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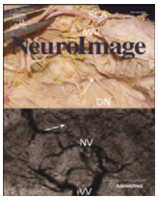

Developmental changes in patterns of brain activity associated with moment-to-moment adjustments in control

Heather A. Wilk, J. Bruce Morton *

Department of Psychology, Western University, Canada

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ABSTRACT

The current study investigated age-related changes in patterns of brain activity associated with moment-to-moment adjustments in control through the use of fMRI. Fifty-eight participants ranging continuously in age from 9 to 32 years were scanned as they performed a task in which the need for rapid adjustments in control was greater in one condition than another. Despite comparable behavioral performance across ages, moment-to-moment adjustments were associated with stronger engagement of anterior cingulate, anterior insula, lateral prefrontal cortex and the intraparietal sulcus in older than in younger participants. The findings confirm the importance of cingulo-insular and fronto-parietal cortices for moment-to-moment adjustments in control, and suggest continuous increases in the utilization of these networks over development.

The ability to detect and resolve conflicts between task-relevant stimuli and distracters is critical for adaptive psychological functioning (Miller and Cohen, 2001). In adults, there is both stable inter-individual (Miyake et al., 2000) as well as dynamic intra-individual variability (Gratton et al., 1992) in the efficacy of conflict processing, suggesting that different contexts elicit different modes of control (Braver et al., 2009). Contexts marked by infrequent conflict, for example, potentially elicit a "react-in-the-moment" mode of control where individual unanticipated instances of conflict are managed on-the-fly, as they occur. This mode of control relies on rapid moment-to-moment adjustments, is associated with greater conflict-related response time costs, and in neuroimaging experiments, with phasic activity in the anterior cingulate cortex (ACC) and lateral prefrontal cortex. Contexts marked by frequent conflict by contrast potentially elicit a future-oriented mode of control where conflict is prospectively anticipated and managed efficiently when it occurs. This mode of control relies on the active maintenance of attention-guiding rules or task-sets, is associated with diminished conflict-related response time costs, and in neuroimaging experiments, with sustained activity in dorsal prefrontal cortex (Braver et al., 2009; MacDonald et al., 2000; Wilk et al., 2011) and attenuated response to conflict in the ACC (Kerns et al., 2004).

Interestingly, there is some evidence that the contextual modulation of conflict processing is less pronounced in children than it is in adolescents and adults (Waxer and Morton, 2011a). In one study, children (9- to 11-year-olds), adolescents (14- and 15-year-olds), and adults (18- to 25-year-olds) were administered a series of interleaved compatible and incompatible stimuli as scalp potentials were measured continuously by means of EEG. For adults and adolescents, response times, N2 amplitudes, and ACC cortical-source activity on incompatible trials were attenuated when these trials were preceded by incompatible trials (i.e., iI trials) as compared to when they were preceded by compatible trials (i.e., cI trials). However, for children, behavioral and brain responses to incompatible stimuli did not vary as a function of preceding trial type — as though children dealt with each instance of conflict as it occurred (Waxer and Morton, 2011a).

Perhaps the most straightforward interpretation of such findings is that children are less likely than older participants to adopt a prospective mode of control, perhaps owing to constraints in the ability to actively maintain attention-guiding rules over time (Morton and Munakata, 2002; Stedron et al., 2005). In the AX Continuous Performance Task (AX-CPT) for example, participants respond to a particular probe (i.e., "X") if it follows a specific contextual cue (i.e., "A") but not if it follows a different cue (e.g., "B"). Whereas older participants adopt a prospective mode of control, as evidenced by a marked increase in mental effort during the presentation of contextual cues and a modulation of responses to subsequent probes, young children adopt a reactive mode of control, as evidenced by a marked increase in mental effort to probes, and little modulation of responses by prior cues (Chatham et al., 2009). Indeed, childhood has been characterized as an important period for development of future-oriented thinking (Haith et al., 1994). Children therefore may be less likely than older participants to adapt a prospective mode of control, and to rely instead on an earlier-developing reactive mode of control.

Very little, however, is actually known about the neuro-cognitive correlates of rapid adjustments in control across development. It is conceivable, therefore, that patterns of brain activity associated with reactive control, such as those that occur in response to sudden or unexpected conflict, change markedly with age. Children, adolescents, and adults show basic differences in conflict processing, with younger

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* Corresponding author. Fax: +1 519 850 2554.
E-mail address: bmorton3@uwo.ca (J.B. Morton).

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participants showing larger conflict-related behavioral interference effects (Davidson et al., 2006; Waxer and Morton, 2011b) but less conflict-related activity in ACC, dPFC, anterior insula (AI), and parietal cortex (PC) compared to older participants (Adleman et al., 2002). Moreover, networks that putatively support moment-to-moment adjustments in control undergo considerable reorganization over development, with the pattern of functional and anatomical connectivity among constituent regions changing markedly over time (Fair et al., 2007; Kelly et al., 2008; Nagy et al., 2004).

The goal of the present study, therefore, was to test for possible age-related differences in patterns of brain activity associated with moment-by-moment adjustments of control by means of functional magnetic resonance imaging (fMRI). Participants ranging in age from 9 to 32 years were administered a standard stimulus–response compatibility task (Kornblum et al., 1990) in blocks of trials that varied in the frequency of compatible trials (25% or 75%). Each trial presented a pair of digits that differed in numerical magnitude and physical size and participants indicated by means of a button press which of the two was numerically larger. Since responses based on differences in physical size are faster and more accurate than those based on differences in numerical magnitude, participants are slower and more error-prone when responding to incompatible stimuli (i.e., stimuli in which the numerically larger digit is physically smaller) than when responding to compatible stimuli (i.e., stimuli in which the numerically larger digit is physically larger), a phenomenon referred to as the size congruity effect, or SCE (Henik and Tzelgov, 1982). Importantly for the present purposes, the SCE—and, by extension, the need for moment-to-moment adjustments in control—is not stable, but increases with the block-level frequency of compatible trials (Borgmann et al., 2011). Therefore, to identify brain regions associated with moment-to-moment adjustments in control, we conducted a whole-brain search for voxels that showed a larger SCE in the 75% than in the 25% conditions using a contrast of two scaled predictors (see Methods). Age-related changes in the resulting pattern of brain activity were then imaged by plotting voxels where the magnitude of this contrast significantly co-varied with age.

On the basis of prior evidence, we made several general predictions. First, we predicted moment-to-moment adjustments in control, as reflected in elevated conflict-related activity when conflict occurs infrequently (i.e., in the 75% compatible condition) as compared to frequently (i.e., in the 25% compatible condition), would be associated with several brain regions, including the ACC, dPFC, AI, and PC. Second, on the basis of evidence showing age-related increases in conflict-related ACC activity and age-related changes in the functional connectivity of the ACC with lateral prefrontal, insular, and parietal cortex, we predicted an age-related increase in the association of the ACC with moment-to-moment adjustments in control, and age-related changes in broader patterns of brain activity associated with moment-to-moment adjustments in control.

Methods

All procedures were approved by the University Research Ethics Board for Health Sciences Research at Western University, Canada, and are in accordance with the 1964 Declaration of Helsinki.

Participants

Fifty-eight individuals (34 males) ranging in age from 9.4 to 32.4 years ($M=16.9$, $SD=5.6$) participated, including 19 children (9 to 12 years), 18 adolescents (13 to 17 years), and 21 adults (18 years and older). Participants younger than 18 years of age ($n=37$) were recruited from Western University's Child Development Participant Pool. Parents of these participants gave written consent to their child's participation and children provided verbal assent. Participants 18 years of age and older ($n=21$) were recruited from the Western University undergraduate and graduate student populations and provided written consent to their participation. All participants were right-handed and had normal or corrected-to-normal vision.

Task

Participants were administered a conflict adaptation paradigm in which individual trials of a size-congruency task (Henik and Tzelgov, 1982) were presented in conditions that differed in the frequency of compatible trials (see Fig. 1). On each trial, two Arabic digits that differed in physical size and numerical magnitude were simultaneously presented for 1950 ms in white on a black background, and participants selected by means of a button press the numerically larger of the two stimuli. Digits ranged in value from 1 to 9. Physically larger digits were presented in a 60-point font; physically smaller digits were presented in a 30-point font. Varying physical and numerical magnitude in this way generated compatible stimuli (i.e., stimuli in which the numerically larger digit was physically larger) and incompatible

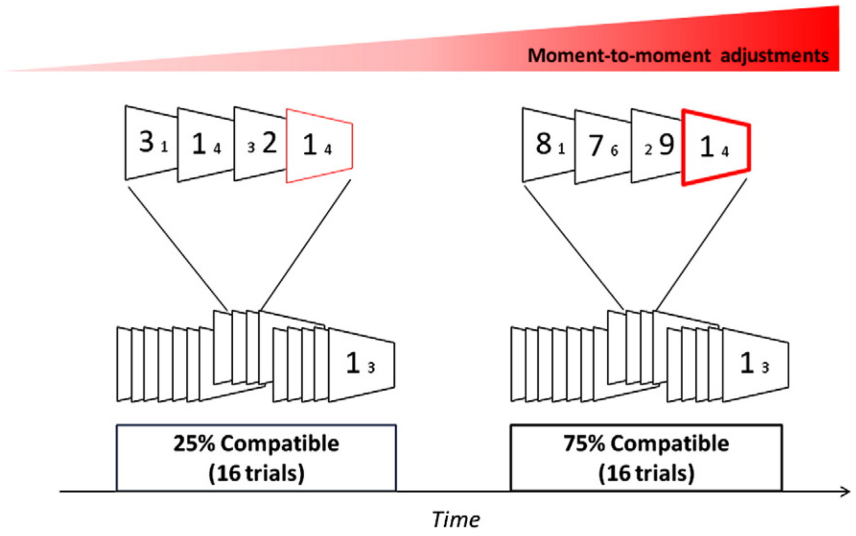

Fig. 1. The size-congruency task administered in the form of a conflict adaptation paradigm. On individual trials, participants were presented with two digits that differed in physical and numerical size, and pressed a button corresponding to the location of the numerically larger digit. On compatible trials, the numerically larger digit was also physically larger. On incompatible trials, the numerically larger digit was physically smaller. Individual trials were administered in conditions that differed in the proportion of overall trials that were compatible (25% or 75%).

stimuli (i.e., stimuli in which the numerically larger digit was physically smaller). Stimuli were administered in 16-trial blocks that differed in the frequency of compatible stimuli: in one condition (termed the 25% condition), 25% of trials (i.e., 4 of 16) were compatible stimuli; and in a second condition (termed the 75% condition), 75% of trials (i.e., 12 of 16) were compatible. The proportion of compatible trials within conditions was not cued explicitly. Instead, three start trials added to the beginning of each condition were used to establish expectations about the frequency of compatible stimuli within conditions. These trials were modeled separately as predictors of no interest. For the 75% condition, all start trials presented compatible stimuli; for the 25% condition, all start trials presented incompatible stimuli. To improve signal-to-noise ratio, 8000 ms null events totaling 12.5% of all trials were added to each condition. To avoid potential stimulus and response repetition effects, digits changed from trial to trial and correct responses were counterbalanced within conditions. The ordering of trials within conditions was fixed for all participants, and individual trials were randomly jittered by means of an inter-trial interval (or ITI) that ranged from 1500 ms to 4500 ms ($M = 3000$ ms). Conditions were presented in a random order fixed for all participants and were separated by 10-second intervals. During all inter-trial intervals, inter-block intervals, and null events, participants remained fixated on a centrally-presented white cross. In total, individual participants completed 14 separate blocks (7 each of the 25% and 75% conditions) for a total of 224 individual trials, administered in four separate 7.8-minute runs. The paradigm was presented using E-Prime software (Psychology Software Tools, Inc.) and was back-projected into the MRI environment. Participants viewed the stimuli through a mirror attached to the head coil and responded with their right index and middle fingers by means of a button box.

fMRI data acquisition

Data were collected using a 3 T Siemens Tim Trio MRI system fitted with a Siemens 32-channel head coil (Erlangen, Germany). Prior to scanning, participants younger than 18 years received training in a mock-scanner facility to aid in their remaining still and to mitigate fear and uncertainty regarding the experimental procedures. Four functional runs, each consisting of 234 whole-brain volumes were collected from each participant in a single scanning session. Due to equipment failure, only 3 runs were collected from 4 participants. Functional volumes consisted of 32-slices (thickness = 3 mm) oriented to the ACPC axis and were collected in an ascending interleaved order using a $T2^*$-weighted echo-planar imaging sequence (TR = 2000 ms; TE = 30 ms; flip angle = 78°), with an in-plane matrix of 64 × 64 pixels and a 21.1 × 21.1 cm field of view, yielding a 3 mm × 3 mm × 3 mm voxel resolution. There were no gaps between slices. To assist in the visualization of functional analyses, a T1-weighted anatomical scan consisting of 192 slices (thickness = 1 mm) with an in-plane 256 × 256 matrix and a 21.1 × 21.1 cm field of view (yielding a 1 × 1 × 1 mm voxel resolution) was also collected as part of the same scanning session.

fMRI data preprocessing

Data were preprocessed in BrainVoyager QX (Brain Innovation BV, Maastricht, The Netherlands). Prior to preprocessing, motion parameters were calculated for each run. Motion was constrained to 2.0 mm within runs, leading to the removal of 1 run for adults, 1 run for adolescents, and 4 runs for children. Data were subsequently motion-corrected by aligning each functional volume with the first volume of the first run, within subjects. Linear trend removal was applied to the time courses of motion-corrected functional runs. T1-weighted anatomical scans were aligned to the ACPC axis, and normalized to Talairach and Tournoux (1998) stereotactic space. $T2^*$-weighted functional volumes were then automatically aligned to unwarped anatomical images by means of a gradient-based affine alignment algorithm. Functional volumes were then warped into Talairach space by applying the translation and rotation parameters used to warp the anatomical images into Talairach space. Functional volumes were then smoothed using an 8 mm full-width at half maximum Gaussian kernel.

Statistical analyses

Data were analyzed using BrainVoyager QX (Brain Innovation BV, Maastricht, The Netherlands). BOLD responses were estimated by means of a whole-brain RFX General Linear Model (GLM) using event-related predictors described below. Contrasts of event-related predictors were conducted as a means of identifying voxels associated with moment-to-moment adjustments in control and co-varied with age in months to test for age-related change.

Age-related changes in moment-to-moment adjustments in control

The current paradigm utilized the stimulus–response compatibility effect (in the form of the SCE) as a basic means of imaging regions associated with cognitive control, and implemented increased demands on rapid adjustments in control by increasing the proportion of compatible trials in a condition from 25% to 75%, given prior evidence that manipulating the block-level frequency of compatible trials in this way leads to a predictable increase in the SCE. Therefore, to map brain regions associated with moment-to-moment adjustments in control, we identified voxels that exhibited a larger SCE in the 75% compared to the 25% condition. This was achieved through the use of a contrast, described in detail below, for which larger values indicated a “better fit” to the pattern of interest (i.e., a larger SCE in the 75% compared with the 25% condition). We then tested for age-related differences in the mapping of moment-to-moment adjustments by testing whether the magnitude of this contrast correlated with age. Positive (negative) correlations indicated regions associated with moment-to-moment adjustments in older (younger) but not younger (older) participants.

The contrast used to identify voxels that exhibited a larger SCE in the 75% compared with the 25% condition was computed as the difference in the beta coefficients of two separate scaled predictors, one for incompatible and one for compatible trials. The scaled predictor for incompatible trials was formed by: (1) defining a vector of onsets for all correct incompatible trials in a run and then using this to create a standard event-related stick-function for all incompatible trials; (2) scaling individual instances (i.e., the height of individual sticks) according to the frequency condition in which they occurred, such that individual incompatible trials in the 75% and 25% conditions were scaled 0.75 and 0.25 respectively; and (3) convolving the resulting stick-function with a canonical sum of two gammas hemodynamic response function. The scaled predictor for the compatible trials was formed the same way except that the initial vector of onsets included all correct compatible trials in the run. In the context of a GLM, the beta coefficients of these predictors are positive when the magnitude of BOLD response increases with condition-level increases in the frequency of compatible trials, and negative when the magnitude of the BOLD response decreases with condition-level increases in the frequency of compatible trials. Therefore, to identify voxels associated with moment-to-moment adjustments in control, we estimated the difference in these scaled predictors (i.e., β_Scaled INC − β_Scaled CON) in the context of a whole-brain RFX ANCOVA, and plotted voxels in which this difference differed from zero. Resulting maps were then corrected for multiple comparisons using a cluster-size thresholding procedure (Forman et al., 1995; Goebel et al., 2006) in which statistically uncorrected maps were submitted to a whole-slab correction criterion based on an estimate of the map's spatial smoothness and an iterative procedure (Monte Carlo simulation) for estimating cluster-level false-positive rates. After 1000 iterations, the minimum cluster-size that yielded a cluster-level false-positive rate (α) of .05 (5%) was used to threshold the statistical maps. Only clusters whose size met or exceeded the threshold value were allowed to remain on the statistical maps.

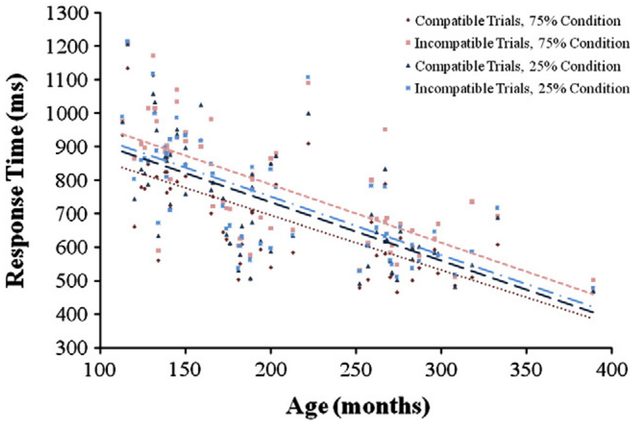

Fig. 2. Behavioral response times (ms) plotted against participant age for compatible and incompatible stimuli (dark and light colors respectively) for both the 25% and 75% conditions (red and blue respectively). Lines represent linear regression of participant age for each trial type. Although there was an overall decrease in response time with increasing age, the compatibility effect was larger in the 75% (red versus pink) than the 25% compatibility condition (turquoise versus navy) for participants of all ages.

Finally, we tested for age-related differences in the mapping of moment-to-moment adjustment by correlating the above contrast estimates (i.e., β_Scaled INC $-$ β_Scaled CON) with age in months. As stated before, regions associated with moment-to-moment adjustments in older (younger) but not younger (older) participants would show positive (negative) correlations.

Results

Behavior

Response times are plotted in Fig. 2 as a function of Age, Condition (25%- and 75%-compatible), and Stimulus Type (compatible and incompatible). In general, response times decreased with increasing age, and were greater to incompatible than compatible stimuli, especially in the 75% compatible condition. A Condition × Stimulus Type repeated-measures ANCOVA with Age as a covariate confirmed that older participants were faster than younger participants, $r\ (58) = -.69$, $p < .001$, and that response times were greater for incompatible ($M = 775$ ms) than compatible stimuli ($M = 722$ ms), $F\ (1,\ 56) = 12.4$, $p < .001$. The effect of Stimulus Type on response times was more pronounced in the 75% ($M = 87$ ms) than in the 25% ($M = 18$ ms) compatible condition, as indicated by a significant Condition × Stimulus Type interaction, $F\ (1,\ 56) = 8.76$, $p < .005$. There were no other effects or interactions.

Because younger participants responded more slowly than adults across all trials, we examined the linear association of age and a percent change interference effect (PECHIE), a measure that mitigates age-related scaling differences in raw RT (see Supplementary materials for a plot of these data). In particular, this was estimated for each individual and each condition as:

$$\text{PECHIE} = (\text{RTincompatible} - \text{RTcompatible}) / \text{RTcompatible} * 100$$

As expected, PECHIE scores were greater in the 75% ($M = 13.0$) than in the 25% conditions ($M = 2.69$), $t\ (57) = 8.28$, $p < .001$. Importantly though, PECHIE scores were uncorrelated with age in both the 75%, $r\ (58) = .128$, $p = $ ns, and 25%, $r\ (58) = .018$, $p = ns$, conditions.

Accuracy was examined as a function of Age, Condition (25%- and 75%-compatible), and Stimulus Type (compatible and incompatible).

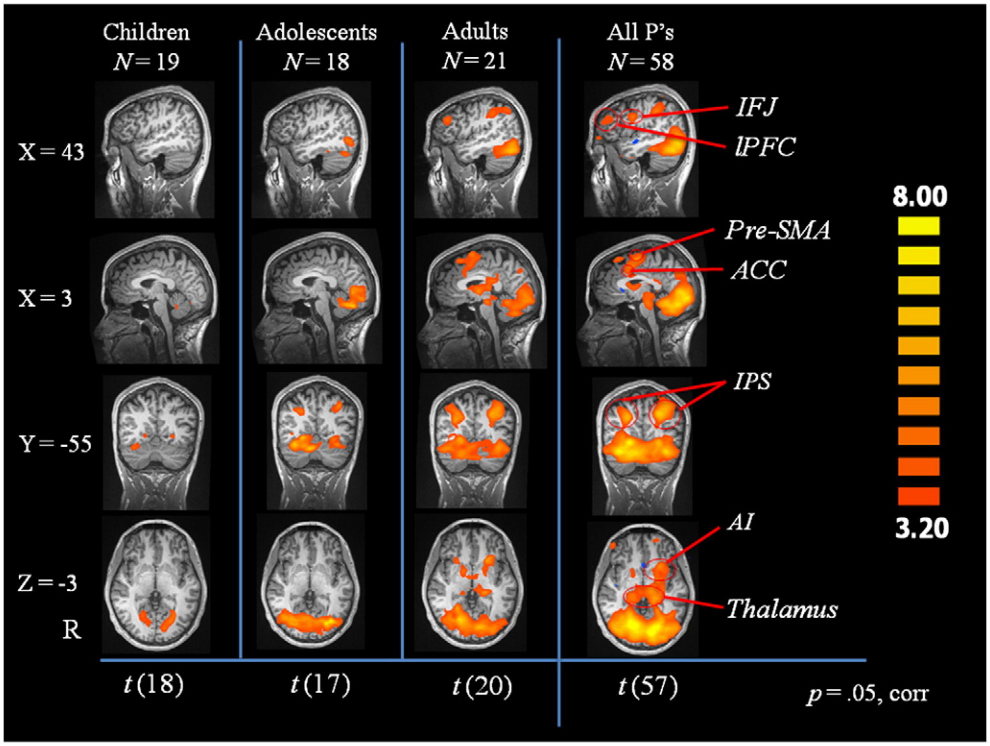

Fig. 3. Regions associated with moment-to-moment adjustments in control in children, adolescents, adults, and the entire sample visualized by computing the difference in scaled incompatible and compatible predictors for the entire sample and separately for children, adolescents, and adults, and plotting this difference at the same threshold for all groups, p (corrected) $< .05$. lPFC = lateral prefrontal cortex; IFJ = inferior frontal junction; ACC = anterior cingulate cortex; pre-SMA = pre-supplementary motor area; AI = anterior insula; IPS = intra-parietal sulcus.

In general, participants of all ages made fewer errors to compatible than incompatible stimuli both in the 25% and the 75% compatible conditions (see Supplementary materials for a plot of these data). A Condition x Stimulus Type repeated-measures ANCOVA with age as a covariate confirmed an effect of Stimulus Type such that participants were more accurate when responding to compatible ($M = .991$) than incompatible stimuli ($M = .961$), F (1, 56) = 8.46, $p < .005$. No other effects or interactions were significant (all p's > .10).

fMRI

Group analysis of moment-to-moment adjustments in control

Brain regions that, for the whole group, showed a pattern of activation consistent with a role in moment-to-moment adjustments in control are shown in Fig. 3, rightmost column. Specifically, these regions, which include the ACC, AI, lPFC, and PC, showed a larger SCE in the 75% than in the 25% compatible conditions, as revealed by a significant difference in scaled incompatible and compatible predictors.

Age-related differences in moment-to-moment adjustments in control

Several brain regions were associated with moment-to-moment adjustments in older but not younger participants (see Figs. 3 and 4), including right anterior insula, right dorsal ACC, right pre-supplementary motor area (pre-SMA), right lateral PFC, and intra-parietal sulcus bilaterally (see Table 1 for a complete list of regions). Specifically, these were regions in which the magnitude of the contrast used to identify regions associated with moment-to-moment adjustment correlated positively with age in months (see Fig. 4, scatterplots).

To aid in the interpretation of these age-related changes, we first defined regions-of-interest from the maps shown in Fig. 4—specifically, regions that were associated with moment-to-moment adjustments in older but not younger participants. These ROIs included right anterior insula, ACC, lPFC, and IPS. We then subdivided the whole sample into separate child ($n = 19$), adolescent ($n = 18$), and adult ($n = 21$) groups, and estimated beta coefficients for separate Condition (25%, 75%) and Stimulus Type (Compatible, Incompatible) predictors for each group in the context of a whole-brain RFX GLM. Finally, we extracted from the ROIs beta coefficients of the four Condition and Stimulus Type predictors separately for each group. Plots of the four beta coefficients for each of the three groups are displayed in Fig. 5.

As expected, adults' beta coefficients showed the signature pattern associated with rapid adjustments in control in all regions (anterior insula, anterior cingulate, left and right IPS), with a larger difference between compatible and incompatible trials in the 75% compatible condition than in the 25% condition. Adolescents' beta coefficients were generally smaller, but trended toward this signature pattern in the left and right IPS. Children's beta coefficients however departed quite strikingly from the signature pattern in all four regions, with the difference between compatible and incompatible trials typically more pronounced in the 25% than in the 75% compatible condition. These patterns were difficult to interpret in any straightforward way, especially given how comparable children's behavioral performance was with that of the older participants.

Moment-to-moment adjustments in control in children, adolescents and adults

To guard against the possibility that the reported age-related trends were driven primarily by an absence of any effects in the younger participants, we calculated the difference in scaled predictors separately for children, adolescents, and adults. These results are presented in Tables 2, 3, and 4, and are plotted in the first three columns of Fig. 3, corrected for multiple comparisons by means of a cluster thresholding procedure (Forman et al., 1995; Goebel et al., 2006). For the children, the resulting map included separate clusters in the posterior cingulate cortex, the left premotor cortex, and the left intraparietal sulcus. As these clusters were not evident in Fig. 5, we redrew these maps and displayed them in Fig. 6. To aid in the interpretation of these maps, estimates of beta coefficients for separate Condition (25%-, 75%-compatible) and Stimulus Type (Compatible, Incompatible) predictors were computed in a whole-brain RFX GLM and extracted from these regions for the purpose of visualization. Plots of the beta coefficients are presented in Fig. 6. In general, these regions showed the signature pattern of betas indicative of a role in moment-to-moment adjustment in control – namely an increase in the magnitude of the compatibility effect in the 75% relative to the 25% compatibility condition – with the pattern clearest in the cingulate and the premotor cortex.

Discussion

While there is some evidence suggesting the ability to prospectively prepare for future cognitive challenges is late-developing (Chatham et al., 2009; Haith et al., 1994; Waxer and Morton, 2011a), relatively little is known about the development of the ability to adjust rapidly to unanticipated cognitive demand. The current study therefore examined age-related changes in patterns of brain activity associated with rapid adjustments in control. Participants aged 9 to 32 years were administered a stimulus–response compatibility task (Kornblum et al., 1990) in blocks that differed in the proportion of compatible trials. Demands on rapid, or moment-to-moment, adjustments in control were expected to be greater given a high (i.e., 75%) as compared to a low (i.e., 25%) proportion of compatible trials in a block, as demands on conflict processing are less anticipated under these conditions (Gratton et al., 1992).

Consistent with these expectations, stimulus–response compatibility effects (i.e., the difference in response time and accuracy for incompatible versus compatible trials) were larger in the 75% as compared to 25% compatible conditions. And, although overall speed of responses increased with increasing age, the magnitude of normalized compatibility effects and their modulation by condition were equivalent for participants of all ages. Thus, observed age-related differences in patterns of brain activity associated with moment-to-moment adjustments in control were not attributable to age-related differences in behavioral performance.

Pronounced age-related changes in patterns of brain activity associated with moment-to-moment adjustments in control were observed. In particular, converging evidence from several analyses suggested that the anterior insula, anterior cingulate, lateral prefrontal cortex, and intraparietal sulcus, were associated with moment-to-moment adjustment in older but not younger participants. First, these regions showed a positive correlation between age and activity related to rapid adjustments in control, such that continuous increases in age were associated with larger differences in beta estimates of scaled predictors for incompatible and compatible trials. Second, an ROI analysis of these regions confirmed that: (a) in adults, there was larger effect of compatibility in the 75% compared to the 25% conditions; (b) in adolescents, this difference was less pronounced; and (c) in children, this

Table 1
Regions that showed continuous age-related increases in their association with moment-to-moment adjustments in control, $p < .05$, corrected.

Region hemisphere		Peak coordinates			Cluster size (mm^3)
		Tal X	Tal Y	Tal Z	
Intraparietal sulcus	R	38	−56	42	4005
	L	−31	−65	33	2130
Anterior cingulate cortex	R	2	28	27	1978
Middle frontal gyrus	R	45	29	34	1906
Ventrolateral PFC	L	36	29	16	1046
Pre-SMA	R	6	8	61	946
Anterior insula	R	22	26	−3	677

difference was largely absent. Third, and finally, separate analyses of child, adolescent, and adult data revealed that age-related increases in the utilization of anterior insula, anterior cingulate, lateral prefrontal and parietal cortices for moment-to-moment adjustment in control were not a spurious by-product of pervasive null effects in the younger participants, nor problems related to warping younger brains to an adult template. Separate analysis of the children's data identified several regions associated with moment-to-moment adjustments in control, including cingulate cortex on the anterior/posterior border and left premotor cortex. The fact that these regions were not in close proximity to regions associated with moment-to-moment adjustments in older participants speaks against the possibility that age-related differences reflect problems related to warping children's brains to an adult template. If children's data had carried the signature moment-to-moment pattern of activity, but been inadequately warped into the common stereotactic space, then a large cluster of voxels showing age differences should have revealed separate but spatially proximal moment-to-moment adjustment regions in each of the three groups. This however, was not observed. Instead, for all regions that showed age differences, there was clear involvement in moment-to-moment adjustments in adults, and no interpretable pattern for the children. Indeed, normalization procedures like those used in the present investigation, are generally considered robust against age-related differences in brain size, at least for children (Burgund et al., 2002). Taken together then, the findings point to age-related increases in the utilization of anterior insula, anterior cingulate, lateral prefrontal, and parietal cortex for rapid adjustments in control.

On a broad level, the findings are consistent with a sizeable body of literature showing age-related increases in lPFC, IPS, ACC, and AI activity associated with cognitive control and conflict processing. Adleman and colleagues for example administered the color-word Stroop task to a group of participants that ranged continuously in age from 7 to 22 years and, as in the present study, found age-related increases in conflict-related activity in the ACC, AI, and lPFC (Adleman et al., 2002). However, as illustrated in this study and others, stimulus–response compatibility tasks, such as the color-word Stroop task, differentially and dynamically engage distinct modes of control depending

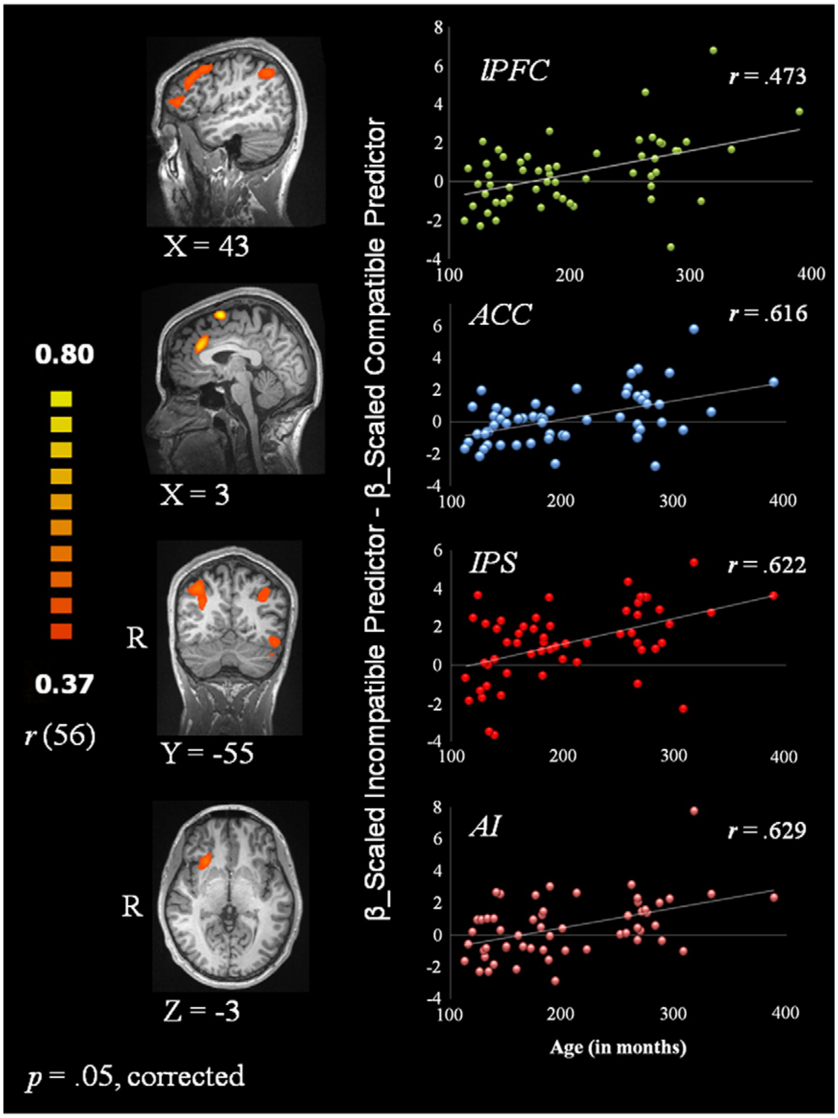

Fig. 4. Brain areas more strongly associated with moment-to-moment adjustments in older than younger participants. Images on the left are plots of the difference of scaled predictors correlated with age in months, and are corrected for multiple comparisons at $p<.05$. Scatterplots on the right illustrate linear associations for lateral prefrontal cortex (lPFC), anterior cingulate cortex (ACC), intra-parietal sulcus (IPS), and anterior insula (AI) by plotting the difference of beta estimates of scaled incompatible and compatible predictors on the y-axis and age in months on the x-axis.

Table 2
Regions associated with moment-to-moment adjustments in children, $p<.05$, corrected.

Region	Hemisphere	Peak co-ordinates		
		Tal X	Tal Y	Tal Z
Intraparietal sulcus	R	29	−80	9
	L	−22	−65	36
Posterior cingulate cortex	L	−7	−17	48
Ventral midbrain	L	−7	−17	−21
Precentral gyrus	L	−22	−8	42
Premotor cortex	L	−41	−6	27
Fusiform gyrus	R	20	−62	−3
	L	−37	−41	−24
Lingual gyrus	L	−25	−71	6
Caudate	L	−16	−20	21
Cerebellum	R	11	−44	−27

Cluster size of individual regions not included as they were peaks within larger a larger cluster.

on their manner of administration (Gratton et al., 1992). The present results therefore represent an important extension of these findings by showing similar age-related trends but under conditions that more definitively engage reactive or moment-to-moment adjustments in conflict processing.

Indeed, in this more specific sense, aspects of the current findings dovetail nicely with models linking rapid adjustments in control to cingulo-opercular and fronto-parietal networks. For example, according to the dual-mechanisms of control account (Braver et al., 2009), moment-to-moment adjustments in control involve a late correction process, in which task goals, maintained by dlPFC, are rapidly reactivated following the detection of interference by the ACC. A similar account posits that AI and dACC form the core of a larger salience network that rapidly activates to stimuli of potential motivational relevance, including those that are temporally or spatially infrequent (Menon and Uddin, 2010; Seeley et al., 2007). These transient signals help direct attention to the external environment by activating and disengaging fronto-parietal and default-mode networks respectively (for discussion, see Menon and Uddin (2010)). Despite their differences, both accounts predict transient cingulo-opercular and fronto-parietal activation in the context of rapid adjustments in control, which is precisely what was observed in the current study, at least in older participants. Younger participants, by contrast, showed very little utilization of these networks in association with moment-to-moment adjustments in control.

Age-related differences in the brain mapping of moment-to-moment adjustments in control evidenced in the current study are

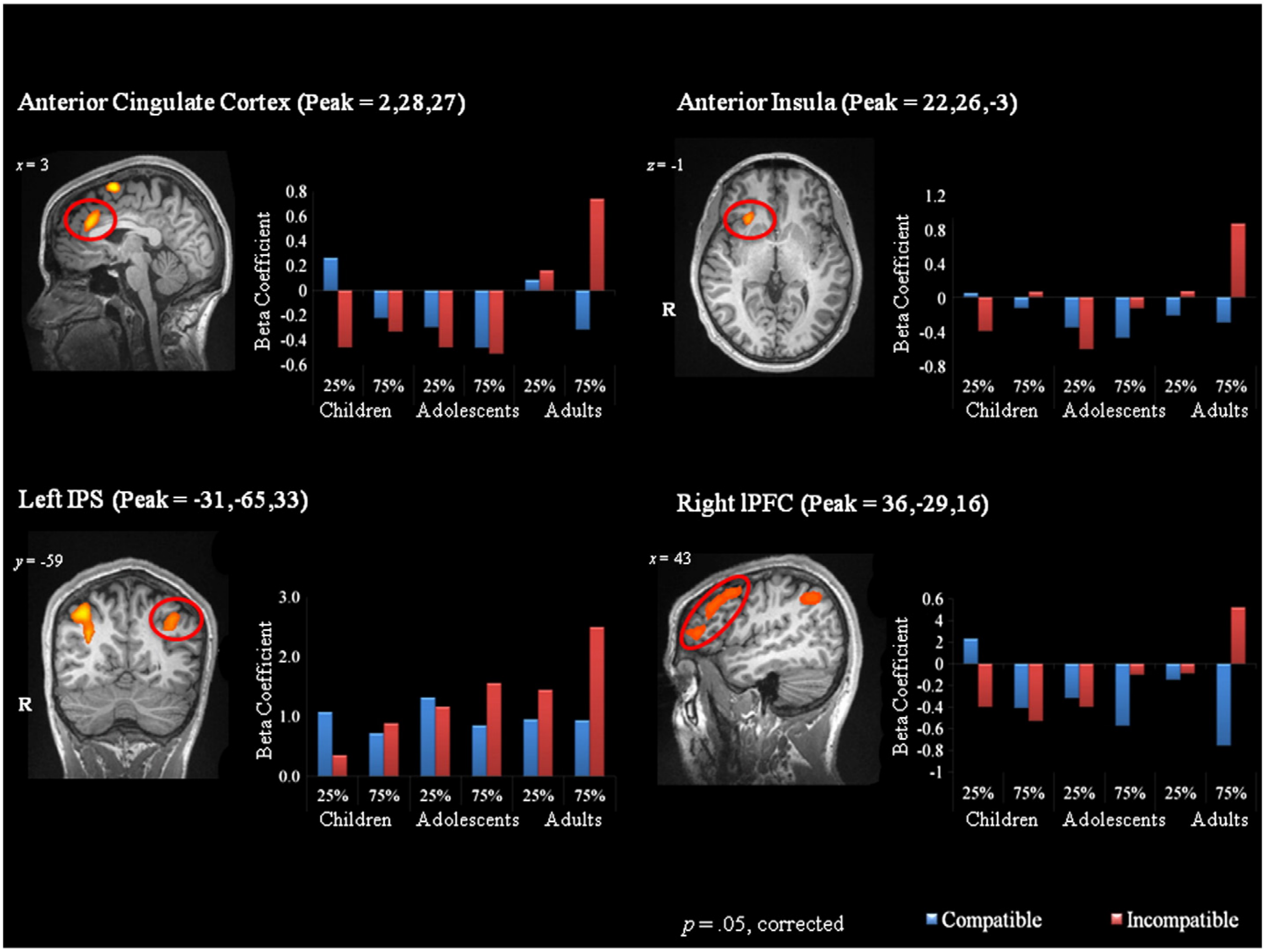

Fig. 5. Brain regions (from Fig. 4) that were more strongly associated with moment-to-moment adjustments in older than younger participants, including anterior cingulate cortex (ACC), anterior insula (AI), intra-parietal sulcus (IPS), and lateral prefrontal cortex (lPFC). To clarify the nature of the correlations plotted in Fig. 4, these regions were defined as ROIs, and for each ROI, beta estimates of compatible and incompatible trials in the 25% and 75% conditions were computed separately for children, adolescents, and adults in the context of a whole-brain RFX GLM. Individual beta estimates appear to the right of each statistical map, and were computed from the average of all voxels in the associated ROI. They are presented without error bars since they were extracted only for the purpose of visualization. For adults, the compatibility effect was more pronounced in the 75% than in the 25% condition in adults in all ROIs, suggesting a role for these regions in moment-to-moment adjustments. This pattern was less evident in these regions for children and adolescents.

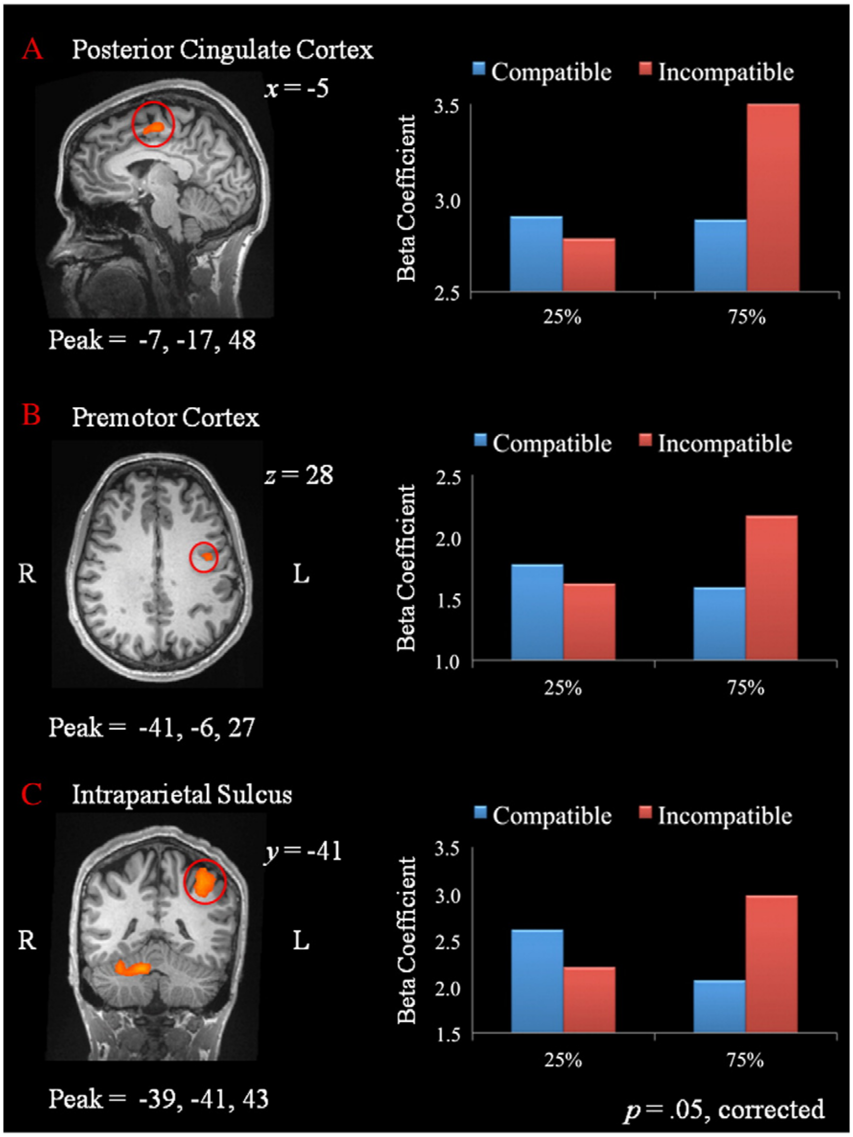

Fig. 6. Images on the left show regions associated with moment-to-moment adjustments in control in children, as revealed by a difference in scaled incompatible and compatible predictors. To clarify the nature of this difference, these regions were defined as ROIs, and beta estimates of compatible and incompatible trials in the 25% and 75% conditions were computed in the context of a whole-brain RFX GLM. Individual beta estimates, on the right, were computed from the average of all voxels in each ROI and are presented without error bars since they were extracted only for the purpose of visualization.

indeed quite striking, especially in view of the fact that all participants evidenced behavioral sensitivity to changes in conflict frequency. What underlying differences might account for this striking pattern of age-related change? One possibility is that younger and older participants used different cognitive/behavioral strategies to achieve comparable levels of performance. Although younger and older participants showed comparable effects of compatibility frequency and trial type on response time and accuracy, younger children were overall slower in their responses than older participants. Thus, although response time and accuracy profiles across participants were comparable, they may nevertheless have been underlying age-related differences in cognitive strategy. A second possibility is that age-related differences in the mapping of moment-to-moment adjustments in control might be explained, at least in part, by changes in connectivity within CO and FP networks. Although much remains to be learned about how CO and FP networks interact in the realization of rapid adjustments in control, and whether these interactions are constrained by differences in structural and functional connectivity, there is emerging evidence that connectivity within and between these networks undergoes considerable reorganization in the age-range under consideration in the present study (Fair et al., 2007; Kelly et al., 2008). Given the magnitude of the observed changes though, basic changes in the underlying anatomy and physiology of the cortex could be at play as well, including changes in cortical thickness (Shaw et al., 2008; Sowell et al., 2004), levels of available dopamine (Dumontheil et al., 2011; Wahlstrom et al., 2007), and dopamine receptor density (Dumontheil et al., 2011; Wahlstrom et al., 2007). These anatomical and physiological differences could have implications for the shape of the hemodynamic response function (hrf) in particular brain regions at particular ages, and the fit of models that assume a canonical hrf. Whatever the underlying causes, the current findings suggest that in addition to age-related changes in cognitive and neural bases of prospective control (Chatham et al., 2009; Waxer and Morton, 2011a), there are also significant changes in patterns of brain activity associated with moment-to-moment adjustments.

Table 3
Regions associated with moment-to-moment adjustments in control in adolescents, $p<.05$, corrected.

Region	Hemisphere	Peak coordinates Tal X	 Tal Y	 Tal Z
Intraparietal sulcus	R	23	−56	33
	L	−37	−53	42
Fusiform gyrus	R	35	−53	−18
	L	−37	−38	−24
Parahippocampal gyrus	R	26	−41	−9
Postcentral gyrus	L	−37	−20	48
Precuneus	R	23	−56	33
Cuneus	R	26	−71	9
Cerebellum	R	20	−74	−18
Premotor cortex	L	−19	−8	69
Precentral gyrus	L	−49	−5	33

Cluster size of individual regions not included as they were peaks within a larger cluster.

Caveats and future directions

One important caveat of the current study is that the findings are based on a particular operational definition of moment-to-moment adjustments in control — namely the conflict adaptation effect. Some critics maintain that conflict adaptation effects do not reflect cognitive control processes, but rather lower-level effects related to stimulus and response repetition ((Mayr et al., 2003) but see (Ullsperger et al., 2005)). Although use of the SCE paradigm in the current study mitigated the untoward influence of these confounds by ensuring that there were no stimulus repetitions across trials and that the probability of a response repetition from trial to trial was close to .5, it is conceivable that the current findings are, to some degree, tied to the use of the conflict adaptation paradigm.

On a related note, age-related differences in performance in the SCE paradigm were minimal, and related mostly to increases in response speed with increasing age. While this affords certain advantages, inasmuch as it controls for possible performance confounds in the interpretation of the brain-imaging findings, it is also at odds with other evidence of age-related changes in conflict adaptation effects. The divergence in behavioral effects may relate to differences in the basic instantiation of conflict (e.g., color-word Stroop task, size-compatibility task, etc.), as well as differences in how adaptation to this conflict is elicited and measured (e.g., either by varying preceding trial compatibility or condition-level compatibility frequency). Although resolving these issues is clearly beyond the scope of the present investigation, it is fair to say on the basis of the present findings that the SCE is a simple and effective means of eliciting conflict adaptation in children as young as 9 years.

The present findings set an important stage for future investigations of age-related changes in cortical networks supporting moment-to-moment adjustments in control. To date, characterizations of these changes are relatively scarce, and are based predominantly on seed-based analyses of resting-state fMRI data. While powerful in many respects, these techniques provide only a limited basis for inferring function, and have proven vulnerable to the untoward effects of participant motion (Power et al., 2012). Multivariate techniques, such as independent component analysis (Calhoun et al., 2009; Stevens et al., 2007), or dynamic causal modeling (Friston et al., 2011), represent an important avenue for future investigation. Applied to event-related data like those reported here, these techniques could aid both in the identification and functional characterization of networks associated with moment-to-moment adjustment in control.

Given the complex and transient nature of everyday experiences, it is important that organisms be able to adapt to subtle changes in environmental regularities (Behrens et al., 2007). The current findings help to identify neural mechanisms associated with the human sensitivity to environmental statistics and highlight the gradual development of this capacity.

Table 4
Regions associated with moment-to-moment adjustments in control in adults, $p<.05$, corrected.

Region	Hemisphere	Peak coordinates Tal X	 Tal Y	 Tal Z
Intraparietal sulcus	R	29	−56	27
	L	−25	−74	39
Anterior cingulate cortex	L	−4	13	24
Anterior insula	R	23	16	−3
	L	−19	19	3
Lateral PFC	R	44	31	30
	R	35	1	30
	R	29	28	15
	L	−4	31	48
	L	−37	43	9
Posterior insula	R	41	−14	3
Pre-SMA	R	5	7	63
Precentral gyrus	R	32	−14	57
	L	−49	−29	48
Fusiform gyrus	L	−37	−71	−15
Lingual gyrus	L	−10	−80	−9
Caudate	L	−10	1	15
Cerebellum	R	26	−47	−30

Cluster size of individual regions not included as they were peaks within a larger cluster.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.neuroimage.2012.06.069.

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