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Folding of the anterior cingulate cortex partially explains inhibitory control during childhood: A longitudinal study

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ABSTRACT

Difficulties in cognitive control including inhibitory control (IC) are related to the pathophysiology of several psychiatric conditions. In healthy subjects, IC efficiency in childhood is a strong predictor of academic and professional successes later in life. The dorsal anterior cingulate cortex (ACC) is one of the core structures responsible for IC. Although quantitative structural characteristics of the ACC contribute to IC efficiency, the qualitative structural brain characteristics contributing to IC development are less-understood. Using anatomical magnetic resonance imaging, we investigated whether the ACC sulcal pattern at age 5, a stable qualitative characteristic of the brain determined in utero, explains IC at age 9. 18 children performed Stroop tasks at age 5 and age 9. Children with asymmetrical ACC sulcal patterns ($n = 7$) had better IC efficiency at age 5 and age 9 than children with symmetrical ACC sulcal patterns ($n = 11$). The ACC sulcal patterns appear to affect specifically IC efficiency given that the ACC sulcal patterns had no effect on verbal working memory. Our study provides the first evidence that the ACC sulcal pattern – a qualitative structural characteristic of the brain not affected by maturation and learning after birth – partially explains IC efficiency during childhood.

1. Introduction

Difficulties in the ability to control impulses and to inhibit a prepotent response (i.e., inhibitory control, hereafter referred to as IC) are related to various pathologic conditions, including Attention Deficit Hyperactivity Disorder (Willcutt et al., 2005), addiction (Goldstein and Volkow, 2011), risk behavior (Quinn and Fromme, 2010), conduct problems (Rothbart et al., 2011), schizophrenia (Insel, 2010) and poor academic performance (Diamond et al., 2007). In healthy subjects, cognitive control including IC efficiency in childhood is a strong predictor of academic and professional successes later in life (Moffitt et al., 2011). The dorsal anterior cingulate cortex (ACC, also labeled the midcingulate cortex, Vogt, 2009) is one of the core structures of the brain functional network responsible for the ability to control impulses and to resolve cognitive conflict

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(Petersen and Posner, 2012). Within the theoretical framework of the conflict-monitoring hypothesis (Botvinick, 2007; Botvinick et al., 2001), the role of the dorsal ACC is to signal conflict in information processing to the cognitive control system supported through dorsolateral prefrontal cortices. The cognitive control system will supposedly increase the activation of task-relevant information and inhibit task-irrelevant information to resolve the information processing conflict (see Egner and Hirsch, 2005).

The ability to control impulses and to inhibit a prepotent response is determined in part by the ACC structure, as suggested by the relationship between interindividual differences in adults' cognitive control efficiency and differences in the cortical thickness (Westlye et al., 2011), surface area (Fjell et al., 2012) and the gray matter volume (Takeuchi et al., 2012) of the ACC. Moreover, the relationship between cognitive control efficiency and these quantitative structural characteristics of the ACC appears to vary during the course of the development (Giedd et al., 2009), with the relationship being stronger for younger children compared to older ones (Fjell et al., 2012). However, the variations in the quantitative characteristics of the brain structure are affected not only by brain maturation but also by learning. Indeed, previous studies have demonstrated that prolonged learning and specific trainings – leading to the improvement of cognitive efficiency – can modify the quantitative structural characteristics of the areas responsible for the trained processes (Draganski et al., 2004, 2006; Hyde et al., 2009). For example, increases in gray matter volume have been reported in adults in response to 3 months of intense training in juggling (Draganski et al., 2004) and to intense learning for medical examinations (Draganski et al., 2006) and in children in response to 15 months of musical training – with a relationship between the quantitative structural brain changes induced by the training and behavioral improvements (Hyde et al., 2009).

Although *quantitative* characteristics of the brain structure reveal the dynamic interplay between brain maturation and learning/training on cognitive development, they provide no information on the early constraint imposed by the structure of the brain on cognitive development. The study of the sulcal pattern, a *qualitative* characteristic of the brain, might provide such information. Indeed, the sulcal pattern is a stable feature of the brain morphology determined in utero (Rakic, 2004; White et al., 2010), and it is not affected by maturation and learning occurring after birth (Sun et al., 2012). Specifically, asymmetry in the sulcal pattern of the ACC between the right and left hemispheres has been associated with increased IC efficiency in preschoolers (Cachia et al., 2014) and in adults (Fornito et al., 2004; Huster et al., 2009). However, there has not yet been evidence that the sulcal pattern of the ACC at a given age explains IC efficiency later in development.

To provide such evidence, we asked the same 18 children to perform Stroop tasks at age 5 and at age 9 – a developmental window in which IC efficiency increases dramatically (Fjell et al., 2012) – and we studied whether a qualitative measure of the ACC morphology (i.e., the sulcal pattern of the ACC) at age 5 was associated with the children's behavioral performance on the Stroop tasks both at age 5 and at age 9. Consistent with previous studies (Cachia et al., 2014; Fornito et al., 2004; Huster et al., 2009), the sulcal pattern of the ACC was classified as a 'single' type when only the cingulate sulcus was present and as a 'double parallel' type when a paracingulate sulcus (PCS) ran parallel to the cingulate sulcus (Ono et al., 1990; Paus et al., 1996a,b) (see Fig. 1A). Children performed the Color-Word Stroop task (Stroop, 1935) at age 9 and the Animal Stroop task (Wright et al., 2003) – an adaptation of the Color-Word Stroop Task for non-reading children – at age 5 (see Fig. 1B). In the Color-Word Stroop task, children named the color of the ink of printed words that denoted colors in a no-conflict condition, in which the ink colors matched the colors denoted by the words (e.g., 'BLUE' appeared in blue ink), and in a conflict condition, in which the colors denoted by the words interfered with the ink colors to be named (e.g., 'RED' appeared in blue ink). Similarly, in the Animal Stroop task, children named the body of animals in a no-conflict condition – i.e., the head matched the animal's body (e.g., a duck's head on a duck's body) – and in a conflict condition – i.e., the head of the animal was replaced by the head of a different animal (e.g., a pig's head on a duck's body). In both Stroop tasks, the difference in response times (i.e., the Stroop interference scores) between the no-conflict and conflict conditions typically reflects the ability to process conflicting information, drawing, in part, on IC efficiency. Critically, the ACC is consistently activated in the Stroop tasks (Petersen and Posner, 2012).

We reasoned that if the sulcal pattern of the ACC constrains IC efficiency during childhood, then the children with asymmetrical ACC sulcal patterns (i.e., the 'single' type in the left hemisphere and the 'double parallel' type in the right hemisphere or vice versa) should have lower Stroop interference scores (i.e., better IC efficiency) than children with symmetrical ACC sulcal patterns (i.e., the 'single' type or the 'double parallel' type in both hemispheres) not only at age 5 but also at age 9. In addition, if the ACC sulcal patterns not only partially explain IC efficiency during childhood but affect the development of IC efficiency per se, then the ACC sulcal patterns should have an effect on the difference in Stroop interference scores between age 5 and age 9.

To assess the specificity of the effect of the ACC sulcal pattern on the development of IC efficiency, we also investigated, in the same sample of children, whether the sulcal pattern of the ACC partially explained the development of their verbal working memory. This investigation was critical given that the Stroop task involves not only the ability to overcome perceptual and cognitive conflicts (MacLeod, 1991) but also a range of other cognitive processes, including working memory (MacLeod et al., 2003). To evaluate the verbal working memory efficiency of children, we asked children at age 5 and age 9 to perform, in addition to the Stroop tasks, the forward and backward digit span tasks from the Wechsler Intelligence Scale for Children (WISC-IV, Wechsler, 2003). Children were instructed to listen to a series of discrete digits, and they subsequently recalled the series of digits in the same (i.e., forward digit span task) or reverse (i.e., backward digit span task) order of presentation. We reasoned that if the sulcal patterns of the ACC constrain specifically IC efficiency during childhood and not other executive functions, then the sulcal pattern of