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The processing of animacy information is disrupted as a function of callous-unemotional traits in youth with disruptive behavior disorders

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ABSTRACT

Atypical amygdala responses to emotional stimuli have been consistently reported in youth with Disruptive Behavior Disorders (DBDs; Conduct Disorder/Oppositional Defiant Disorder). However, responding to animacy stimuli has not been systematically investigated. Yet, the amygdala is known to be responsive to animacy stimuli and impairment in responsiveness to animacy information may have implications for social cognitive development. Twenty-nine youth with DBDs and 20 typically developing youth, matched for IQ, age (M_{age} = 14.45, SD = 2.05) and gender, completed a dot probe task during fMRI. Stimuli consisted of negative/faces, negative/objects, neutral/faces and neutral/objects images. Youth with DBDs, relative to typically developing youth, showed: i) reduced amygdala and lateral temporal cortex responses to faces relative to objects. Moreover, within the group of youth with DBDs, increasing callous-unemotional traits were associated with lesser amygdala responses to faces relative to objects. These data suggest that youth with DBDs, particularly those with high levels of CU traits exhibit dysfunction in animacy processing in the amygdala. This dysfunction may underpin the asociality reported in these youth.

1. Introduction

Disruptive Behavior Disorders (DBDs), which include Conduct Disorder and Oppositional Defiant Disorder, are a leading cause of referrals to mental health practitioners for children and adolescents (Kazdin et al., 2006). Youth with DBDs are at increased risk for aggression and antisocial behavior (Frick et al., 2005). Furthermore, prognosis is poor, with many of these youth showing significant aggression in adulthood (Fergusson et al., 2010; Robins, 1966). Recent neuroimaging work has implicated amygdala dysfunction in the pathology of DBDs (Blair et al., 2014). However, the functional characteristics of this amygdala dysfunction remain under-studied.

The amygdala engages in emotional processing (LeDoux, 2012) showing greater responses to threat and appetitive stimuli relative to neutral stimuli (Zald, 2003), stimuli previously associated with aversive reinforcers relative to stimuli not associated with such reinforcers (Pape and Pare, 2010) and fearful expressions relative to neutral expressions (Murphy et al., 2003). The amygdala is thought to prime representations of emotional stimuli within temporal cortex, through reciprocal interactions with this region (Desimone and Duncan, 1995; Pessoa and Ungerleider, 2004; Vuilleumier, 2005). The amygdala is also sensitive to animacy information. The amygdala shows greater responses to animate stimuli, particularly faces (Gobbini et al., 2011; Yang et al., 2012), but also animals (Coker-Appiah et al., 2013; Yang et al., 2012), and inanimate objects moving in animate ways (Martin and Weisberg, 2003; Wheatley et al., 2007) relative to inanimate stimuli. Lateral regions of temporal cortex, including lateral fusiform gyrus and posterior superior temporal sulcus, show increased response to animate relative to inanimate stimuli (Martin, 2007). It is assumed that the amygdala similarly primes cortical representations of animate stimuli within these regions, similar to representations of emotional stimuli (Dunsmoor et al., 2014).

Youth with DBDs show disrupted amygdala responses to emotional stimuli (Crowe and Blair, 2008; Marsh and Blair, 2008) together with reduced lateral temporal cortex responses (for meta-analysis see Alegria et al., 2016), presumably due to reduced priming by the amygdala. The severity of amygdala disruption is positively associated with the level of a particular symptom set; callous-unemotional (CU) traits (lack of guilt/

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empathy, deficient affect; Viding et al., 2012; White et al., 2012a). CU traits represent an important subgroup of antisocial youth (Frick et al., 2014) and are captured by the "with Limited Prosocial Emotions" specifier for Conduct Disorder in the Diagnostic and Statistical Manual of Mental Disorders – 5th Edition (American Psychiatric Association, 2013).

Notably though, the functional integrity of other roles of the amygdala, for example responsiveness to animacy, in youth with DBDs and their relationship with CU trait severity remains unknown. One prototypical animate stimulus, known to activate the amygdala, is the human face (Gobbini et al., 2011; Yang et al., 2012). Considerable previous work has examined responsiveness to face stimuli in youth with conduct problems and CU traits (see Marsh and Blair, 2008 for meta-analysis). However, the majority of these studies have examined the contrast between responsiveness to emotional relative to neutral face stimuli (Jones et al., 2009; Marsh et al., 2008; Viding et al., 2012; White et al., 2012a). In other words, work has not typically specifically examined group differences in responsiveness to *neutral* face stimuli. Responsiveness to neutral stimuli has been treated as a high-level baseline stimulus, which allows for contrasting the responsiveness to emotional face stimuli. One exception to this, Marsh et al. (2008) did suggest intact responding to neutral faces in a sample of youth with DBD and psychopathic traits. However, our preliminary recent re-analysis of neutral face data from White et al. (2012a) revealed reduced responsiveness in youth with DBD and elevated CU traits to neutral faces. As such, we considered it useful to examine responsiveness to this form of animate stimuli in a targeted study of youth with DBD.

Determining the functional integrity of the amygdala during animacy processing in youth with DBDs, particularly as a function of CU traits, is important for two reasons. First, response to animacy information is considered critical for social engagement (Wheatley et al., 2007), particularly within the amygdala (Ochsner, 2008). As such, dysfunctional animacy processing might contribute to the social disengagement associated with CU traits (e.g., attachment problems; Bohlin et al., 2012; Pasalich et al., 2012) and/or the disruption of socialization reported in youth with CU traits (Frick et al., 2014; Frick and White, 2008). Second, response to animacy information has implications for future interventions. As interventions become targeted for specific neuro-cognitive impairments, it is important to know whether the clinician's target should be modifying the individual's amygdala responsiveness to emotional stimuli selectively or generally increase amygdala responsiveness.

The current study utilized a dot probe paradigm (MacLeod et al., 1986). Such a paradigm allows assessment of both behavioral responses and neural responsiveness to both neutral and emotional animate stimuli. More critically, it allows assessment of responsiveness to these variables "passively"; without task demands that focus on the core variables. That is, to respond to the dot probe, not the animacy/emotional components of the visual stimuli. As such, this paradigm shared similarities with our previous work that has examined amygdala responsiveness to distress cues in this population (task demands in this work focus on the person's gender rather than their affect; e.g., Mitchell et al., 2007; White et al., 2012a). In addition, such a paradigm allows assessment of the participant's capacity for response inhibition via their differential responsiveness to the congruence/incongruence of the visual location of the visual stimulus and the probe. Notably, an association between dysfunctional response inhibition and externalizing behaviors (Patrick et al., 2013; Young et al., 2009), particularly impulsivity (Krueger et al., 2007; Loeber et al., 2009), has been made for some time. Moreover, recent work has indicated that youth with DBDs show reduced responsiveness in systems mediating response inhibition (although this impairment relates to impulsiveness rather than CU traits; Hwang et al., 2016).

The current study tests two hypotheses. First, youth with DBDs, relative to TD youth, would show reduced responses to negative relative to neutral images and animate relative to inanimate stimuli within the amygdala and lateral temporal cortex. Second, within the youth with DBD, CU traits would be inversely associated with responsiveness to negative and animate stimuli within the amygdala and lateral temporal cortex.

2. Methods

2.1. Participants

Fifty-two youth participated, though the final sample was 49 youth: 29 youth with DBDs and 20 typically developing (TD) youth aged 10–17 years. Three youth (1 TD youth and 2 youth with DBDs) were excluded for excessive movement (see MRI parameters and data preprocessing). Youth were recruited from the community through advertising and referrals from area mental health practitioners. A statement of informed assent and consent was obtained from participating youth and parents. The NIH Combined Neurosciences Institutional Review Board approved this study. All youth and parents completed the Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS; Kaufman et al., 1997) assessments conducted by a doctoral-level clinician as part of a comprehensive psychiatric and psychological assessment. The K-SADS has demonstrated good validity and inter-rater reliability (kappa $>$ 0.75 for all diagnoses; Kaufman et al., 1997). The K-SADS assesses for substance abuse and substance dependence but, due to exclusion criteria, no children in either group met criteria for these diagnoses. IQ was assessed with the Wechsler Abbreviated Scale of Intelligence (two-subtest form; Wechsler, 1999). Exclusion criteria were pervasive developmental disorder, Tourette's syndrome, lifetime history of psychosis, depression, bipolar disorder, generalized, social or separation anxiety disorder, post-traumatic stress disorder, neurologic disorder, history of head trauma, history of substance abuse, and IQ $<$ 70. In addition, parents completed the Inventory of Callous-Unemotional Traits (Frick, 2004), a measure of callous-unemotional traits. Youth meeting K-SADS criteria for Conduct Disorder or Oppositional Defiant Disorder were included in the DBDs group, while comparison subjects did not meet criteria for any K-SAD diagnosis. The groups did not differ significantly on IQ ($t = 1.511$, $p = 0.138$), age ($t = -1.134$, $p = 0.263$), or gender ($\chi^2 = 1.793$, $p = 0.181$).

2.2. Study measures

2.2.1. Inventory of Callous-Unemotional Traits (ICU; Frick, 2004)

The ICU is a 24-item parent-report scale designed to assess CU traits in youth. The construct validity of the ICU has been supported in community and juvenile justice samples (Essau et al., 2006; Kimonis et al., 2008).

2.2.2. The Animacy Attention Task

The current study used a version of a dot probe task (White et al., 2014). The stimuli consisted of images that were negative and animate (i.e., fearful faces), negative and inanimate (e.g., gun, knife), neutral and animate (i.e., neutral faces), or neutral and inanimate (e.g., mug, hairdryer). Importantly, stimuli were matched such that facial expression stimuli did not differ from the object stimuli on valence, arousal, or luminance (White et al., 2014). Each trial began with a 30 ms fixation, followed by a 300 ms stimulus presentation on either the left of the right side of the screen occupying 40% of the width and 45% of the height of the screen. The stimuli were immediately followed by the presentation of a probe (*) for 1000 ms. During congruent trials the probe appeared on the same side of the screen as the stimulus. During incongruent trials, the probe appeared on the opposite side of the screen to the stimulus. Following the probe was a 970 ms fixation. Participants were asked to make a button press corresponding to the side of the screen the probe appeared on as quickly as possible after the presentation of the probe. The task included 4 runs of 2 m and 10 s each, each consisting of 10 negative faces, 10 negative objects, 10