Development of temperamental effortful control mediates the relationship between maturation of the prefrontal cortex and psychopathology during adolescence: A 4-year longitudinal study

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ABSTRACT

This study investigated the relationship between the development of effortful control (EC), a temperamental measure of self-regulation, and concurrent development of three regions of the prefrontal cortex (anterior cingulate cortex, ACC; dorsolateral prefrontal cortex, dlPFC; ventrolateral prefrontal cortex, vlPFC) between early- and mid-adolescence. It also examined whether development of EC mediated the relationship between cortical maturation and emotional and behavioral symptoms. Ninety-two adolescents underwent baseline assessments when they were approximately 12 years old and follow-up assessments approximately 4 years later. At each assessment, participants had MRI scans and completed the Early Adolescent Temperament Questionnaire-Revised, as well as measures of depressive and anxious symptoms, and aggressive and risk taking behavior. Cortical thicknesses of the ACC, dlPFC and vlPFC, estimated using the FreeSurfer software, were found to decrease over time. EC also decreased over time in females. Greater thinning of the left ACC was associated with less reduction in EC. Furthermore, change in effortful control mediated the relationship between greater thinning of the left ACC and improvements in socioemotional functioning, including reductions in psychopathological symptoms. These findings highlight the dynamic association between EC and the maturation of the anterior cingulate cortex, and the importance of this relationship for socioemotional functioning during adolescence.

1. Introduction

Self-regulation refers to internal and/or transactional processes that regulate emotion, cognition and behavior (Karoly et al., 2005; Steinberg, 2005). It plays a crucial role in the development of various aspects of functioning, and has been associated with increased social competence (Spinrad et al., 2006), superior coping abilities (Eisenberg et al., 1997), and academic success (Duckworth and Seligman, 2005; Eisenberg et al., 2010). Poorer

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regulatory capabilities, on the other hand, are related to problems with attention and hyperactivity, sexual risk taking, and addiction (Crockett et al., 2006; Quinn and Fromme, 2010), as well as other externalizing and internalizing problems (Eisenberg et al., 2010; Valiente et al., 2004).

Self-regulation has often been studied by developmental researchers within a temperamental framework (Bridgett et al., 2013; Zhou et al., 2012). Effortful control (EC), a construct that consistently arises from factorial analyses of temperament questionnaires, describes the ability to shift and focus attention, and inhibit a dominant response and/or activate a subdominant response (Rothbart and Rueda, 2005). The current study examined EC using a self-report measure of temperament specifically designed for adolescents: the Early Adolescent Temperament Questionnaire-Revised (EATQ-R; Capaldi and Rothbart, 1992; Ellis and Rothbart, 2001). EC is composed of three subscales within the EATQ-R; activity control, inhibitory control, and attentional control. Individuals with high levels of EC have been found to exhibit greater regulation of their attention, emotions and behavior, which is thought to have positive effects for their social and emotional functioning (Eisenberg and Spinrad, 2004).

Rothbart et al. (2003) propose that individual differences in EC are determined by the functioning of the executive attention network (Posner, 2012; Rothbart et al., 2007), which is thought to comprise the anterior cingulate cortex (ACC) and lateral prefrontal cortices (Posner, 2012; Rothbart and Rueda, 2005). Specifically, the ACC is thought to monitor competition between conflicting processes and signal this information to the lateral PFC (Botvinick et al., 1999; Casey et al., 2001). Within the lateral PFC, the dorsolateral prefrontal cortex (dlPFC) is involved in keeping goals active within working memory and directing attention, and the ventrolateral prefrontal cortex (vlPFC) is implicated in selection of goal-appropriate responses based on information from semantic memory, such as the causes, significance and potential outcomes of the situation (Kalisch, 2009; Ochsner and Gross, 2008; Ochsner et al., 2012).

1.1. Adolescent development

Adolescence is characterized by significant improvements in self-regulatory abilities. Although the development of EC has not been examined during this period, numerous studies have identified improvements in related constructs. For example, performance on tasks of cognitive control that tap into the same executive attention network that is implicated in EC has been found to improve into early adulthood (Leon-carrion et al., 2004; Luna et al., 2004). Similarly, emotion regulatory abilities have been found to continue to develop through adolescence (Garnefski and Kraaij, 2006; McRae et al., 2012). Furthermore, there is also marked cortical maturation during adolescence, including post-pubertal reductions in gray matter thickness (Brown et al., 2012; Mills et al., 2012; Mutlu et al., 2013; Shaw et al., 2008; Tamnes et al., 2010a). Specifically, higher-order association cortices within the prefrontal region, such as those underlying EC, have been found to exhibit protracted development into the early adult years (Gogtay et al., 2004).

However, little is known about the development of EC in relation to structural maturation of its presumed neurobiological substrates during adolescence. Although investigators have postulated that the protracted development of self-regulation may be attributed to delayed prefrontal cortical maturation (Nelson et al., 2005; Sowell, 2004), limited research has specifically investigated this relationship. To our knowledge, only one longitudinal study has directly examined within-subject change in gray matter structure in relation to change in self-regulatory abilities. Tamnes et al. (2013) found that improvements in working memory were related to reductions in cortical volume of the prefrontal and posterior parietal regions between 9 and 20 years of age. Cross-sectional studies are also limited, with inconsistent results to date (Fjell et al., 2012; Tamnes et al., 2010b; Østby et al., 2011). Therefore, further research is needed to examine the relationship between cortical maturation and development of self-regulatory processes.

Adolescence is also a period of increasing prevalence of various forms of psychopathology, such as depression, anxiety, substance use, and conduct problems (Paus et al., 2008). There is now a well-established role of regulatory processes in the development of psychopathology. Low levels of EC have consistently been related to the presence of internalizing symptoms, such as depression and anxiety, as well as externalizing symptoms, such as aggression, conduct problems, risk taking and hyperactivity (Eisenberg et al., 2001; Muris and Meesters, 2009; Oldehinkel et al., 2004; Valiente et al., 2004). Therefore, EC may be one potential indirect pathway through which neurobiological changes in the prefrontal regulatory regions impact on behavioral outcomes.

1.2. The current study

Given the paucity of research examining concurrent development of neurobiology and behavior, the current study investigated the relationship between development of EC and concurrent maturation of three hypothesized neural substrates (ACC, dlPFC, and vlPFC), in a community sample of adolescents. The study also investigated whether change in EC mediated the relationship between cortical maturation and the development of internalizing and externalizing symptoms. Sex effects in these relationships were also explored as there is some evidence of differences between males and females in cortical maturation (Mutlu et al., 2013; Raznahan et al., 2010) and in EC (Else-Quest et al., 2006).

A longitudinal design was employed to assess within-subject change between early- and mid-adolescence, with the age range of the sample being strictly constrained at both periods of assessment. To our knowledge, no longitudinal research has been conducted in this area using self-reported termperamental assessment of self-regulation, or using measures of psychopathology symptoms. Given that cortical maturation is characterized by reductions in thickness during adolescence, and more rapid thinning has been associated with higher levels of