Cortical gray-matter thinning is associated with age-related improvements on executive function tasks

Maria Kharitonova[a], **Rebecca E. Martin**[b], **John D.E. Gabrieli**[c], and **Margaret A. Sheridan**[a,*]

[a]Laboratories of Cognitive Neuroscience, Division of Developmental Medicine, Boston Children's Hospital, Harvard Medical School, Boston, MA, United States

[b]Department of Psychology, Columbia University, New York, NY, United States

[c]Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, MA, United States

Abstract

Across development children show marked improvement in their executive functions (EFs), including the ability to hold information in working memory and to deploy cognitive control, allowing them to ignore prepotent responses in favor of newly learned behaviors. How does the brain support these age-related improvements? Age-related cortical gray-matter thinning, thought to result from selective pruning of inefficient synaptic connections and increases in myelination, may support age-related improvements in EFs. Here we used structural MRI to measure cortical thickness. We investigate the association between cortical thickness in three cortical regions of interest (ROIs), and age-related changes in cognitive control and working memory in 5–10 year old children. We found significant associations between reductions in cortical thickness and age-related improvements in performance on both working memory and cognitive control tasks. Moreover, we observed a dissociation between ROIs typically thought to underlie changes in cognitive control (right Inferior Frontal gyrus and Anterior Cingulate cortex) and age-related improvements in cognitive control, and ROIs for working memory (superior parietal cortex), and age-related changes in a working memory task. These data add to our growing understanding of how structural maturation of the brain supports vast behavioral changes in executive functions observed across childhood.

Keywords

Brain development; Executive functions; Cognitive control; Structural MRI

[*]Corresponding author at: Laboratories of Cognitive Neuroscience, Boston Children's Hospital, 1 Autumn St, AU 645, Boston, MA 02215, United States. Tel.: +1 857 218 5220; fax: +1 617 730 0518. sheridan.margaret@childrens.harvard.edu, sheridan.margaret@gmail.com. .

1. Introduction

As children age, they show marked improvements in the ability to deploy cognitive control to enable learning new rules and ignoring old ones, and to hold information in mind over the course of delays. In adults and children, functions of the prefrontal, anterior cingulate, and parietal regions of the brain are thought to support these examples of cognitive control and short-term memory (e.g., Bunge and Wright, 2007; Hedden and Gabrieli, 2010; Fuster, 2001; MacDonald et al., 2000; Miller and Cohen, 2001; Todd and Marois, 2004).

Simultaneous with behavioral improvements, the brain itself is undergoing a number of significant maturational changes, including an increase in overall cortical volume, an increase in white-matter volume, and cortical gray-matter thinning (Gogtay et al., 2004; Hua et al., 2009; Lenroot and Giedd, 2006; O'Donnell et al., 2005; Shaw et al., 2008; Sowell et al., 2004; Supekar et al., 2009; Tau and Peterson, 2009; Toga et al., 2006). The precise contribution of each of these factors to the development of cognition is not yet known; however, gray-matter thinning is thought to be critical for age-related cognitive improvements (Casey et al., 2005; Sowell et al., 2004; Tau and Peterson, 2009). Here we explored the role of gray-matter thinning in age-related improvements in cognitive control and working memory span in children ages 5–10, using structural MRI.

Many studies have identified substantial decreases in gray-matter thickness in prefrontal and parietal cortices beginning in early childhood and continuing into adolescence (Gogtay et al., 2004; O'Donnell et al., 2005; Pfefferbaum et al., 1994; Sowell et al., 2004; Wilke et al., 2007). These studies include both cross-sectional examinations using automatic gray-white matter parcellation techniques similar to those used in the current paper (Ostby et al., 2009) and longitudinal examinations of children 5–10 years old (Sowell et al., 2004). In contrast to these studies reporting age-related cortical thinning, a few studies have observed non-linear patterns of cortical thickening in early childhood followed by thinning in later childhood or adolescence (e.g. Shaw et al., 2006, 2008). Other studies found that developmental thickening of the cortex is limited to ventromedial prefrontal cortex and left-lateralized language areas (Sowell et al., 2004); these regions were not examined in this study.

Developmental cortical gray-matter thinning is thought to result from both synaptic pruning and myelination (Dosenbach et al., 2010; Sowell, 2001; O'Donnell et al., 2005; Sowell et al., 2004; Toga et al., 2006). Over the course of childhood, white-matter volume expands (via myelin proliferation) and replaces gray matter (Sowell et al., 2004). This process results in smaller estimates of cortical gray-matter thickness. Although changes in function would be the likely consequence of synaptic pruning and myelination, few studies have explored the relationship between brain maturation and age-related improvements on executive function measures in the same group of children.

Studies have begun to identify associations between cortical thinning and age-related improvement in task performance. For example, cortical thickness in the frontal lobes was negatively related to verbal learning in children ages 7–16 (Sowell, 2001). In a different study, developmental gray-matter thinning in the left hemisphere (frontal and inferior parietal regions) was specifically related to an increase in vocabulary but not spatial task performance (Sowell et al., 2004). Similarly, cortical thickness in frontal, parietal, and occipital regions negatively correlated with performance on working memory and anti-saccade tasks in 8–19 year old participants (Tamnes et al., 2010).

These studies have shed light on the development of the structure-function relationship in the brains of children from ages 7 through adolescence, but little if anything is known about structure-function relations in younger children. Here we examined brain-behavior relations in children ages 5–10 in regards to executive functions, which improve remarkably in this

developmental period (Best et al., 2009; Brocki and Bohlin, 2004; Crone et al., 2009; Davidson et al., 2006). As half of our sample consists of children five to seven years of age, we were able to examine brain-behavior associations during this time of rapid change.

Our structural analyses focused on regions of interest (ROIs) associated with executive function in children and adults, and examined how these brain regions were associated with age-related gains on two behavioral measures of executive functions. Furthermore, we performed a mediation analysis to identify if changes in cortical thickness statistically explained the association between age and task performance, allowing for identification of a possible mechanism through which children improve their executive function across childhood.

One behavioral measure employed was the Simon task, in which participants pressed a button on the same side of the screen as the stimulus if the stimulus was in one color (side-congruent trials), and the opposite side from the stimulus if it was in a different color (side-incongruent trials). On the side-incongruent trials participants must have ignored the prepotent response (to press on the same side) in favor of a less common conflicting response (to press on the opposite side). During the Simon task, adults reliably recruit the right Inferior Frontal Gyrus (rIFG) and the anterior cingulate cortex (ACC) when ignoring the prepotent response in favor of a conflict response (Fan et al., 2003; Huettel and McCarthy, 2004; Kerns, 2006; Peterson et al., 2002). We thus predicted that cortical thickness of the rIFG and the ACC would be related to age-related improvements on the Simon task, and would mediate the age-performance association in this task.

The rIFG has been hypothesized to support response inhibition (Aron, 2007; Aron et al., 2004), suggesting that this region might be particularly sensitive to incongruency in the Simon task. However, more recent research has suggested that rather than being primarily involved in response inhibition, this region plays a general role in monitoring the environment for currently relevant information in the service of task goals. In this account, attention-based *context monitoring* is the primary function supported by the rIFG, rather than response inhibition per se (Chatham et al., 2011; Dodds et al., 2011; Hampshire et al., 2010; Sharp et al., 2010). Our study may shed some light on these conflicting accounts of the role of the rIFG. The inhibitory account predicts a selective relationship between rIFG thickness and performance on the *incongruency effect* in the Simon task (incongruent trial performance, controlling for congruent performance) because the prepotent same-side response needs to be ignored in favor of the conflicting opposite side response. In contrast, we hypothesize that consistent with the attentional context monitoring account, there will be a significant association between rIFG thickness and performance on both the congruent and the incongruent trials because both require goal-directed context monitoring and response selection.

The ACC is commonly activated during tasks requiring resolution of conflicting stimuli or rules (Botvinick et al., 1999, 2004). This conflict resolution process can be dissociated using fMRI from overall goal maintenance, subserved in turn by the PFC (MacDonald et al., 2000). Because the Simon task requires resolution of conflict in the incongruent blocks (pressing on the side of the screen opposite of the stimulus), we hypothesized that the thickness of this region will be selectively associated with and mediate the incongruency effect.

To investigate the specificity of brain-behavior associations, we also assessed short-term memory capacity using the digit span task in a subset of children ($N = 27$) for whom these data were available. There are two components in the digit span task: in the digits forward task, participants hear an increasingly longer series of digits and then must recite them. In

the digits backwards task, participants also hear an increasingly longer series of digits and then must perform mental manipulation by reciting them in the reverse order. We predicted that performance on the digit span task would be selectively related to cortical thickness in the superior parietal region, consistent with previous work using a variety of methods to examine neural substrates supporting short-term memory storage, including transcranial direct current stimulation to superior parietal cortex (e.g. Berryhill et al., 2010), patients with superior parietal lesions (Koenigs et al., 2009) and fMRI studies (e.g. Tsukiura et al., 2001). Moreover, we predict that superior parietal thickness will be more related to performance on the forward than the backward digit span task, consistent with the notion that the parietal cortex accumulates information in working memory (e.g., Jonides et al., 1998; McNab and Klingberg, 2007; Todd and Marois, 2004), and thus might serve as a neural correlate for working memory storage.

We assessed regional specificity of the relation of cortical thinning to task function by defining three regions of interest (ROIs) in the prefrontal, cingulate, and parietal cortex. Specifically, we examined cortical thickness in the right inferior frontal gyrus (rIFG), the bilateral anterior cingulate cortex (ACC), and the bilateral superior parietal cortex. We hypothesized a dissociation, such that cortical thinning in the rIFG and the ACC should be selectively related to improvements in task performance for context monitoring and cognitive control (respectively), whereas cortical thinning in the superior parietal region should be associated with improvement in short-term memory span. If shown, this would be the first demonstration of the correlation between age-related changes in structural maturity of regions typically recruited in the context of executive function tasks and age-related improvement in those tasks in early and middle childhood.

2. Material and methods

2.1. Subjects

Thirty-two children participated in this study (*M* age = 8.34 years; *SD* = 1.64; range: 5.7–10.7 years old; 14 female; *N* = 16 for age 7 and under; see Fig. 1 for a histogram of ages). One participant was Hispanic (3.1% of the sample), 2 were African-American (6.3%), 2 were Asian (6.3%), 26 were Caucasian (81.2%), and 1 had mixed ethnicity (3.1%). Eleven additional participants were excluded for failure to understand the Simon task (3), excessive movement (2), claustrophobia (2), or technical difficulties (4). Only 27 children completed the digit span task, due to changes in testing procedures. All study procedures were approved by the Institutional Review Boards at Massachusetts Institute for Technology and at Children's Hospital Boston. Informed consent and assent was provided by each participant. These data were collected as part of a larger study, in which functional MRI data was collected along with additional behavioral tasks, which will be reported elsewhere.

2.2. Imaging

2.2.1. Acquisition—Structural magnetic resonance images were acquired at Athinoula A. Martinos Imaging Center at MIT on a Siemens 3T TrioTim scanner. Images were obtained using a MPRGAGE sequence producing multi-echo T1-weighted images (TE 1 = 1.64 ms, TE 2 = 3.5 ms, TE 3 = 5.36 ms, TE 4 = 7.22 ms, TR = 2530 ms, flip angle = 7 degrees, 176 slices with $1 \times 1 \times 1$ mm isometric voxels) using a 32-channel head coil. To reduce the imaging acquisition time parallel imaging was used with an acceleration factor of 3.

2.2.2. Measurement of cortical thickness in individual subjects—Cortical thickness estimates were calculated with the FreeSurfer image analysis suite, which is documented and freely available for download online (http://surfer.nmr.mgh.harvard.edu). FreeSurfer morphometric procedures have demonstrated good test-retest reliability across

scanner manufacturers and field strengths (Han et al., 2006). In addition, these procedures have been successfully used in studies of children as young as age four (Ghosh et al., 2010).

FreeSurfer processing includes motion correction of a volumetric T1 weighted image, removal of non-brain tissue using a hybrid watershed/surface deformation procedure (Ségonne et al., 2004), automated Talairach transformation, previously validated in pediatric populations (Burgund et al., 2002) and segmentation of the subcortical white matter and deep gray matter volumetric structures, separately validated for use with pediatric populations (Ghosh et al., 2010).

FreeSurfer provided thickness estimates for 148 cortical regions (74 for each hemisphere), according to the 2009 atlas (Destrieux et al., 2010). Of these regions, we examined three a priori ROIs outlined above, based on hypotheses about regions that should be most critical for performance on the Simon and the digit span tasks (Fig. 2 depicts these ROIs). The superior parietal region was calculated by averaging the thickness across the left and the right superior parietal gyri, based on previous evidence suggesting that the integrity of both right and left superior parietal regions are necessary for verbal working memory storage (e.g.,Koenigs et al., 2009). The ACC region was calculated by averaging the thickness of the left and the right anterior cingulate region. Finally, rIFG was calculated based on the thickness of the right pars triangularis region.

2.3. Tasks

2.3.1. Simon task—In this task (adapted from Davidson et al., 2006), performed while children underwent MRI scanning, children were presented with two kinds of stimuli (e.g., pink and yellow circles, Fig. 3). These stimuli were presented one at a time on either the right or left side of the screen. Children were told to press the side-congruent button for one of these stimuli (pink circles) and the side incongruent button for the other stimuli (yellow circles). This task allowed us to examine both context monitoring and inhibitory demands; both the side-congruent and the side-incongruent trials have context monitoring demands because the correct motor response must be selected and executed. In contrast, only the side-incongruent trials have an additional inhibitory demand: i.e., ignoring the prepotent side-congruent response, and selecting the conflicting side-incongruent response. These trials were grouped into three types of blocks: side-congruent, side-incongruent, and fixation, each lasting 22 seconds. Non-fixation blocks included 11 trials, lasting two seconds each. There were two runs, each of which included 12 blocks, the order of which was counterbalanced, and with a total of 88 side-congruent and 88 side-incongruent trials. For each trial, accuracy and reaction time (RT) was recorded. Total time on task was approximately 4.5 minutes per each of the two runs for each child.

The three dependent variables (DV) were RTs from the side-incongruent trials (*incongruent RT*), side-congruent trials (*congruent RTs*), and incongruent RTs controlling for congruent RTs (i.e. congruent RTs were used as a covariate; *incongruency effect*). The latter DV allows us to selectively examine variance due to processing incongruency, which we hypothesize to be related to the functioning of the ACC. Another approach to examining the incongruency effect would be to calculate a difference score between incongruent and congruent RTs and use this difference score as the DV; however, the difference score approach lacks in power and reliability (Cronbach and Fruby, 1970; DeGutis et al., 2013; Edwards, 2001; Judd et al., 2009), and is thus not used here.

2.3.2. Digit span task—The forward and backward digit span subtests of the Weschler Intelligence Scale for Children, Forth Edition (WISC-IV) were administered. In the forward digit span, children were asked to recite increasingly longer strings of digits in the same order as the experimenter read them. In the backward digit span, children were asked to

recite increasingly longer strings of digits in the reverse order, starting from the last digit heard. Strings started out at two digits long and incrementally increased, up to eight digits long. There were two strings per length. The task was terminated when a child incorrectly recited both strings of a given length. The raw, non-adjusted for age lengths of the string at which the forward and the backward tasks were terminated were used here as the DVs because we were interested in examining the effect of age on task performance. These tasks were performed outside the scanner.

2.4. Statistical analyses

2.4.1. Behavioral results—Overall performance levels (accuracy and RTs) were established using a repeated-measures ANOVA with task condition (incongruent vs. congruent for the Simon task, and digits forward vs. digits backward for the digit span task) as within-subjects factors and gender as a between-subjects factor. The association between age and behavioral performance was assessed using ordinary least squares (OLS) linear regression with task condition and age as factors; all analyses controlled for gender.

2.4.2. Brain-behavior relationships—We examined the relation between cortical thickness in three a priori defined ROIs and task performance on the Simon task and digit span task. We performed this analysis using ordinary least squares (OLS) linear regression, using gender as a control variable.

2.4.3. Mediation analysis—To test whether the thickness of cortical structures could explain the relationship between age and task performance, we performed a mediation analysis. We hypothesized that cortical thickness in the rIFG and ACC regions selectively mediates the association between age and specific aspects of performance on the Simon task. According to the context monitoring account of rIFG function, rIFG thickness should mediate the age-performance relationship for both congruent and incongruent trials, because both require monitoring the context for relevant task features. According to the conflict monitoring account of ACC function, ACC thickness should mediate only the incongruency effect, given the role that this region plays in processing conflicting information. To test these hypotheses, we examined whether rIFG and ACC thickness mediates the link between age and incongruent RTs, age and congruent RTs, and age and the incongruency effect (incongruent RTs, additionally controlling for congruent RTs), respectively.

According to the classic approach to mediation, four criteria must be statistically significant (Baron and Kenny, 1986): (1) the relationship between a predictor variable (age) and an outcome variable (task performance); (2) the relationship between the predictor variable (age) and the potential mediators (cortical thickness); (3) the relationship the between potential mediators (cortical thickness) and outcome variable (task performance), which (4) must be mitigated by the addition of the mediator. With small sample sizes it is recommended that step 4, testing the significance of the mediated (or indirect) effect, be completed using a non-parametric bootstrapping approach (Hayes, 2009; MacKinnon et al., 2000; Preacher and Hayes, 2004, 2008; Shrout and Bolger, 2002). Generating this distribution allows the construction of a 95% confidence interval (CI) from which the statistical significance of the indirect effect can be evaluated for each mediator separately. Confidence intervals that do not include zero indicate a significant indirect effect of the predictor (age) on the outcome (task performance) through the mediators (cortical thickness), while controlling for gender. This approach for testing mediation has been recommended for use with small samples because it does not rely on assumptions of normality, which are often violated in small samples (Preacher and Hayes, 2004). Here we complete steps 1–3 of the Baron and Kenny approach using OLS linear regression, with

gender as a covariate. Consistent with previous studies using small sample sizes, we complete step 4 using the non-parametric bootstrapping approach.

3. Results

3.1. Simon task

3.1.1. Behavioral results—Accuracy and RT data are provided in Table 1. Accuracy was comparable across both types of trials, F(1,30) = .15, p = .70, but responses were faster for congruent than incongruent trials, F(1, 30) = 26.8, p < .001. Age was associated with better accuracy for both congruent trials (β = .043, p = .001) and incongruent trials (β = .034, p = .003). Age was marginally associated with faster RTs on congruent trials (β = −.23.3, p = .054) and showed a non-significant trend for faster RTs on incongruent trials (β = −18.6, p = .13). Because accuracy was consistently high and not differentiated across trial types, only RTs are used in all subsequent analyses.

3.1.2. Brain-behavior associations—As shown in Table 2, rIFG thickness was positively associated with RTs (thinner regions associated with faster RTs) on both types of trials (β = 281.8, p = .02 for incongruent RTs; β = 297.8, p = .01 for congruent RTs). Similar patterns were found for the association between ACC thickness and task performance (β = 299.8, p = .008 for incongruent RTs; β = 265.0, p = .02 for congruent RTs). As predicted, cortical thickness in the superior parietal cortex was not related to performance on the Simon task, all p's > .47.

3.1.3. Mediation analysis—We tested whether cortical thickness in the rIFG and the ACC regions mediated the relationship between age and Simon task performance. We predicted that the rIFG thickness would mediate this relationship for both types of trials, whereas the ACC would selectively mediate the relationship between the incongruency effect and age. As described above, we examined the criteria for performing a mediation analysis using the Baron and Kenny (1986) approach, and tested the significance of the mediation using the bootstrapping approach (Hayes, 2009; Preacher and Hayes, 2004, 2008) (Fig. 4).

Age was negatively associated with rIFG thickness (β = −.052, p = .002). RIFG thickness was positively related to both incongruent RTs (β = 281.8, p = .02) and congruent RTs (β = 297.8, p = .01). Age was negatively related to congruent RTs (β = −23.3, p = .05) and had a non-significant trend with the incongruent RTs (β = −18.6, p = .13). To test the significance of the indirect effect between age and Simon task performance, bootstrap resampling was used (95% confidence intervals are reported; significant confidence intervals do not include 0). This analysis revealed that consistent with our predictions, rIFG thickness was a significant mediator of age-performance relationship, as the confidence interval (CI) did not include zero for both congruent RTs CI: [−33.5, −1.5] and incongruent RTs CI: [−37.9, −1.1]. RIFG thickness did not predict incongruent RTs when controlling for congruent RTs, an estimation of the incongruency effect (β = 5.5, p = .92), and age was also not significantly related to the incongruency effect (β = 3.5, p = .51). However, the lack of a direct effect between the IV and the DV does not preclude examination of the indirect effect through the mediator (Hayes, 2009; MacKinnon et al., 2000; Rucker et al., 2011; Shrout and Bolger, 2002). Thus, we again used the bootstrap resampling and found, as predicted, rIFG thickness was a not significant mediator of the relationship between age and the incongruency effect CI: [−8.8, 3.2].

Similar steps were executed for examining whether ACC thickness mediated the age-performance association. Age was negatively related to ACC thickness (β = −.051, p = .

006). ACC thickness was significantly related to both incongruent RTs (β = 299.8, p = .008) and congruent RTs (β = 265.0 p = .02), but not the incongruency effect (β = 64.2, p = .22). We again used the bootstrap resampling and found that ACC thickness was not a significant mediator of the relationship between age and congruent RT CI: [−27.4, 2.0], but was a significant mediator of the relationship between age and incongruent RTs (CI: [−36.5, −.78]) and the incongruency effect, (CI: [−13.5, −.04]), consistent with the role of ACC in conflict processing.

Superior parietal cortical thickness was not related to age, incongruent RTs, congruent RTs, or the incongruency effect, all p's > .4. Further, thickness of the superior parietal cortex did not mediate the association between age and any behavioral dependent variables: CI for incongruent RTs = [−14.6, 2.3], CI for congruent RTs = [−11.5, 1.6], CI for the incongruency effect = [−1.5, 4.4].

3.2. Digit span

3.2.1. Behavioral results—Children correctly recalled more items when doing the forward (M = 4.5, SD = 1.2) than the backward (M = 3.6, SD = 1.1) components of the digit span task, F(1,24) = 17.3, p < .001. Performance improved with age for both the forward (β = .33, p = .02) and the backward components (β = .32, p = .009) of the task (Fig. 5).

3.2.2. Brain-behavior associations—As seen in Table 3, only the thickness of the Superior Parietal region reliably predicted forward digit span (β = −2.3, p = .046), while rIFG (β = −2.4, p = .051) and superior parietal thickness (β = −1.7, p = .099) both marginally predicted backward span. In contrast, thickness of the ACC region was not related to performance on either the forward or the backward span (both p's > .5). Interestingly, while there was a significant association between both age and digit span performance, and between superior parietal cortex thickness and digit span performance (for both forward and backward), superior parietal cortex did not mediate the association between age and digit span performance for either digits forward or digits backward (CI for forward digit span = [−.099, .13]; CI for backward digit span = [−.080, .084]; Fig. 5). This lack of mediation might be explained by the finding that in our sample there was no association between superior parietal thickness and age, unlike for the ACC or rIFG (Fig. 2).

4. Discussion

Our findings elucidate relationships between age-related improvement on measures of cognitive control and working memory span and structural maturation in three a priori defined cortical regions. The mediation analysis enabled us to look beyond simple correlations and investigate whether changes in cortical thickness could statistically explain age-related changes in behavior. These relationships were task and region-specific, with a dissociation across our two tasks and the three cortical regions. Specifically, cortical thinning in the rIFG significantly mediated the link between age and faster performance on the Simon task on both congruent and incongruent trial types, consistent with the context monitoring role of this region(Chatham et al., 2011; Hampshire et al., 2010; Munakata et al., 2011). In contrast, developmental thinning of the ACC mediated the relationship between age and incongruent RTs and between age and incongruency effect in the same task, consistent with its role in processing conflicting information (Botvinick et al., 1999, 2001). The cortical thickness mediation of the age-performance associations was task-specific, in that it was significant for the Simon, but not the digit span task. In addition, these effects were region-specific, such that the thickness in our third ROI, the superior parietal region, was not related to performance on the Simon task through either regression or mediation analyses. Instead, thickness in the superior parietal region, known to be critical for working

memory storage, was associated with performance on the digit span measure (Berryhill and Olson, 2008; Koenigs et al., 2009; Tsukiura et al., 2001), In contrast to the superior parietal region, the ACC did not show any association with performance on this task in either analysis, and rIFG only showed a marginal association with the backward digit span performance for the regression analysis.

Superior parietal thickness was associated with digit span performance, but not age, and did not mediate age-related changes in digit span performance in this sample. This finding might be explained if the superior parietal cortex is on a faster developmental trajectory than the rIFG or ACC, whereby our observed differences in thickness of the superior parietal area reflected stable individual differences instead of fluctuating changes in thickness associated with age. Some areas of the superior parietal cortex do appear to thin relatively early in childhood (Gogtay et al., 2004); however, a follow-up study with younger participants is needed to test this possibility. Previous work has demonstrated that different areas of cortex mature at different rates (e.g. Gogtay et al., 2004; Sowell et al., 2001, 2004; Shaw et al., 2008, 2006); here we additionally demonstrate that these stages of maturity are differentially predictive for assessments of various aspects of cognitive function.

Our results help inform an ongoing debate regarding the functional role of the rIFG. This region has long been postulated to be critical for supporting response inhibition (e.g. Aron et al., 2004; Aron, 2007), but recent theoretical and empirical work has argued that it is instead involved in contextual monitoring (Chatham et al., 2011; Dodds et al., 2011; Hampshire et al., 2010; Munakata et al., 2011). In our study, developmental thinning of the rIFG was associated with faster performance on the Simon task, irrespective of the trial type. This finding is consistent with the context monitoring account, given that both types of trials have monitoring demands and require detection of task-relevant information (stimulus color and location), but only the incongruent trials carry inhibitory demands. Our findings are also consistent with previous theoretical arguments against the constructs of inhibition existing at the *cognitive* level (e.g., MacLeod, 2003). Finally, our findings are consistent with empirical work that examined components of executive functions using the tri-partite model including shifting, updating, and inhibition (Miyake et al., 2000), and found no evidence for the inhibition factor in children (Huizinga et al., 2006; van der Sluis et al., 2007) or variance that is specific to the inhibition factor after controlling for variance that is common to other executive functions in adults (Friedman et al., 2008; see also Hedden and Gabrieli, 2010).

We found significant age-related thinning in the ACC and rIFG regions, consistent with findings of age-related decreases in cortical thickness (Giedd et al., 1999; Lenroot et al., 2007; Ostby et al., 2009; Sowell et al., 2004; Tamnes et al., 2010; Tau and Peterson, 2009). However, several other studies have reported age-related cortical *thickening* that occurs before thinning takes place, typically in later childhood or early adolescence. While some authors report age-related thickening in regions similar to the ones we examine here (e.g. Shaw et al., 2008), others find that thickening is selective to *left* frontal language regions and ventromedial prefrontal cortex, inferior to the ACC (Sowell et al., 2004): regions that we did not examine in our study. The specific shape of age-based trajectories varies greatly across different brain regions (e.g. Shaw et al., 2006, 2008); thus, the trajectories within our ROIs could differ from the large areas of cortex explored in previous studies (Shaw et al., 2006, 2008).

5. Limitations

One major limitation of our study is our cross-sectional design. It is possible that our results are driven, at least in part, by individual differences of participants that are not limited to age. We see evidence for this in superior parietal cortex, where there was no association

between thinning and age, and no significant mediation of age-related changes in digit span performance. However, our findings in the ACC and rIFG are less consistent with that interpretation, given that we see strong associations between age and cortical thinning, as well as significant brain mediation of age-related changes in performance. Nevertheless, a longitudinal follow-up would more precisely elucidate the role of the developing brain in supporting age-related task improvements in executive function tasks. A relatively small sample size is another limitation of our study; however, our sample is of similar size to previous studies examining brain-behavior relationships in children (e.g. Sowell et al., 2001, 2004).

6. Conclusions

Despite these limitations, we believe this study is an important first step in understanding the development of brain-behavior associations. To the best of our knowledge, our study is the first to investigate the relationship between neural structure and executive function performance in theory-driven, a priori defined regions during early and middle childhood: a time of dramatic improvement in executive functions. Establishing region-specific developmental trajectories could prove useful in helping to develop neural markers for diagnosing developmental disorders, such as the attention deficit-hyperactivity disorder (ADHD), which shows delayed maturation of developmental cortical thickness trajectories (Shaw et al., 2007, 2009). Before using cortical thickness measures for clinical and diagnostic purposes, however, a more solid understanding of the structure-function relationship in the developing brain is required. Here we show that these relationships show a high degree of specificity across different aspects of executive function tasks and neural regions. These data add to our understanding of how the structural maturation of the brain is associated with vast behavioral changes observed across childhood.

Acknowledgments

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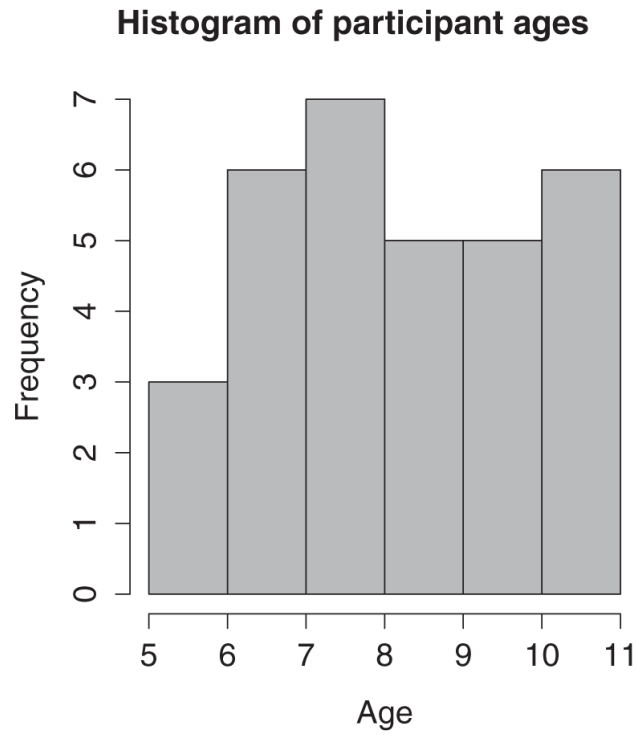
Histogram of participant ages

Fig. 1.
Histogram of participants' ages shows a comparable number of participants in each age bin.
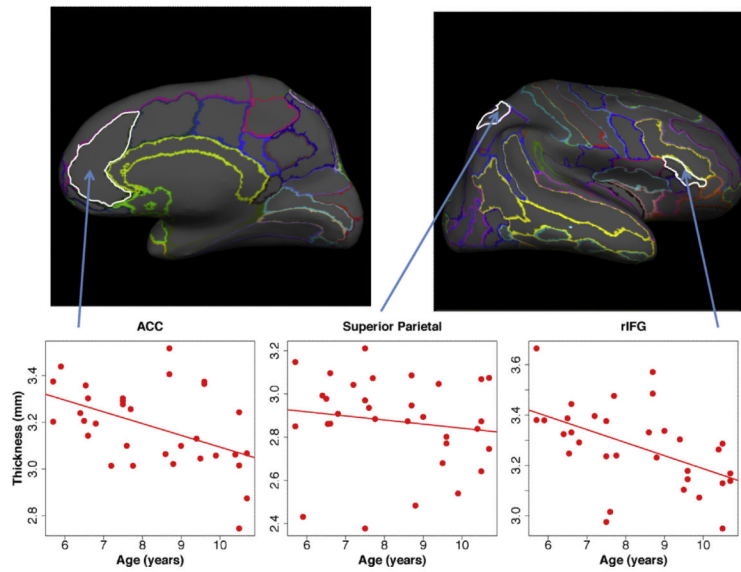
Fig. 2.
The association between cortical thickness and age for the three ROIs examined here. Abbreviations: rIFG: right Inferior Frontal Gyrus; ACC: Anterior Cingulate Cortex. The ROIs are outlined in white for one representative subject; only the right side is depicted here, but the ACC and the Superior Parietal regions were examined bilaterally. Thickness decreases linearly with age for the two of the three ROIs investigated here (rIFG, ACC).
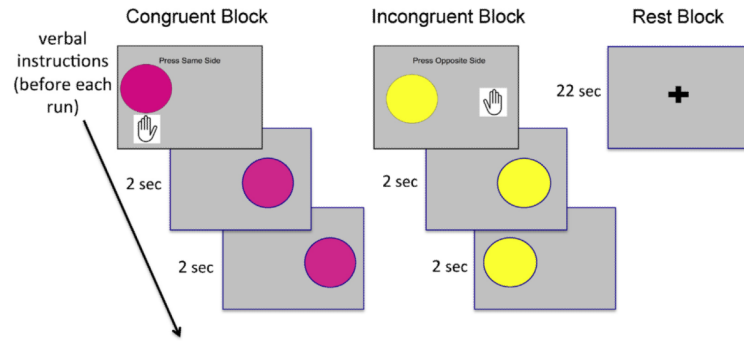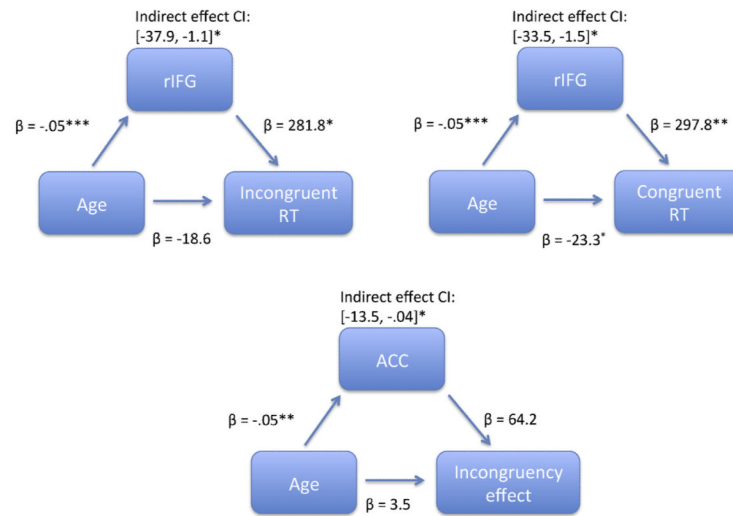
Fig. 3.
The design of the Simon task.

Fig. 4.
Mediation analysis results for the Simon task. Abbreviations: Sup Par: superior parietal cortex. ***Significant at .005 level, **Significant at .01 level, *Significant at .05 level, [x]Marginal at .1 level; all 2-sided tests.
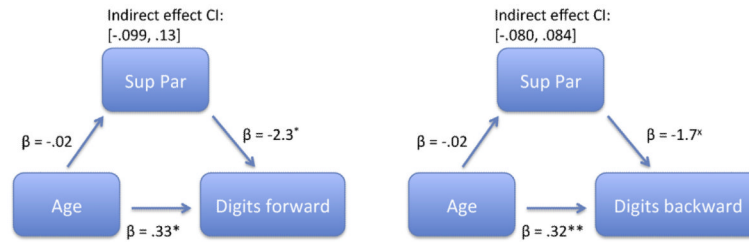
Fig. 5.
Mediation analysis results for the Digit span task. Abbreviations: Sup Par: superior parietal cortex. ***Significant at .005 level, **Significant at .01 level, *Significant at .05 level, ^{x}Marginal at .1 level; all 2-sided tests.

Table 1

Mean Accuracy (% correct) and RT data (ms), with standard deviations in parentheses.

Accuracy (% correct)		Reaction times (ms)	
Congruent	Incongruent	Congruent	Incongruent
90.8 (12.2)	91.7 (11.3)	625.5 (108.8)	665.7 (109.6)

Table 2

Regression output for cortical thickness predicting performance on the Simon task.

Simon Task: Brain-behavior relationships, controlling for gender		
Incongruent RT	**Congruent RT**	**Incongruency effect**
β**(SE)**	β**(SE)**	β**(SE)**
rIFG	281.8 (114.2)[*]	297.8 (110.9)[**]	5.5 (56.4)
ACC	299.8 (105.6)[**]	265.0 (107.0)[*]	64.2 (51.4)
Sup Par	55.3 (98.0)	69.9 (96.4)	−10.1 (39.9)

Abbreviations: rIFG: right Inferior Frontal Gyrus; ACC: Anterior Cingulate Cortex; Sup Par: Superior Parietal Cortex.

[***] Significant at .005 level,

[**] Significant at .01 level,

[*] Significant at .05 level,

[x] Marginal at .1 level; all 2-sided tests.

Table 3

Regression output for cortical thickness predicting performance on the Digit span task.

Digit Span Task: Brain-behavior relationships, controlling for gender		
	Digit span forward	Digit span backward
	β (SE)	β (SE)
rIFG	−1.5 (1.4)	−2.4 (1.1)[x]
ACC	−1.1 (1.4)	−.76 (1.2)
Sup Par	−2.3 (1.1)[*]	−1.7 (.97)[x]

Abbreviations: rIFG: right Inerior Frontal Gyrus; ACC: Anterior Cingulate Cortex; Sup Par: superior parietal cortex.

[***] Significant at .005 level,

[**] Significant at .01 level,

[*] Significant at .05 level,

[x] Marginal at .1 level; all 2-sided tests.