Antisocial Behavior is Associated with Reduced Frontoparietal Activity to Loss in a Population-Based

Sample of Adolescents

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Draft version 1, 6/2/21. This manuscript is currently under peer review. Please do not copy or cite without author's permission

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Abstract

Background: Adolescent antisocial behavior (AB) is a public health concern due to the high financial and social costs of AB on victims and perpetrators. Neural systems involved in reward and loss processing are thought to contribute to AB. However, investigations into these processes are limited: few have considered anticipatory and consummatory components of reward, response to loss, nor whether associations with AB may vary by level of callous-unemotional (CU) traits.

Methods: A population-based, community sample of 128 predominantly low-income youth (mean age =15.9 years; 42% male) completed a monetary incentive delay task during fMRI. A multi-informant, multi-method latent variable approach was used to test associations between AB and neural response to reward and loss anticipation and outcome, and whether these associations were moderated by CU traits.

Results: AB was not associated with neural response to reward but was associated with reduced frontoparietal activity during loss outcomes. This association was moderated by CU traits such that individuals with higher levels of AB and CU traits had the largest reductions in frontoparietal activity. Co-occurring AB and CU traits were also associated with increased precuneus response during loss anticipation.

Conclusions: Findings indicate that AB is associated with reduced activity in brain regions involved in cognitive control, attention, and behavior modification during negative outcomes. Moreover, these reductions are most pronounced in youth with co-occurring CU traits. These findings have implications for understanding why adolescents involved in AB continue these behaviors despite severe negative consequences (e.g., incarceration).

Introduction

Antisocial behavior (AB) refers to acts of aggression, rule-breaking, and delinquency, and is the foundation of the diagnosis of Conduct Disorder (CD) in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013). Adolescent AB is a major public health concern due to the chronic trajectory of AB, leading to substantial long-term costs for perpetrators, victims of AB, and to society broadly (Foster & Jones, 2005). Despite theory and behavioral research emphasizing the role of dysfunctional reward and punishment-related decision making in AB (Blair, 2015a; Fowles, 1980; Hoppenbrouwers, Neumann, Lewis, & Johansson, 2015), there is relatively little research investigating the associations between AB and neural response to reward and punishment (Byrd, Loeber, & Pardini, 2014; Murray, Waller, & Hyde, 2018).

Reward Processing in Antisocial Behavior

Behavioral and neurobiological studies indicate that youth engaging in high levels of AB persist with previously rewarded behaviors, even when reward contingencies change (Blair, 2015a, 2015b; Byrd et al., 2014). Several studies have examined the neural mechanisms that underlie disrupted reward processing in youth AB (Bjork, Chen, Smith, & Hommer, 2010; Cohn et al., 2015; Crowley et al., 2010; Finger et al., 2011; Gatzke-Kopp et al., 2009; Murray, Shaw, Forbes, & Hyde, 2017; Veroude et al., 2016; White et al., 2013). These studies have primarily focused on the ventral striatum (VS), a hub of the reward circuit that is key for reward motivation, valuation, and response (Haber & Knutson, 2010; Heekeren et al., 2007). Yet, the direction of the associations between youth AB and reward-related neural processing are mixed (for reviews see, Byrd et al., 2014; Murray et al., 2018). For example, prior work has shown that adolescents with “externalizing” behaviors have increased VS activation during reward outcomes (Bjork et al., 2010) and when expected rewards are not received (Gatzke-Kopp et al., 2009), while other studies have linked adolescent AB to reduced VS reactivity during risky-decision making (Crowley et al., 2010), and passive avoidance learning (Finger et al., 2011).

There are several possible explanations for the seemingly conflicting findings regarding the relationship between AB and reward processing. First, AB is a heterogeneous construct with subgroups that have potentially different etiologies. Callous-Unemotional (CU) traits – which includes low empathy, remorse, and interpersonal affect – delineate a group of youth high on AB, with a more stable and severe pattern of AB, and different behavioral, genetic, and neural correlates (Frick, Cornell, Barry, Bodin, & Dane, 2003a). Thus, the DSM-5 added CU traits as a specifier of the CD diagnosis (“with limited prosocial emotions”) to delineate youth that may have a different trajectory and etiology to their AB (American Psychiatric Association, 2013). Discrepancies in findings of reward-related neural functioning may be attributed to the (often unmeasured) presence (or absence) CU traits in each sample. To date, few studies have investigated how CU traits might influence associations between AB and reward processing in youth (Cohn et al., 2015; Murray et al., 2017).

A second factor potentially contributing to conflicting findings is the considerable methodological heterogeneity across neuroimaging investigations of reinforcement processing. Reward and loss processing include distinct phases (e.g., anticipation, consumption, learning), which have unique patterns of neural activation across a network of corticolimbic brain regions (Berridge & Robinson, 2003; Knutson & Greer, 2008). AB and impulsive-antisocial psychopathic traits have been linked to increased neural reactivity in frontostriatal regions during reward anticipation, but not outcome (Buckholz et al., 2010; Murray et al., 2018), highlighting the importance of examining potential neural dysfunction within specific phases of reward processing.

Beyond explaining discrepancies in the existing (small) literature, two other limitations of the literature need to be addressed. First, despite behavioral research that indicates abnormal punishment processing as playing a key role in AB (Matthys, Van Goozen, Snoek, & Van Engeland, 2004; Newman, Widom, & Nathan, 1985), few studies have examined associations between AB and neural responses to *negative outcomes* such as monetary loss (Byrd, Hawes, Burke, Loeber, & Pardini, 2018; Gregory et al.,

2015). Second, most neuroimaging research on AB is conducted using either relatively small groups of youth with severe AB or samples of very healthy participants who reside near major research universities. Both of these sampling strategies have their respective strengths and limitations, either by examining neural response to reward in extreme groups, thus not capturing the dimensional nature of AB (Krueger, Markon, Patrick, Benning, & Kramer, 2007), or by recruiting non-representative, advantaged and very healthy community samples, which may limit the reliability and generalizability to the general population (e.g., across a range of racial/ethnic groups and socioeconomic status) (Button et al., 2013; Chiao, 2009; Chiao & Cheon, 2010). Recruiting participants from under-represented and underserved groups (e.g., African Americans) is particularly important for research on AB due to these groups' disproportionate exposure to systemic racism, which leads to greater exposure to low-income, dangerous neighborhoods, which place youth at greater risk for AB (Leventhal & Brooks-Gunn, 2000). Moreover, youth of color are more likely to experience harsher consequences for risky-behavior than non-minority youth (e.g., incarceration) (Burch, 2015). Questions of generalizability and replicability of neuroimaging findings to broader, more representative samples highlight the critical importance of examining brain-behavior relationships in well-sampled cohorts that include substantial representation of participants of color (Falk et al., 2013; Hyde, Thompson, Creswell, & Falk, 2015).

Current Study

The current study contributes to a small but growing body of work on neural reward and loss processing in youth AB. The study seeks to fill gaps in the previous literature by investigating associations between AB and neural activity during both anticipatory and consummatory phases of reward and loss processing in a sample of primarily low SES adolescents, the majority of which identify as youth of color. In addition to examining associations to neural response to both reward and loss, the study examines whether CU traits moderate any associations between AB and neural activity during

adolescence, a critical developmental period when AB becomes more common and severe (Shaw, Hyde, & Brennan, 2012).

Method

Participants

Participants were 237 youth from the Study of Adolescent Neural Development (SAND) who participated in the longitudinal Fragile Families and Child Wellbeing Study (FFCWS; Reichman, Teitler, Garfinkel, & McLanahan, 2001). The FFCWS is a longitudinal population-based sample of infants born in hospitals in twenty US cities (population >200,000) between 1998 and 2000. The study was oversampled 3:1 for non-marital births. Based on this sampling frame (urban, non-marital births), the resulting sample was enriched for families with lower-income and substantial representation of families of color. At the time of recruitment, 42% of the sample reported an annual household income of <\$25,000. Families in the FFCWS completed interview-based assessments when target youth were 1, 3, 5, 9, 15 years old. The current sample consists of youth born in three of the original 20 cities: Detroit, MI, Toledo, OH, and Chicago, IL. 195 youth completed the fMRI scanning session. Of the 128 youth with usable fMRI data in the present analyses (Supplemental Table 1), the average age was 15.9 years old (range 15.0-17.6); 58% were female; 76% were Black/African American, 12% were White/European American; and 40.6% had an annual family income of below \$25,000 (Supplemental Table 2; Murray, Lopez-Duran, Mitchell, Monk, & Hyde, 2020). Youth also completed self-report questionnaires and a psychiatric interview. Primary caregivers completed self-report questionnaires, questionnaires about their child, and psychiatric interviews about their and their child's mental health. The University of Michigan institutional review board approved all procedures.

Measures

Monetary incentive Delay task. Participants completed a point-based, modified version of the Monetary Incentive Delay (MID) task during fMRI (Supplemental Figure 1; Murray et al., 2020). The task

consisted of 90 trials, presented in two, 45-trial, 9.4-minute runs. In each trial, participants saw a cue indicating the trial type (potential win, loss, or no-change/neutral), then a variable fixation crosshair delay, then a target (white square), followed by a jittered inter-trial interval. Participants were instructed to respond to the target with their right index finger to win or avoid losing points. Task difficulty was adjusted using a performance tracking algorithm so that each participant successfully responded to ~50% of the trials. Participants completed a practice session outside of the scanner to ensure task understanding and to determine the initial response window. The task used in the current study produced a robust response in the extended corticolimbic circuit and was also able to separate the anticipation and consumption phases of reward and loss via additional jitter (2-4 sec) between trials (Murray et al., 2020).

Antisocial Behavior. AB was assessed using a multi-informant, multi-method approach which combined several indicators of AB using self-report, parent-report, and clinical diagnostic assessment as done previously in this sample (Dotterer et al., 2020). AB was assessed using the (a) total score from the youth-reported Self-Report of Delinquency (Elliott, Huizinga, & Ageton, 1985), (b) rule-breaking, and (c) aggression subscales from the parent-reported Child Behavior Checklist (CBCL; Achenbach, 1991; Achenbach, Dumenci, & Rescorla, 2003), and (d) combined lifetime CD and oppositional defiant disorder (ODD) symptom counts from the clinician-rated Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime diagnostic interview (K-SADS; Kaufman et al., 1997). The four measures were modestly-to-strongly correlated (range, $r=.30-.81$, all $ps <.001$; Supplemental Table 3). To create a multi-method, multi-informant, dimensional measure of AB, we used confirmatory factor analysis (CFA) in Mplus (Version 7.3; Muthén & Muthén, 2014) with maximum likelihood estimation with robust standard errors. Scale loadings on the latent AB factor were moderate-to-high ($\beta=.39-.93$, $p <.001$; Supplemental Table 3).

Assessment of Callous-Unemotional Traits. Similar to the assessment of AB, we used several indicators to create a multi-informant, multi-method dimensional measure of CU traits (Dotterer et al., 2020). CU traits were assessed using total scores from the (a) parent-reported and (b) youth-reported Inventory of Callous-Unemotional Traits (Frick, 2004), and (c) clinician-rated total lifetime symptom counts from the Michigan Addendum to the K-SADS (Walker et al., 2020), which consisted of items derived from the Clinical Assessment of Prosocial Emotions (CAPE; Frick, 2016) to assess the Limited Prosocial Emotions specifier of CD in the DSM-5. The three measures were modestly correlated ($r = .13-.35$, all $ps < .05$; Supplemental Table 4). A latent factor was created in MPlus (Muthén & Muthén, 2014) using CFA with full information maximum likelihood estimation with robust standard errors. Scale loadings were moderate-to-high ($\beta = .35-.86$, $p < .001$; Supplemental Table 4).

Other Variables included as Covariates. To account for potential demographic or developmental effects, we included the following covariates in all fMRI analyses: (a) self-reported race, a social construct used here to address differences in exposures to personal and systemic racism and other unequal exposures (two dichotomous codes: Black/African American vs. Other; White/European American vs. Other) (Phinney, 2010); (b) parent-reported annual family income; (c) youth age (months); (d) self-reported gender; and (e) self-reported pubertal development, using the Pubertal Development Scale (Murray et al., 2020; Petersen, Crockett, Richards, & Boxer, 1988).

Analysis

BOLD fMRI acquisition and pre-processing. Youth were scanned with a GE Discovery MR750 3T MRI scanner with an 8-channel head coil. T1-weighted gradient echo images were taken before the functional scans (TR/TE = 9.0/1.8 ms, TI = 500 ms, flip angle = 15°, FOV = 26 cm; slice thickness = 1.4 mm; 256 x 256 matrix; 40 slices). Functional T2*-weighted BOLD images were acquired using a reverse spiral sequence with interleaved contiguous axial 3mm slices (TR/TE = 2000/30 ms, flip angle = 90, FOV = 22 cm) aligned with the AC-PC plane. Functional images were positioned to maximize limbic coverage. An

auto-shimming procedure was conducted to reduce field inhomogeneity. The standard pre-processing procedure from the University of Michigan fMRI Center was applied, including removing outliers from the raw k-space data, image reconstruction, fieldmap correction, and slice-timing correction. Using SPM12 (<http://www.fil.ion.ucl.ac.uk/spm/>), high-resolution anatomical images were re-oriented to the AC-PC plane, gray matter segmented, and functional images were realigned, co-registered, normalized, and smoothed with an 8mm FWHM Gaussian filter.

Artifact detection Tools (ART) software (http://www.nitrc.org/projects/artifact_detect/) was used to identify motion outliers (>2mm movement or 3.5° rotation) that were removed in the statistical model via spike regression. Due to our focus on the VS, participants were only included in subsequent analyses if there was a minimum of 70% coverage in the VS using an anatomically defined bilateral region of interest (ROI). Two spheres of 10mm radius were created in WFU PickAtlas Tool v3.0.5 around the Montreal Neurological Institute (MNI) coordinates $x=\pm 12$, $y=12$, and $z=-10$ to encompass the bilateral VS (Murray et al., 2017). Data were also visually inspected for signal drop out and poor whole brain coverage (particularly in reward-related regions including the prefrontal cortex and limbic system). As described previously in this task and sample (Murray et al., 2020), additional data quality assessments were done to assess for outliers. Six subjects were excluded due to having several large, or many small movement artifacts, despite having fewer than 20% outlier scans identified with ART. Analyses including these subjects are similar to those reported in the main text (Supplemental Table 5). Participant exclusions due to MRI contraindications, behavioral data, and MRI processing are presented in Supplemental Table 1.

In addition to testing associations between AB and reward- and loss-related neural response at the whole-brain level, we also examined associations within the VS, a key node of the reward circuit, using a small-volume correction. 3dClustSim (Cox, Chen, Glen, Reynolds, & Taylor, 2017) was used for multiple comparison correction using a Monte Carlo simulation to achieve a correction of $p<.05$. Spatial

autocorrelation (ACF) values for a random 10% of the sample were calculated from the first level model residuals using 3dFWHMx in AFNI. ACF values (mean values: 0.512, 6.737, 12.656) were used in 3dClustSim to estimate the noise smoothness using a Gaussian plus mono-exponential function. We used a voxel-wise correction of $p < .001$. Resulting cluster thresholds were $k=5$ for the VS ROI and $k=131$ for whole-brain analyses.

Neural response to reward and loss in AB. To test for associations between AB and neural response to reward and loss, multiple regression analyses were conducted using SPM12. Separate multiple regression analyses of AB and CU traits as predictors were examined in contrasts allowing for the separation of anticipation and consumption phases: 1) Reward Anticipation > Reward Win 2) Loss Anticipation > Loss Outcome. Neural responses for expected versus unexpected outcomes within the context of reward and loss trials were also examined: 3) Reward Win > No-Win Trials, and 4) Loss Outcome > No Loss. We also examine the potential moderating effect of CU traits on associations between AB and neural response. We hypothesized that AB would be associated with increased VS response during reward anticipation and that CU traits would not be associated with reward function (Murray et al., 2018). Given the limited research on neural response to loss, we hypothesized that AB would be associated with neural response to loss and that CU traits would moderate this association; however, we did not make specific directional hypotheses.

We present the results of models that include the primary predictor (i.e., AB or CU traits) and demographic covariates (i.e., age, gender, pubertal status, annual family income, and self-reported race), and for the moderation analyses, the AB x CU interaction term, the main effects of AB and CU traits, and demographic covariates. Analyses of the zero-order associations (e.g., AB without covariates) and analyses accounting for shared variance of AB and CU traits (e.g., AB controlling for CU traits) were similar to those reported in the main text (Supplemental Table 6).

Results

Is AB related to Neural Response to Reward?

AB was not associated with neural reactivity to Reward Anticipation > Reward Outcome, nor Reward Win > No Win contrasts.

Is AB related to Neural Response to Loss?

AB was negatively correlated with several large clusters (i.e., reduced reactivity) during Loss Outcome > No Loss (Table 1, Figure 1). This included the inferior frontal gyrus ($t = -6.34$, $k = 2732$, $x = -48$, $y = 16$, $z = 20$), inferior and superior parietal lobules ($t = -6.17$, $k = 10030$, $x = 22$, $y = -62$, $z = 52$), inferior and middle temporal gyrus ($t = -4.70$, $k = 158$, $x = 58$, $y = -46$, $z = -12$), fusiform and lingual gyri ($t = -4.45$, $k = 697$, $x = -42$, $y = -62$, $z = -14$), occipital gyrus ($t = -4.32$, $k = 176$, $x = -18$, $y = -94$, $z = 8$), and caudate ($t = -4.30$, $k = 332$, $x = 18$, $y = 10$, $z = 20$). AB was not associated with neural reactivity to Loss Anticipation > Loss Outcome, nor was AB associated with loss-related reactivity in the VS ROI.

Are CU traits related to Neural Response to Reward?

CU traits were not associated with neural reactivity to Reward Anticipation > Reward Outcome, nor Reward Win > No Win contrasts.

Are CU traits related to Neural Response to Loss?

CU traits were associated with reduced neural response to Loss Outcome > No Loss in the middle frontal gyrus ($t = -4.23$, $k = 436$, $x = -44$, $y = 18$, $z = 40$) and the superior parietal lobule ($t = -3.95$, $k = 186$, $x = -22$, $y = -54$, $z = 50$) (Table 1, Figure 2). These regions overlapped with those identified in the AB analyses, and did not survive when controlling for AB (Supplemental Table 6). CU traits were not associated with Loss Anticipation > Loss Outcome, nor loss-related reactivity in the VS ROI.

Do CU traits Moderate on Neural Response to Reward and Loss in AB?

There was a significant interaction between AB and CU Traits for both loss-related analyses. Specifically, the interaction of AB and CU traits predicted increased activity in the right precuneus and angular gyrus during Loss Anticipation > Loss Outcome ($t = 4.54$, $k = 441$, $x = 30$, $y = -64$, $z = 40$), and this

effect was driven by a reduced response in those with low CU traits, and an increased response in those with high CU traits (Table 1, Figure 3).

The interaction of AB and CU traits predicted reduced frontoparietal reactivity to Loss Outcome > No Loss such that the pattern of reduced activation was strongest for those with high levels of CU traits (Table 1, Figure 1C). Clusters largely overlapped with the results of the AB analyses. The largest frontoparietal cluster included the inferior frontal gyrus, superior parietal lobule, cingulate, and precuneus ($t = -6.74$, $k = 14315$, $x = -52$, $y = 8$, $z = 28$) and additional clusters included the middle and inferior temporal gyri ($t = -5.67$, $k = 192$, $x = 56$, $y = -62$, $z = -2$), and mid-cingulate ($t = -3.93$, $k = 241$, $x = -14$, $y = 14$, $z = 38$).

Discussion

The current study investigated associations between AB, CU traits, and neural processing of reward and loss in a population-based sample of youth born in medium-sized US cities. We improved upon previous research by (a) using a task designed to measure neural responses to the anticipation *and* consumption, (b) including the examination of reward *and* loss, and (c) examining whether co-occurring levels of CU traits impacted findings using a multi-method multi-informant latent variable approach. Contrary to our hypothesis, AB and CU traits were not associated with neural response to reward. In line with our hypotheses, AB and CU traits were associated with neural processing of loss. Specifically, AB was associated with decreased reactivity across a widespread frontoparietal network during loss outcomes. These links were moderated by CU traits such that the pattern of reduced reactivity was strongest for youth with higher levels of CU traits. Finally, although AB and CU traits were not independently linked to neural response during loss anticipation, the interaction of AB and CU traits was associated with greater angular gyrus and precuneus activity during loss *anticipation*. Our findings of reduced neural response to loss in AB and CU traits provide support for loss-processing as an important target for continued research to inform our understanding of AB. Moreover, these findings underscore

the importance of investigating the unique and moderating effects of CU traits in youth who engage in AB and the decomposition of anticipation versus consumption of reward and loss.

AB was associated with a large cluster of reduced frontoparietal activation during loss outcomes. The regions of reduced neural activation, including the inferior parietal lobes and inferior and middle frontal gyri, correspond with key nodes of the frontoparietal control network (Dixon et al., 2018; Seeley et al., 2007). This network is engaged during tasks requiring working memory and behavioral and cognitive control (Seeley et al., 2007), and components of this network have distinct connections with the default mode network and dorsal attention network (Dixon et al., 2018). Prior work suggests that activation in these regions contributes to mapping stimulus-response associations and their relationship to reward outcomes (Dixon & Christoff, 2012). Also, prior work has found that youth AB is associated with reduced resting-state functional connectivity (Lin, Tseng, Lai, Matsuo, & Gau, 2015) and reduced task-based activation during loss processing (Schwenck et al., 2017) within the frontoparietal network. Thus, our findings may suggest that youth high on AB fail to recruit cognitive and attentional neural circuitry necessary for behavior modulation in response to negative outcomes. These results are also consistent with behavioral studies of youth AB (Byrd et al., 2014), showing impairments in passive avoidance learning (e.g., Newman & Kosson, 1986) and response reversal (e.g., Budhani & Blair, 2005), both of which require related cognitive and attentional resources.

The association between AB and reduced frontoparietal response to loss was most pronounced in youth with higher levels of CU traits. Reduced reactivity to loss outcomes may suggest that youth high on AB and CU traits may be less sensitive to losses and potentially more sensitive to unexpected positive outcomes (i.e., “no loss” trials indicate a positive, loss avoidance outcome). Reduced loss sensitivity in youth with AB and CU traits is consistent with behavioral research indicating that individuals with AB and CU/psychopathic traits may overvalue positive feedback (Scerbo et al., 1990), undervalue negative feedback (Blair, Colledge, & Mitchell, 2001), have difficulty modulating responses in the context of

reward and punishment (Newman & Kosson, 1986), and persevere on previously rewarded stimuli despite increasing punishment (Frick et al., 2003b). The literature on neural response to loss in AB and CU traits in youth is still very limited (Byrd et al., 2014; Dugré et al., 2020). Nevertheless, the current study adds to a growing body of literature implicating blunted loss processing in individuals high on AB and CU traits.

Although AB and CU traits were not directly associated with neural response during loss *anticipation*, there was a significant interaction of AB and CU traits during loss anticipation. AB was associated with increased reactivity in the precuneus and angular gyrus during loss anticipation in those with higher levels of CU traits but reduced reactivity in those with lower levels of CU traits. These regions are nodes of the default mode network and are typically downregulated during goal-directed activity (Buckner, Andrews-Hanna, & Schacter, 2008). Previous research indicates that individuals with psychopathic traits have attenuated down-regulation of the default mode network during a go/no-go task (Freeman et al., 2015) and display altered patterns of attention allocation when processing negative information that is secondary to the primary task goals (Baskin-Sommers, Curtin, & Newman, 2011). Our results suggest that youth with high levels of both AB and CU traits may have reduced task-induced down-regulation of the default mode network during negative anticipatory cues and thus may not allocate attentional resources towards affective information to guide performance. These results also highlight the need to separate anticipatory versus consummatory phases of neural loss processing in AB and CU traits, as we found divergent findings: reduced frontoparietal activity during loss *receipt* but greater activation of default-mode hubs during loss *anticipation*.

We found no associations between AB or CU traits and neural response to reward, which is surprising given previous literature linking these traits to reward-related neural dysfunction (Byrd et al., 2014; Murray et al., 2018). However, a recent meta-analysis of youth and adults did not find significant associations between neural reward function and AB (Dugré et al., 2020), though the authors

emphasized caution given the small number of studies in this area. It is also possible that the point-based incentive in our version of the MID task may not have been sufficiently stimulating for youth with AB who may require increased sensory input to obtain positive affect (Quay, 1965, 1993).

Although the current study has many strengths, including a large, well-sampled cohort of youth in a narrow age range, the use of multi-method and multi-informant dimensional measures of AB and CU traits, and assessment of anticipation and outcome phases of reward and loss processing, the study has several limitations that should be considered. First, to avoid potential confounding effects in our primarily low-income sample, the MID task provided non-monetary, point-based incentives (instead of money, which may be valued differentially depending on family income). It is possible that the point rewards did not provide the same motivational salience as monetary rewards. Second, we did not record participant responses that occurred outside of the response window. Thus, we were unable to distinguish too-slow responses from non-responses. We addressed this issue by carefully inspecting the data and excluding subjects with inconsistent responding. Nevertheless, we are encouraged that the task main effects (Murray et al., 2020) are consistent with prior meta-analyses of the MID (Dugré, Dumais, Bitar, & Potvin, 2018; Oldham et al., 2018). Finally, the population-based sampling strategy and dimensional approach for assessing AB and CU traits included a range of youth, from those with no conduct problems to those with clinically significant symptoms of CD, ODD, and CU traits. This approach is consistent with dimensional conceptualizations of psychopathology (Blair, 2015a; Insel et al., 2010). However, though several youth did meet diagnostic criteria for AB psychopathology (10 youth had a lifetime diagnosis of CD and/or ODD), the size of those with full diagnoses was too small to allow for case-control analyses. Our findings may not generalize to samples with more severe AB and will require replication in clinical/forensic samples to determine whether the current associations exist linearly across a wider range of AB and CU traits.

Conclusion

In a well-sampled cohort of adolescents from medium-sized US cities and primarily low-income environments, AB was associated with decreased frontoparietal response to loss but was not associated with neural response to reward. CU traits moderated associations between AB and loss-related neural functioning, with results being more pronounced in youth with higher levels of CU traits. These results demonstrate that AB is associated with differences in neural circuitry involved in attention, executive control, and behavior modification while processing negative outcomes. Reduced attention and executive control recruitment in response to negative outcomes may contribute to inappropriate cost-benefit evaluations and may explain why youth who engage in AB persist in harmful, risky-behaviors despite severe consequences. Improving our understanding of the role of reward and loss-processing in the development and persistence of AB and CU traits is key for improving the treatment and prevention of this costly mental illness.

Table 1: Neural Reactivity during Reward and Loss Processing in Antisocial Behavior and Callous Unemotional Traits

	<i>t</i>	Cluster Size	MNI Coordinates	Brain Region
Reward Anticipation > Reward Outcome				
No significant clusters				
Reward Win> No Win				
No significant clusters				
Loss Anticipation > Loss Outcome				
AB x CU Traits	4.54	441	30 -64 40	Precuneus, angular gyrus
Loss Outcome > No Loss				
AB	-6.34	2732	-48 16 20	Bilateral inferior and middle frontal gyrus
	-6.17	10030	22 -62 52	Precuneus, bilateral inferior and superior parietal lobule
	-5.09	599	2 40 42	Superior frontal gyrus, supplementary motor area
	-4.82	274	-8 -34 6	Extra nuclear, vermis
	-4.70	158	58 -46 -12	Inferior and middle temporal gyrus
	-4.45	697	-42 -62 -14	Fusiform gyrus, lingual gyrus, cerebellum
	-4.32	176	-18 -94 8	Middle occipital gyrus
	4.30	332	18 10 20	Caudate
CU Traits	-4.23	436	-44 18 40	Middle frontal gyrus
	-3.95	186	-22 -54 50	Superior parietal lobule
AB x CU Traits	-6.74	14315	-52 8 28	Bilateral inferior frontal gyrus, bilateral superior parietal lobule, anterior cingulate, precuneus
	-5.67	192	56 -62 -2	Right middle and inferior temporal gyrus
	-3.93	241	-14 14 38	Mid-cingulate

Note. Associations between AB factor scores, CU traits factor scores, and neural response to reward and loss. All models included age, gender, pubertal status, annual family income, and self-reported race as covariates and were significant at $p < .001$ and $\alpha = .05$, cluster threshold $k = 131$. Supplemental analyses of zero-order associations and analyses controlling for the overlap between AB and CU traits were highly similar (Supplemental Table 6).

Figure 1. Callous-Unemotional traits Moderate Associations between Antisocial Behavior and Frontoparietal Activation during Loss Outcome. (A) Cortical surface rendering of the association between AB and neural response to Loss Outcome > No Loss. (B). Multi-slice activation map of the association between AB and neural response to Loss Outcome > No Loss. (C) Association between AB and neural response to Loss Outcome > No Loss as a function of CU traits. Mean cluster beta-weights were extracted at from main cluster encompassing bilateral inferior frontal gyri and superior parietal lobules ($t=-6.74$, $k=14315$, MNI: $x=-52$ $y=8$ $z=28$). Simple slopes plotted at mean, high, and low levels CU traits, asterisk indicates significant slope at high level of CU traits $p<.001$. High CU traits was coded as + 1SD from the CU traits factor mean, whereas low was coded as the lower bound of the CU traits factor due to there being no subjects 1 SD below the mean. The grey area indicates the level of AB at which the association is significant (AB factor score < 0.85 and > 1.99).

Figure 2. Callous-Unemotional Traits are Associated with Reduced Middle Frontal Gyrus Activity during Loss Outcome. (A) The CU traits factor score was associated with reduced response in the middle frontal gyrus during Loss Anticipation > Loss Outcome (centered at peak voxel MNI: $x=-44$ $y=18$ $z=40$; $t=4.23$, $k=436$). (B) Scatterplot of association between CU traits and neural response to Loss Outcome > No Loss.

Figure 3. Callous-Unemotional traits Moderate Associations between Antisocial Behavior Angular Gyrus Activation during Loss Anticipation. (A) CU traits significantly moderated the association between AB and neural response in the angular gyrus and precuneus during Loss Anticipation > Loss Outcome (centered at peak voxel MNI: $x=30$ $y=-64$ $z=40$; $t=4.54$, $k=441$). (B) Association between AB and neural response to Loss Anticipation > Loss Outcome as a function of CU traits. Mean cluster beta-weights were extracted at from angular gyrus/precuneus cluster ($t=4.54$, $k=441$, MNI: $x=30$ $y=-64$ $z=40$). Simple slopes plotted at mean, high, and low levels CU traits, asterisk indicates significant slope at low level of CU traits $p=.04$. High CU traits was coded as + 1SD from the CU traits factor mean, whereas low was coded as the lower bound of the CU traits factor due to there being no subjects 1 SD below the mean. The grey area indicates the level of AB at which the association is significant (AB factor score < 0.32 and > 2.36).

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Supplemental Information

Figure 1

Modified Monetary Incentive Delay task. A schematic of a single MID trial. Trial type was indicated by a up arrow, down arrow or a horizontal double arrow to indicate reward, loss and neutral trials, respectively (2 s). After a variable delay (2–2.5 s) a white square (target) appeared. Participants were instructed to respond as quickly as possible to the target. A fixation cross appeared that included a delay (2 s) and a catch-up period to account for variability in participant response. Feedback was presented (1.65 s), followed by a jittered inter-trial interval (2, 3 or 4 s). The task was modified from common versions of the MID (e.g., Casey et al., 2018; Knutson, Fong, Adams, Varner, & Hommer, 2001) by adding a jittered intertrial interval to allow for more temporal separation of anticipation and consumption phases of reward and loss processing. Figure reproduced, with permission from (Murray, Lopez-Duran, Mitchell, Monk, & Hyde, 2020).

Supplemental Table 1: Summary of Available Data for Analyses

	Number lost	Participants with data
Original sample		237
Sample with imaging data		
- Refused MRI	7	
- Exceeded MRI table weight limit/couldn't fit in scanner	5	
- Medical restriction	3	
- Braces or other metal in body	13	
- Risk of pregnancy	1	
- Missed scanning appointment	1	
- Excluded for diagnosis of Autism Spectrum Disorder	2	
- Incomplete fMRI data	12	
Total lost	44	193
Sample with usable imaging data		
- Task administration issue (i.e., wrong version, wrong hand)	2	
- fMRI scan quality issues (distortion, artifact, signal drop out)	17	
- Low ventral striatum coverage (<70%)	7	
- Motion outlier (>20% TRs with ART)	1	
- Poor Task Performance (<6 trials per outcome condition)	26	
- Poor Task Performance (>10 consecutive trials without a recorded button press)	6	
- Activation outlier	6	
Total lost	65	128

Note. Participants with complete and usable MRI data from the full sample. Consistent with previous work in this sample (Murray et al., 2020), fMRI data were excluded if there was signal drop out in the VS ROI (< 70% coverage) or in reward-related limbic and prefrontal regions via visual inspection of individual whole brain maps. Six subjects were identified with large outlier parameter estimates ($\pm > 3$ s.d. from sample mean) in contrasts of interest. For these participants, individual functional scans were further inspected to confirm either a few large or many small movements that caused abnormal parameter estimates. Analyses including these subjects is presented in Supplemental Table 5. Behavioral data from the MID task were analyzed to ensure sufficient responding during the task. Youth with <6 trials of each outcome were excluded due to poor task responding. Also, for participants with <10 trials per outcome, behavioral data were visually inspected to ensure consistent participant engagement.

Supplemental Table 2: Descriptive Statistics of Demographic Measures for the Final Analytic Sample

Measure	Count (%)
Adolescent Gender	
- Male	54 (42.2)
- Female	74 (57.8)
Adolescent Self-Reported Race	
- Black / African American	97 (75.8)
- White / Caucasian	15 (11.7)
- More than one race	5 (3.9)
- Other Non-Hispanic Groups	5 (3.9)
Adolescent Self-Reported Ethnicity	
- Not Hispanic	122 (95.3)
- Hispanic	6 (4.7)
Measure	Range
	Mean (SD)
- Age (Years)	15.0-17.6
	15.88 (0.53)

Supplemental Table 3: Descriptive Statistics and Bivariate Correlations between Measures Included in Antisocial Behavior Factor Score

	CBCL Aggression	CBCL Rule-Breaking	SRD Total Score	KSADS ODD/CD Symptoms
CBCL Rule-Breaking	.81***			
SRD Total Score (no drug items)	.39***	.30***		
KSADS ODD/CD Symptom Count	.64***	.61***	.47***	
<i>M (SD)</i>	3.84(2.82)	2.00(4.79)	5.77 (6.88)	4.85(9.04)
Range	0-25	0-18	0-44	0-51
Factor Loading	.88***	.93***	.39***	.69***

Note. [†]p < .10, *p < .05; **p < .01; ***p < .001. CBCL= Child Behavior Checklist; SRD = Self-Report of Delinquency; KSADS = Kiddie Schedule for Affective Disorders and Schizophrenia; ODD = oppositional defiant disorder; CD = conduct disorder; df = degrees of freedom; TLI = Tucker–Lewis index; CFI = comparative fit index; RMSEA = root mean square error of approximation; SRMR = standardized root mean residual. Correlations were computed for whole sample (n = 237). Analyses performed using maximum likelihood estimation with robust standard errors (which can accommodate skewness) in Mplus version 7.3 (Muthén & Muthén, 2014). Chi-Square test of model fit = 2.67, df=1, p=.10; CFI=.99, TLI=.96, RMSEA=.08, SRMR=.01. Based on modification indices, two scales' residuals (SRD Total score and KSADS ODD/CD Symptom Count) were allowed to correlate.

Supplemental Table 4: Descriptive Statistics and Bivariate Correlations between Measures Included in Callous-Unemotional Traits Factor Score

	ICU Parent Total	ICU Self Total	Limited Prosocial Emotions Symptoms
ICU Parent-Report Total Score			
ICU Self-Report Total Score	.13*		
CAPE/KSADS Limited Prosocial Emotions Symptom Count	.35***	.29***	
<i>M (SD)</i>	18.99(8.99)	21.78(8.24)	.97 (2.69)
Range	1-52	4-44	0-16
Factor Loading	.40***	.35***	.86***

Note. [†]p < .10, *p < .05; **p < .01; ***p < .001. ICU = Inventory of Callous-Unemotional Traits; KSADS = Kiddie Schedule for Affective Disorders and Schizophrenia; CAPE = Clinical Assessment of Prosocial Emotions; df = degrees of freedom; TLI = Tucker-Lewis index; CFI = comparative fit index; RMSEA = root mean square error of approximation; SRMR = standardized root mean residual. Consistent with prior studies that have used the ICU, we used a total score for 22 of the original 24 items dropping two items based on an examination of polychoric inter-item correlations (Waller et al., 2015). Correlations were computed for whole sample (n = 237). Measures of CU traits were significantly skewed. Analyses performed using maximum likelihood estimation with robust standard errors (which can accommodate skewness) in Mplus version 7.3 (Muthén & Muthén, 2014). Model was fully saturated.

Supplemental Table 5: Neural Reactivity during Reward and Loss Processing in Antisocial Behavior and Callous Unemotional Traits with fMRI Outliers Included

	<i>t</i>	Cluster Size	MNI Coordinates	Brain Region
Loss Anticipation > Loss Outcome				
No significant clusters				
Reward Win> No Win				
No significant clusters				
Loss Anticipation > Loss Outcome				
AB x CU Traits	4.54	441	30 -64 40	Precuneus, angular gyrus
Loss Outcome > No Loss				
AB	-5.67	1265	30 -50 60	Superior parietal lobule
	-5.33	1468	-34 -56 56	Inferior parietal lobule
	-5.08	345	48 40 14	Inferior frontal gyrus
	-4.58	613	32 -8 60	Superior and middle frontal gyrus
	-4.43	272	-4 -30 24	Posterior cingulate
	-4.09	168	4 4 22	Caudate
	-3.64	235	-52 32 16	Inferior frontal gyrus
AB x CU Traits	-6.32	1323	-20 -66 58	Bilateral superior parietal lobule
	-5.19	2006	0 36 14	Anterior cingulate, middle frontal gyrus

Note. Associations between AB and CU traits factors and neural response to reward and loss including fMRI outliers. Six youths were excluded from the analyses due to excessive movement-related signal artifacts that could potentially influence the findings. Analyses including these subjects (total n=134) controlled for demographic variables (age, gender, pubertal status, annual family income, self-reported race) and were significant at $p < .001$ and $\alpha=.05$., cluster threshold $k=131$.and were largely similar to those reported in the main text and showed reduced frontoparietal activity to loss outcome > no loss in AB that was also moderated by CU traits. However, the association between CU traits and neural response to Loss Outcome > No Loss and the interaction of AB and CU traits to Loss Anticipation > Loss Outcome were not significant with the outliers included.

Supplemental Table 6: Neural Reactivity during Reward and Loss Processing in Antisocial Behavior and Callous Unemotional Traits

	<i>t</i>	Cluster Size	MNI Coordinates	Brain Region
Reward Anticipation > Reward Outcome				
No significant clusters				
Reward Win> No Win				
No significant clusters				
Loss Anticipation > Loss Outcome				
AB x CU Traits (no covariates)	4.43	391	30 -66 42	Precuneus, angular gyrus
Loss Outcome > No Loss				
AB (no covariates)	-6.56	2351	-48 16 20	Bilateral inferior and middle frontal gyrus
	-6.35	8110	-18 -68 56	Precuneus, bilateral inferior and superior parietal lobule
	-5.44	1599	48 38 12	Superior and inferior frontal gyrus
	-4.85	459	2 40 40	Superior medial frontal cortex, supplemental motor area
	-4.75	234	-8 -34 6	Extra nuclear, posterior cingulate
	-3.98	347	-20 -76 2	Middle occipital gyrus
AB (with CU traits & demographic covariates)	-6.80	2702	24 -64 52	Superior and inferior parietal lobule
	-6.34	1223	48 40 14	Inferior and middle frontal gyrus
	-6.04	1158	-48 16 20	Inferior and middle frontal gyrus
	-5.55	1851	-16 -68 56	Superior and inferior parietal lobule
	-5.26	950	22 -8 48	Middle frontal gyrus
	-5.12	1101	-12 -32 28	Extra nuclear, posterior cingulate
	-4.92	497	2 42 40	Superior medial frontal cortex, dorsal anterior cingulate, supplemental motor area
	-4.19	151	-30 -4 44	Precentral gyrus
AB x CU Traits (no covariates)	-7.04	4931	-50 10 28	Inferior and middle frontal gyrus, inferior and superior parietal lobule
	-6.66	8923	10 -72 54	Inferior parietal lobule, superior parietal lobule, angular gyrus, anterior cingulate, middle frontal gyrus
	-5.44	159	56 -62 -2	Middle temporal gyrus

Note. Associations between AB and CU traits factors and neural response to reward and loss. Additional analyses were conducted to thoroughly assess neural response to reward and loss in AB and CU traits. Analyses tested zero-order associations (i.e., AB without covariates, CU traits without covariates, ABxCU traits interaction without covariates) and when accounting for the overlap between AB and CU traits (i.e., AB controlling for CU traits and demographic covariates and vice versa). Results were largely similar to those reported in the main text, however associations between CU traits and Loss Outcome>No Loss were not significant without including demographic covariates or when controlling for overlap with AB.

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