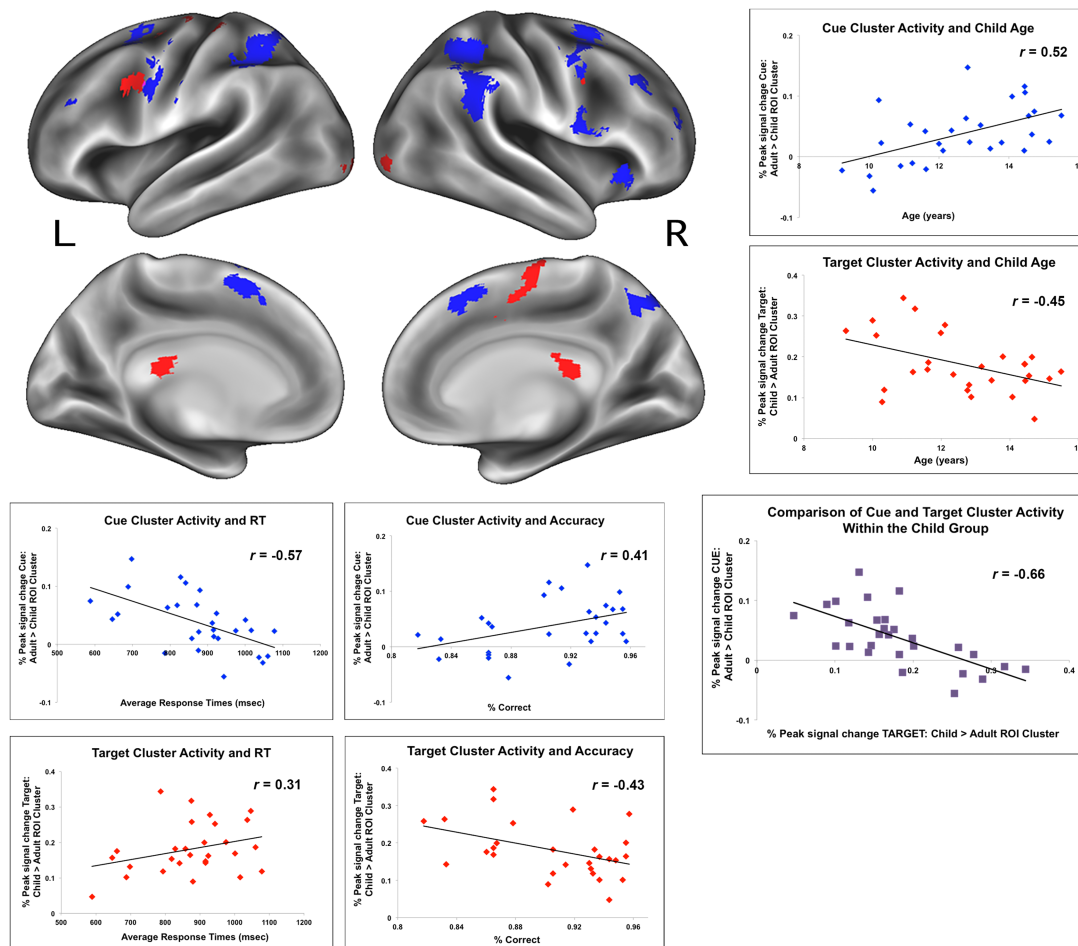
ACC was also positively correlated with engagement of the Cue cluster ( $r = 0.41$ ,  $P < 0.05$ ) and negatively correlated with engagement of the Target cluster ( $r = -0.43$ ,  $P < 0.05$ ) in the child group, but not in the adult group. Engagement of the Cue period in frontal and parietal regions by a child strongly correlated with faster RTs to the Target ( $r = -0.57$ ,  $P < 0.005$ ), and there was a slight correlation with engagement of the Target cluster and slower

RTs ( $r = 0.31$ ,  $P = 0.11$ ). There was no correlation with estimated IQ in the children for either signal (Cue:  $r = -0.05$ ,  $P = 0.80$ ; Target:  $r = -0.04$ ,  $P = 0.84$ ).

## Discussion

We report an examination of cue signal processing separate from task execution (the Target period) during a cued switching task in children/adolescents and young adults. We use an incisive method (separating cue from target signaling) within a developmental population to study preparatory processing directly.

We predicted that putative adaptive task-control regions, particularly those in the fronto-parietal network, would be particularly engaged during task preparation on a trial-by-trial basis, and might change over development. We found that those regions were indeed differentially active between children and adults, but that other putative task-control networks, including cingulo-opercular and ventral attention, were as well. Furthermore, we observed control network (fronto-parietal and cingulo-opercular) engagement during the Target period, but this activity was, on the whole, more similar between children and adults. Perhaps most intriguing were the activity differences observed between the child and adult groups during the Cue period, and the relationship between Cue activity and Target activity



**Figure 8.** Study of Cue-Target interactions within the Child group. Brain: 25 frontal and parietal regions from the Cue-Age interaction (all Adult > Child) were clustered (blue regions). Seventeen Target signal regions (Child > Adult) were clustered from the Target-Age interaction (red regions). Scatterplots: top right: The engagement of the Cue cluster (blue dots) increased with age between 9 and 15 years, and the engagement of the Target cluster (red dots) declined. Bottom right: Individual children who engaged the Cue cluster more during the Cue signal tended to engage the Target signal cluster less during the Target period (purple scatter plot). Bottom left: RTs and ACC for the study also showed improvements correlated with Cue cluster engagement (blue dots) and poorer performance correlated with greater engagement of the Target cluster (red dots). None of these effects were significant in the adult group.

within the child participants. We demonstrate functional significance of the cue processing by its relationship with ACC and RTs within the child group. We contend that these results reflect, on a trial-by-trial basis, the manner by which engagement of preparatory task control improves during development, directly relating to improvements in goal-directed behavior and task performance. While some prior research has suggested that children aged 8 years and older may be good engagers of preparatory control (Chatham et al. 2009), during this task there is still an observable difference between early adolescents and adults, indicating that this aspect of task control is still developing.

### Substantial Differences Observed in Cue Processing: These Differences Tracked with Age and Behavioral Performance

During the Cue period, many brain regions were more active in adults than in children, even when subgroups were matched for average ACC, RTs, IQ, or postscrubbing movement (see [Supplementary Material](#)). While there were fewer age differences during the Target period, many of those exhibited greater activity in children and were primarily frontal and sensorimotor regions, suggestive of a late or possibly compensatory strategy by the

child group as a consequence of failing to fully engage the cue effectively prior to the target arrival.

When we directly examined individual child engagement of a cluster of frontal and parietal regions with greater adult activity in the Cue period compared with a cluster of regions with greater activity in children in the Target period, we saw a strong correlation, such that more “adult-like” engagement of frontal and parietal regions during the Cue period correlated with less use of these potential “compensatory” regions during the Target period (Fig. 8). Furthermore, engagement of the Cue cluster correlated strongly with better performance both in terms of greater ACC and faster responses. This engagement of the Cue cluster became more adult-like over age, indicating that this aspect of task control continues to mature, in our sample, between the ages of 9 and 15 years. Our finding that adults demonstrate greater engagement of task-control networks as a result of moment-to-moment task-control demands is consistent with previous findings in this age range (Wilk and Morton 2012); here, we show that this group difference is largely specific to cue processing relative to target response. The mature system has greater separation of these signals, and activity does not differ over the age range within our adult group, though it could differ between individuals due to non-age-related factors. These data support the hypothesis that

preparatory control engagement is relatively slow to mature, and results in a significant improvement in task-level control.

Our ability to find differences in Cue preparation over age is due to application of the catch-trial design to study task-control development. In so doing, we reveal tradeoffs in processing emphasis over age, as well as dramatically different foci of activity for each signal type in the brain (i.e., greater fronto-parietal control-related processing in the Cue for adults and greater control and sensorimotor processing in the Target for children).

### Trial-by-Trial Cueing Produces Strong Age Differences in Performance

Despite our previous task-initiation (start-cue) signal study (Church, Wenger, et al. 2009) that suggested children and adults had similar adaptive control signaling when starting tasks, we found numerous age-related differences using this more intensive trial-by-trial cueing paradigm. As would be expected from the brain data, we also found numerous behavioral differences between children and adults. Previous studies have found that task-switching behavior does not appear to be adult-like in children ages 9–15 years (Cepeda et al. 2001; Crone, Bunge, et al. 2006; Bunge and Wright 2007; Huizinga and Van der Molen 2011; Wendelken et al. 2011; Chevalier et al. 2013). Our study provides a possible explanation for why: children are ineffective in their use of the preparation phase of the trial. This finding builds on prior results from behavior, EEG, and eye-tracking approaches (e.g., Chevalier et al. 2010, 2015; Holt and Deák 2015) by showing brain regions associated with cue processing in children relative to adults.

We hypothesized that children, having failed to process the Cue effectively, would engage more processing-related activity during the Target period. Our results were consistent with that hypothesis, revealing numerous cognitive control network age effects during the Cue period, but few during the Target period.

### Multiple Task-Control Networks Are Engaged by Preparatory Cue Processing

The main effect of the Cue signal overlapped with multiple control networks, including fronto-parietal, cingulo-opercular, and ventral and dorsal attention, and not just fronto-parietal network regions as predicted (Fig. 3A; Corbetta and Shulman 2002; Power et al. 2011, 2014). In both the Cue and Target main effect images, the peaks of activity were well defined by the overlaid resting-state functional area borders. For example, note the well-circumscribed medial superior frontal cortex activity in the putative cingulo-opercular network during the Cue period; Fig. 3B.

The Cue activity in task-control areas is seen to a lesser extent in the Target signal activity, where the main effect regions also involve motor, visual, and insula regions (Fig. 3C). However, it is noteworthy that there is a prominent asymmetry in the main effect Target image, such that there are 2 nodes of activity in the left fronto-parietal network that are minimally present in the right hemisphere. The more posterior of these 2 left frontal regions has a significant age effect (compare left lateral hemisphere of Fig. 3C with Fig. 5): There is greater activity in children than in adults for the Target, but the reverse for the Cue.

### RSFC Control Networks Are Engaged by Preparatory Cue Processing

When we applied 18 previously reported regions from cingulo-opercular and fronto-parietal networks to the Cue and Target signals in children and adults, the Cue signal showed significant age

differences, with greater engagement in adults, while the Target signal only had one region of difference over age (the right thalamus ROI, which was also greater in adults). These data, combined with the resting-state functional areas described above, support the model of multiple control network engagement during preparatory task control. This engagement increased well into adolescence for both whole-brain and applied ROI analyses.

More work needs to be done over typical and atypical development to understand the maturational profile of different types of task-control signals (e.g., switching, task initiation, and errors) in the brain. Yet, RSFC is able to distinguish between putative control networks in a highly reliable way (Power et al. 2011; Power and Petersen 2013; Cole et al. 2014). Developmental task-based fMRI and rest-based connectivity MRI studies have indicated potential subtle changes in within- and between-network relationships (e.g., Sherman et al. 2014) and has previously indicated that resting network relationships can relate to task performance measures (e.g., Barber et al. 2013). The present results suggest that the relative “timing” of engagement of regions, in addition to the relative “amount” of activity is important to consider, during a trial.

### Task-Switching Activity Is Similar Over Age

Somewhat surprisingly, the task-switching aspect of this study did not interact with the large age effects found for the Cue and Target signal. There were numerous regions of the brain that had a different (in magnitude) timecourse for switching rather than repeating task trials, as has been seen previously, but these were similar for both age groups (Braver et al. 2003; Ruge et al. 2011; Wendelken et al. 2012). The left lateralization evident for the Cue-switching effects has been observed previously even with nonlexical items (Bunge et al. 2003; Wendelken et al. 2012); future studies could investigate how different types of Cues may interact with age and switching effects.

### Limitations and Further Questions

Despite our best efforts to address the numerous confounding behavioral factors differing between the child and adult groups, it is quite possible that we are reporting effects that are not purely related to development (e.g., attributable to task performance). Furthermore, our child age range was large, which is both a limitation and advantage; we are underpowered to look at smaller age bins due to our sample size, but the broad age range allowed us to study cue–target signal differences at a correlational level. Thus, further research should investigate smaller age bins with greater power and work to examine performance separate from age. However, it is possible that it is precisely the developmental differences that are creating the performance differences observed in this report: The children’s lack of task-control engagement during task preparation periods may lead directly to the behavioral effects. Thus, a deeper understanding of task control on a trial-by-trial level is a challenge worthy of future experiments. These further experiments could address whether there are adaptations to the task that would encourage children to engage the Cue signal, or whether there are training paradigms that could influence a child’s brain activity pattern to be more adult-like.

A limitation of this particular task was its lexical nature, which could potentially generate age differences separate from actual Cue engagement. Future explorations could use tasks that remove the lexical aspect of the Cue. Finally, it remains an

open question how these developmental differences compare with differences seen in aging, or with developmental disorders.

## Conclusions

We report a study of children (aged 9–15 years) and adults (aged 21–30 years) performing a demanding trial-by-trial Cue–Target task, where we were able to analyze the Cue and Target BOLD signals separately. The brain data presented here indicate that engagement of control networks during the preparatory Cue period relates to faster and more accurate task performance. Cue signal engagement increased over age, and most likely relates to loading of task parameters consistent with visual attention models (e.g., Logan and Gordon 2001). Preparatory control engagement thus allows less processing demand for Target-specific information (e.g., selection of correct response mapping). Individuals who fail to sufficiently prepare during the Cue period must combine all of these stages during the Target period, resulting in slower responses, as is seen in the child group of this study. As a whole, these results suggest that preparatory (engagement during the Cue period) task control develops during late childhood and early adolescence, and benefits cued task performance.

By studying task-control development in typical development, we can start to construct the expected developmental trajectory of these types of signals. These trajectories then provide a context with which to study task control in different disorders (Baym et al. 2008; Church, Fair, et al. 2009).

## Supplementary Material

Supplementary material can be found at: <http://www.cercor.oxfordjournals.org/>.

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## Notes

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