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

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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.

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

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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.