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Boys with conduct problems and callous-unemotional traits: Neural response to reward and punishment and associations with treatment response

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ABSTRACT

Abnormalities in reward and punishment processing are implicated in the development of conduct problems (CP), particularly among youth with callous-unemotional (CU) traits. However, no studies have examined whether CP children with high versus low CU traits exhibit differences in the neural response to reward and punishment. A clinic-referred sample of CP boys with high versus low CU traits (ages 8–11; n = 37) and healthy controls (HC; n = 27) completed a fMRI task assessing reward and punishment processing. CP boys also completed a randomized control trial examining the effectiveness of an empirically-supported intervention (i.e., Stop-Now-And-Plan; SNAP). Primary analyses examined pre-treatment differences in neural activation to reward and punishment, and exploratory analyses assessed whether these differences predicted treatment outcome. Results demonstrated associations between CP and reduced amygdala activation to punishment independent of age, race, IQ and co-occurring ADHD and internalizing symptoms. CU traits were not associated with reward or punishment processing after accounting for covariates and no differences were found *between* CP boys with high versus low CU traits. While boys assigned to SNAP showed a greater reduction in CP, differences in neural activation were not associated with treatment response. Findings suggest that reduced sensitivity to punishment is associated with early-onset CP in boys regardless of the level of CU traits.

1. Introduction

Although childhood-onset conduct problems (CP) have been consistently associated with the development of severe and chronic antisocial behavior, many children who exhibit severe CP do not engage in severe delinquency during adolescence or adulthood (Moffitt, 1993; Byrd et al., 2012). A growing number of studies have found that callous-unemotional (CU) traits (e.g., lack of empathy and guilt) may help further delineate a subgroup of children with CP at heightened risk for exhibiting severe and persistent delinquency (Frick et al., 2013). As a result, CU traits have recently been added as a specifier for conduct disorder in The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5; American Psychiatric Association, 2013) and there is increasing interest in identifying unique etiological factors may underlie the development of CP among youth with CU traits.

Abnormalities in reward and punishment processing have long been implicated in the development of CP, particularly among youth with CU traits (Byrd et al., 2013; Blair et al., 2016; Hyde et al., 2013). Theoretically, researchers have suggested that a heightened sensitivity to reward and reduced sensitivity to punishment (i.e., loss of a desired stimulus or presentation of an unpleasant stimulus) increase risk for the development and persistence of CP. Behavioral studies have found that CP youth exhibit a greater affinity for large, immediate rewards using risk taking paradigms (Fairchild et al., 2009; Syngelaki et al., 2009; Schutter et al., 2011), and difficulty inhibiting a previously rewarded response in the face of increasing punishment during passive avoidance (Hartung et al., 2002) and response reversal paradigms (O'Brien et al., 1994; O'Brien and Frick, 1996; Matthys et al., 1998). Moreover, there is some evidence to suggest that these deficits are most pronounced among CP youth with high CU traits (Budhani and Blair, 2005; Frick et al., 2013, 2003; Byrd et al., 2013). However, these studies assess 'overall performance' using behavioral tasks that include aspects of both reward *and* punishment processing, limiting our ability to disentangle whether the observed performance differences are due to abnormalities in processing reward, punishment, or both. Additionally, it is unclear whether CP youth exhibit deficits in processing reward and

Abbreviations: CP, conduct problems; CU, callous-unemotional; HC, traits healthy controls; SNAP, Stop-Now-And-Plan

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punishment at a particular stage of learning (e.g., initial encoding/receipt, acquisition, extinction) or across multiple stages (Balsam et al., 2010).

Over the last several years, neuroimaging studies have attempted to address these limitations by disaggregating the neural response to reward and punishment across various stages of learning. Some evidence indicates that, relative to healthy controls (HC), youth with CP exhibit functional abnormalities in regions associated with reward processing (i.e., ventral and dorsal striatum), punishment processing (i.e., amygdala), and higher-order regulatory function (i.e., medial prefrontal cortex, mPFC; anterior cingulate cortex, ACC) (for reviews see Byrd et al., 2013; Hyde et al., 2013; Blair et al., 2016; Alegria et al., 2016). This altered functional activation has been documented using tasks involving either reward or punishment anticipation and/or receipt (Bjork et al., 2010; Cohn et al., 2015b, 2013) as well as tasks incorporating aspects of both reward and punishment during acquisition and/or extinction (Finger et al., 2008, 2011; White et al., 2013, 2016; Crowley et al., 2010; Cohn et al., 2015a). While prominent theory posits that a hypersensitivity to reward and a hyposensitivity to punishment underlies the development of CP and CU traits (Newman and Wallace, 1993; Frick et al., 2014), the neuroimaging literature is not entirely consistent, with noted discrepancies in directionality of results (i.e., hyper- versus hypo-activation) (Byrd et al., 2013; Blair et al., 2016; Hyde et al., 2013). Though inconsistencies may be associated with task-specific differences or an inability to completely disambiguate responsivity to reward and punishment processing at individual stages of learning (Richards et al., 2013), additional limitations regarding sample heterogeneity may also obscure findings.

Many studies in this area have focused on functional differences in reward/punishment processing between heterogeneous groups of CP youth and healthy controls (e.g., Rubia et al., 2008; Bjork et al., 2010; Crowley et al., 2010), potentially obfuscating important etiological differences. Those studies that have assessed CU traits report mixed findings and this may be attributable to an extreme group approach (i.e., CP youth with high CU traits versus healthy controls; Finger et al., 2008, 2011) or suppressor effects arising from a failure to account for unique associations between CP versus CU traits and variation in neural response to reward/punishment (see Cohn et al., 2015a, 2013). Additionally, these studies have focused almost exclusively on adolescence, a developmental period characterized by substantial changes in the neural circuitry underlying reward and punishment processing (Steinberg and Morris, 2001). Thus, the current study sought expand on previous research by focusing on potential differences in reward/punishment processing *between* subgroups of pre-adolescent youth with CP and high versus low CU traits.

1.1. Implications for intervention

The examination of reward and punishment processing among subgroups of youth with CP is particularly important from an intervention perspective. Although multimodal interventions that include child-focused cognitive-behavioral therapy (CBT) and parent management training (PMT) are generally effective at reducing CP among children (Webster-Stratton et al., 2004), it is well-documented that these interventions are not equally effective for all youth (Hawes et al., 2014; Matthys et al., 2012). Some have suggested that CP youth with CU traits may be more responsive to reward-based intervention and more resistant to punishment focused strategies (Hawes et al., 2014). However, we are aware of no existing studies that have examined whether functional abnormalities in reward and/or punishment processing are associated with treatment response among CP youth with high versus low CU traits.

1.2. Current study

To address noted gaps in the literature, the current study used functional magnetic resonance imaging (fMRI) to assess neural responsivity to the receipt of reward and punishment among pre-adolescent boys with CP and varying levels of CU traits, and HC. To examine potential differences *between* CP boys with high versus low CU traits, group-based analyses were used. Additionally, CP and CU traits were examined dimensionally in continuous analyses. Consistent with theory and prior research, we hypothesized that CP would be associated with reduced sensitivity to punishment and greater sensitivity to reward as evidenced by decreased amygdala activation to punishment, increased striatal activation to reward and reduced activation in the mPFC and ACC to both reward and punishment. Moreover, we hypothesized that these neural abnormalities would be most pronounced in those boys with CP and high CU traits. Finally, in exploratory analyses, this study examined whether abnormalities in the neural correlates of reward and/or punishment processing predicted post-treatment levels of CP following random assignment to an empirically supported multi-modal intervention (i.e., Stop-Now-And-Plan; SNAP).

2. Methods

2.1. Participants

Participants were 64 boys 8- to 11-years-old ($M = 10.68$; $SD = 1.18$): 37 boys exhibiting CP and 27 matched HC. CP youth were recruited from a larger treatment study (Burke and Loeber, 2014) and deemed eligible if they presented with clinically significant behavior problems (i.e., externalizing composite T-score > 64; aggressive behavior, rule breaking, conduct problems subscale T-scores > 70) according to the Child-Behavior Checklist (CBC-L; Achenbach, 1991) For further details on inclusion and exclusion of CP youth, see Burke and Loeber (2015).

HC were recruited predominantly from local pediatricians' offices in the community and matched as a group to CP youth on age and race. Inclusion criteria necessitated problems below the at-risk threshold on all externalizing and internalizing scales of the CBCL (T-score < 60). All procedures were reviewed and approved by the Institution Review Board. Written informed consent was obtained from parents/guardians and youth provided assent prior to each assessment.

2.2. Procedure

All CP youth and HC controls completed a baseline assessment, which included measures of CP, CU traits and covariates (e.g., demographics, IQ). Eligible CP and HC youth also completed an fMRI scan. Following the fMRI scan session, CP youth were randomly assigned to one of two treatment conditions: 1) a multimodal CBT/PMT intervention (i.e., SNAP; n = 21) or 2) standard services (SS; n = 16) in the community as a part of the larger treatment study (see Burke and Loeber, 2015). Finally, CP youth were reassessed 3-months later, after treatment was completed. Due to attrition, post-treatment data was only collected on 34 CP boys (19 assigned to SNAP; 15 assigned to SS). For review of the larger intervention, see Burke and Loeber (2015).

2.3. SNAP intervention

The SNAP program is an empirically supported, manualized intervention and takes a multimodal approach by focusing on two core components: 1) child CBT groups emphasizing self-control skills and problem-solving techniques; 2) parent PMT groups focused on behavioral strategies for consistent reward and punishment implementation. Groups use modeling, behavioral rehearsal/role plays and home practice exercises and are offered simultaneously for 90-min for 12 consecutive weeks. For further details on this intervention see Augimeri et al. (2007).