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Cognitive control network connectivity in adolescent women with and without a parental history of depression

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ABSTRACT

Background: Adolescent women with a parental history of depression are at high risk for the onset of major depressive disorder (MDD). Cognitive theories suggest this vulnerability involves deficits in cognitive control over emotional information. Among adolescent women with and without a parental history of depression, we examined differences in connectivity using resting state functional connectivity analysis within a network associated with cognitive control over emotional information.
Methods: Twenty-four depression-naïve adolescent women underwent resting state functional magnetic resonance imaging (fMRI). They were assigned to high-risk ($n = 11$) and low-risk ($n = 13$) groups based their parents' depression history. Seed based functional connectivity analysis was used to examine group differences in connectivity within a network associated with cognitive control.
Results: High-risk adolescents had lower levels of connectivity between a right inferior prefrontal region and other critical nodes of the attention control network, including right middle frontal gyrus and right supramarginal gyrus. Further, greater severity of the parents' worst episode of depression was associated with altered cognitive control network connectivity in their adolescent daughters.
Conclusions: Depressed parents may transmit depression vulnerability to their adolescent daughters via alterations in functional connectivity within neural circuits that underlie cognitive control of emotional information.

1. Introduction

Adolescent women with a parental history of depression are at unusually high risk for major depressive disorder (MDD). Between the ages of 13 and 15, girls begin to experience depression at twice the rate as boys of the same age (Nolen-Hoeksema and Girgus, 1994; Hankin and Abramson, 2001; Hyde et al., 2008) These rates increase by 2–3-fold among girls who have a parental history of depression (Beardselee et al., 1998; Weissman et al., 2006). Adolescent depression is particularly pernicious, as it frequently leads to chronic and recurrent MDD in adulthood (Lewinsohn et al., 1999; Rao et al., 1999). Thus, there is a clear need to elucidate the mechanisms underlying depression vulnerability in this high-risk, adolescent population.

Neural models of depression broadly implicate deficits in the recruitment of regions associated with cognitive

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control, particularly control over mood congruent information (e.g., sad images) (Mayberg, 1997; Phillips et al., 2003). These regions include ventral and dorsal lateral prefrontal cortex, anterior cingulate cortex, and posterior parietal cortex (Disner et al., 2011). Recent work using resting state fMRI suggests that current depression is associated with abnormalities in the functional connectivity between these regions, which comprise key nodes of the so-called cognitive control network (CCN) (Schlösser et al., 2008; Vasic et al., 2009; Sheline et al., 2010; Veer et al., 2010; Alexopoulos et al., 2012). Thus, a growing body of evidence supports the idea that CCN function is altered in depression. What remains unclear is whether differences in CCN network are due to current symptomatology or are evident prior to symptom onset. Alterations within the CCN network must predate onset of depression for CCN connectivity to be considered a viable risk factor for depression.

To investigate this possibility, we used seed-based, resting state functional connectivity analysis to explore differences in CCN connectivity among adolescent women with and without a parental history of depression. Our exploration focused specifically on a set of CCN regions implicated in attentional control. Cognitive models of depression posit that deficits in attentional control over emotional stimuli play a key role in depression vulnerability (Beck, 1967; Ingram, 1984; Teasdale, 1988). Behavioral studies suggest that these deficits predict the onset of depression in adults (Beevers and Carver, 2003; Beevers et al., 2011). Recent behavioral work also suggests that a parental history of depression predisposes adolescent women to deficits in attentional control for emotional stimuli (Joormann et al., 2007).

Importantly, difficulty with attentional control over emotional stimuli in depression appears to be associated with functional alterations within the CCN network. An imaging study examining attentional control over emotional information found that depression was associated with altered activity several key CCN regions, including right inferior frontal gyrus (rIFG), right middle frontal gyrus (rMFG), and right supramarginal gyrus (rSMG) (Beevers et al., 2010). The rIFG in particular is thought to play a key role in mediating the success of cognitive control over emotional stimuli (Ochsner and Gross, 2005; Wager et al., 2008). This region has been implicated in behavioral inhibition, suppression of unwanted thoughts, attention shifting, and efforts to reappraise emotional stimuli (Aron et al., 2004; Anderson et al., 2004; Hampshire and Owen, 2006; Hampshire et al., 2010).

Given its important role in the cognitive control over emotion stimuli, we selected the rIFG region as a seed region for functional connectivity analyses in adolescent women with and without a parental history of depression. In addition to this whole brain approach, we performed a region of interest (ROI) analysis using the rMFG and rSMG locations identified in our previous study (Beevers et al., 2010). This analysis allowed us to explore the specificity of deficits in this previously defined network using an unbiased approach. We also supplemented group comparisons with analyses using severity of parents' worst episode of depression as a more continuous index of adolescent depression risk. This variable was then used to examine connectivity between the rIFG seed and rMFG/rSMG targets in the ROI analysis.

We are not aware of any studies examining functional connectivity within the CCN among adolescents at high risk for depression. Two recent studies suggest that adolescent depression is associated with decreased connectivity within putative resting state networks, including frontolimbic and default mode networks (Bluhm et al., 2009; Cullen et al., 2009). Results in depressed adults are mixed; there is recent evidence of decreased (Veer et al., 2010; Alexopoulos et al., 2012) and increased connectivity within the CCN (Sheline et al., 2010). This is in contrast to a more consistent pattern of increased DCN connectivity in depressed adults (e.g., Sheline et al., 2010; Greicius et al., 2007).

Based on the adolescent and recent adult depression literature, we predicted that adolescent women at high-risk for MDD by virtue of parental history of depression would demonstrate decreased connectivity within the CCN. More specifically, we expected decreased connectivity between rMFG/rSMG targets and the rIFG seed. We also speculated that severity of parents' worst depressive episode would be associated with lower levels of connectivity between rMFG/rSMG targets and the rIFG seed.

2. Methods

2.1. Sample

The sample included 27 adolescents and one of their adult parents (for 96% of the girls, this was their mother). One individual was removed from analysis due to excessive movement during imaging. Two other individuals were removed from the analysis because we could not confidently assign them to a group (parental history or no parental history) due to conflicting reports about depression history. In both cases, the parent who completed the study materials did not report a history of depression; however, their daughters reported a history of depression in the other parent (who did not participate in the study) on a family history self-report questionnaire. In two cases we could not verify the daughter's self-report using standardized measures (i.e., attempts to have the other parent complete the depression history screening and questionnaire were unsuccessful); therefore, we removed these two individuals from the analysis. As a result, the final sample included 24 adolescent girls between the ages of 13 and 15. Girls were then assigned to high-risk ($n = 11$) and low-risk ($n = 13$) groups based on criteria used to classify their parents' history of depression (see below). There were no significant differences with respect to age and race across vulnerability groups (see Table 1 for demographic information).

2.2. Measures

Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS). The Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) (Puig-Antich and Chambers, 1978) is a structured