Amygdala reactivity predicts adolescent antisocial behavior but not callous-unemotional traits

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**A R T I C L E I N F O**

**Article history:**
Received 17 October 2016
Accepted 22 February 2017
Available online 27 February 2017

**Keywords:**
Antisocial behavior
Callous-unemotional traits
Amygdala
Threat
fMRI

**A B S T R A C T**

Recent neuroimaging studies have suggested divergent relationships between antisocial behavior (AB) and callous-unemotional (CU) traits and amygdala reactivity to fearful and angry facial expressions in adolescents. However, little work has examined if these findings extend to dimensional measures of behavior in ethnically diverse, non-clinical samples, or if participant sex, ethnicity, pubertal stage, and age moderate associations. We examined links between amygdala reactivity and dimensions of AB and CU traits in 220 Hispanic and non-Hispanic Caucasian adolescents (age 11–15; 49.5% female; 38.2% Hispanic), half of whom had a family history for depression and thus were at relatively elevated risk for late starting, emotionally dysregulated AB. We found that AB was significantly related to increased right amygdala reactivity to angry facial expressions independent of sex, ethnicity, pubertal stage, age, and familial risk status for depression. CU traits were not related to fear- or anger-related amygdala reactivity. The present study further demonstrates that AB is related to increased amygdala reactivity to interpersonal threat cues in adolescents, and that this relationship generalizes across sex, ethnicity, pubertal stage, age, and familial risk status for depression.

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1. Introduction

Antisocial behavior (AB) includes behaviors such as rule breaking, lying, and aggression. AB is a major public health concern because of its high prevalence and the negative impact of AB on perpetrators, victims, and their families (Foster and Jones, 2005; Nock et al., 2006; Odgers et al., 2007). Recent research has suggested that youth with AB are a heterogeneous group (Frick and Viding, 2009), which may undermine intervention success. Thus, research that examines the divergent etiologies of specific dimensions within AB has the potential to inform more effective, personalized treatments (Frick and Nigg, 2012; Kahn et al., 2012; Moffitt et al., 2008).

1.1. Divergent pathways of amygdala reactivity

One recent approach to parsing AB into etiologically distinct subtypes is to measure the presence of callous-unemotional (CU) traits. CU traits were added as a subtyping specifier to the antisocial behavior diagnosis of Conduct Disorder in the latest version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013), titled “with limited prosocial behavior.” These traits are characterized by low empathy, lack of remorse, and shallow interpersonal affect (Frick and White, 2008; Viding et al., 2012). AB in the presence of CU traits is more highly heritable (Viding et al., 2005), and research is beginning to suggest that AB and CU traits may have divergent relationships with neural reactivity, particularly in the amygdala (Hyde et al., 2013). The amygdala has been implicated in cognitive and affective processes believed to underlie behavioral deficits characteristic of youth AB, such as poor fear conditioning and impaired...
emotional regulation, potentially via two divergent pathways (Blair et al., 2014; Hyde et al., 2013). In one pathway, in those high on CU traits, relatively decreased amygdala reactivity to signals of interpersonal distress may prevent the processing of interpersonal distress cues, and disrupt important conditioning early in life that contributes to the development of empathy (Blair et al., 2014). In a second pathway, in those low on CU traits, but high on AB, relatively increased amygdala reactivity to cues of social threat may result in over-reactivity to threat and lead to emotional dysregulation, manifesting behaviorally as increased reactive aggression and AB (Hyde et al., 2013; Viding et al., 2012). Consistent with a dual pathway model, antisocial adolescents with high levels of CU traits (AB+/CU+) demonstrate relatively decreased amygdala reactivity to signals of interpersonal distress such as fearful facial expressions with directed eye gaze (Jones et al., 2009; Lozier et al., 2014; Marsh et al., 2008; Viding et al., 2012). In contrast, antisocial adolescents low on CU traits (AB+/CU−) exhibit relatively increased reactivity of the amygdala to negative emotional stimuli, particularly interpersonal signals of threat, such as angry facial expressions with directed eye gaze (Herpertz et al., 2008; Sebastian et al., 2012; Sebastian et al., 2014; Viding et al., 2012).

Though a growing literature supports a dual pathway model for AB+/CU+ versus AB+/CU− adolescents, the majority of these studies have focused on small case-control samples of those extreme on AB and CU traits. Thus, beyond a few exceptions (e.g., Viding et al., 2014), studies of adolescents have been unable to separate the relative contribution of amygdala reactivity to AB versus CU traits. As evidence continues to accumulate emphasizing the dimensional nature of AB and CU traits (Blonigen et al., 2006; Krueger et al., 2007), research is needed to test these relationships across the distribution of AB and CU traits, particularly in samples with non-clinical levels of AB. Although recent studies have begun to examine AB dimensionally in healthy and at-risk adults (e.g., Carré et al., 2013; Hyde et al., 2014), it is important to examine this question in early adolescence at the cusp of the emergence of serious AB and other psychopathology. Thus, the primary goal of our study was to examine the relationships between AB, CU traits, and amygdala reactivity to fearful and angry facial expressions in a relatively large sample of teens with variability in AB and CU traits but without diagnosable levels of AB.

1.3. Present study

The goal of the present study was to investigate relationships between amygdala reactivity and dimensional measures of AB and CU traits in a sample of adolescents with nonclinical levels of AB at the start of adolescence. We examined reactivity to fearful and angry facial expressions compared to a non-face control condition to evaluate the differential contribution of reactivity to interpersonal distress or threat, respectively. Consistent with prominent theories of AB and CU traits (Blair et al., 2014), we expected that AB would be related to increased amygdala reactivity to angry facial expressions, whereas CU traits would be uniquely related to decreased amygdala reactivity to fearful facial expressions. Finally, given previous research suggesting differential neural correlates for AB between men and women (Carré et al., 2013), as well as across race/ethnicity (Hyde et al., 2016), and research suggesting that pubertal onset may influence amygdala reactivity (Crone and Dahl, 2012), we examined these relationships in an early adolescent sample containing substantial proportions of Hispanic participants and girls during early to middle adolescence to analyze potential moderation of findings based on sex, ethnicity, pubertal timing, and age. Though sex, ethnicity and puberty based analyses were exploratory, we expected that relationships between AB, CU traits, and amygdala reactivity would be strongest in male participants and Caucasians in early stages of puberty, given that prior research in this area has focused on Caucasian boys during early adolescence (Jones et al., 2009; Sebastian et al., 2014; Viding et al., 2012). Finally, though we focused on the amygdala globally, given the different roles in fear learning, potential implications for the development of later psychopathology (Moul et al., 2012), as well as the different afferent and efferent connections of the centro-medial (CM) versus the basolateral (BL) regions (Amunts et al., 2005), we also conducted exploratory analyses within the CM versus BL sub-regions. We examined these questions in a large sample of psychiatrically healthy participants, in a sample that was enriched with adolescents with familial risk for depression (50% of the sample) and thus potentially at risk for later comorbid and emotionally dysregulated late onset AB.
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