Psychological Medicine (2016), **46**, 1485–1496. © Cambridge University Press 2016
doi:10.1017/S0033291716000118

ORIGINAL ARTICLE

Dual neurocircuitry dysfunctions in disruptive behavior disorders: emotional responding and response inhibition

S. Hwang[1]*, Z. T. Nolan[2], S. F. White[3], W. C. Williams[4], S. Sinclair[5] and R. J. R. Blair[5]

[1] *University of Nebraska Medical Center, Omaha, NE, USA*
[2] *Penn State College of Medicine, MD/PhD Program, Hershey, PA, USA*
[3] *Boystown National Research Hospital, Boystown, NE, USA*
[4] *Department of Psychology, Stanford University, Stanford, CA, USA*
[5] *Department of Health and Human Services, Section on Affective Cognitive Neuroscience, National Institute of Mental Health, National Institutes of Health, Bethesda, MD, USA*

Background. To determine the functional integrity of the neural systems involved in emotional responding/regulation and response control/inhibition in youth (age 10–18 years) with disruptive behavioral disorders (DBDs: conduct disorder and/or oppositional defiant disorder) as a function of callous-unemotional (CU) traits.

Method. Twenty-eight healthy youths and 35 youths with DBD [high CU (HCU), $n = 18$; low CU (LCU), $n = 17$] performed the fMRI Affective Stroop task. Participants viewed positive, neutral, and negative images under varying levels of cognitive load. A 3-way ANOVA (group×emotion by task) was conducted on the BOLD response data.

Results. Youth with DBD-HCU showed significantly less activation of ventromedial prefrontal cortex (vmPFC) and amygdala in response to negative stimuli, compared to healthy youth and youth with DBD-LCU. vmPFC responsiveness was inversely related to CU symptoms in DBD. Youth with DBD-LCU showed decreased functional connectivity between amygdala and regions including inferior frontal gyrus in response to emotional stimuli. Youth with DBD (LCU *and* HCU) additionally showed decreased insula responsiveness to high load (incongruent trials) compared to healthy youth. Insula responsiveness was inversely related to ADHD symptoms in DBD.

Conclusions. These data reveal two forms of pathophysiology in DBD. One associated with reduced amygdala and vmPFC responses to negative stimuli and related to increased CU traits. Another associated with reduced insula responses during high load task trials and related to ADHD symptoms. Appropriate treatment will need to be individualized according to the patient's specific pathophysiology.

Received 4 June 2015; Revised 4 January 2016; Accepted 5 January 2016; First published online 15 February 2016

Key words: Amygdala, callous-unemotional trait, disruptive behavior disorder, emotional responding, response inhibition.

Introduction

The disruptive behavioral disorders (DBDs) of conduct disorder (CD) and oppositional defiant disorder (ODD) are characterized by aggressive behavior, poor emotional regulation, and relationship difficulties (APA, 2013). There have been recent claims that the impairments shown by these patients might relate to forms of dysfunction in several different neurocognitive mechanisms that manifest as specific forms of behavioral disturbance (Blair, 2013). Thus, considerable data indicate that a group of youth with DBDs show *reduced* amygdala responses to distress cues, the degree of which is positively associated with callous-unemotional (CU) traits (i.e. reduced guilt and empathy) and instrumental aggression (White *et al.* 2012; Lozier *et al.* 2014). These youths also showed atypical responses to reward and punishment within ventromedial prefrontal cortex (vmPFC) and caudate compared to typically developed youth (Finger *et al.* 2008, 2011) and youth with attention deficit hyperactivity disorder (ADHD; Finger *et al.* 2008). A recent study suggested that these functional difference reflect compromised representation of reinforcement expectancies within the vmPFC and aberrant prediction error signaling within the caudate (White *et al.* 2013). There are also some data indicating a second group of youths show *increased* amygdala responses to threat and low CU traits (Viding *et al.* 2012; Blair, 2013; Sebastian

* Address for correspondence: S. Hwang, M.D., Department of Psychiatry, University of Nebraska Medical Center, 987830 Nebraska Medical Center, Omaha, NE 68198, USA.
(Email: soonjo.hwang@unmc.edu)

et al. 2014). Indeed, the importance of CU traits is recognized in DSM-5 with the inclusion of the limited prosocial emotions specifier for CD (APA, 2013).

Two additional neurocognitive mechanisms have been hypothesized, when dysfunctional, to increase the risk of antisocial behavior/relate to the behavior problems of youth with CD (Patrick *et al.* 2009; Young *et al.* 2009; Miyake & Friedman, 2012; Blair *et al.* 2013). The first of these is top-down attention [related to prefrontal (dorsomedial and lateral) regions; Buhle *et al.* 2014]. Top-down attention is implicated in emotional regulation in explicit cognitive reappraisal paradigms where subjects alter stimulus representations by priming non-emotional features (Buhle *et al.* 2014) and implicit attention distraction paradigms (e.g. the Affective Stroop task; aST) where subjects prime task features at the expense of the representation of emotional distracters (Pessoa *et al.* 2005; Blair *et al.* 2007). As such dysfunction in top-down attention might lead to emotional dysregulation and an increased risk for reactive aggression. Indeed, studies have reported increased amygdala responses to negative stimuli in youth with conduct problems and low CU traits (Viding *et al.* 2012; Sebastian *et al.* 2014). It has been suggested that this might reflect *deficient* top-down attention-based emotion regulation (Blair, 2013; Blair *et al.* 2013). However, no previous functional magnetic resonance imaging (fMRI) work has investigated this possibility.

The second neurocognitive mechanism hypothesized, when dysfunctional, to increase the risk of antisocial behavior/relate to the behavior problems of youth with CD is response control/response inhibition (Patrick *et al.* 2009; Young *et al.* 2009; Miyake & Friedman, 2012). Response control/response inhibition is thought to be mediated by dorsomedial and inferior frontal/anterior insula cortices (Criaud & Boulinguez, 2013). Response control/inhibition is important for avoiding sub-optimal choices and can be indexed by the Stop, Go/No-Go and Stroop tasks (Criaud & Boulinguez, 2013). Impairment in response control/inhibition should result in an individual who will 'impulsively' express behaviors (including antisocial behaviors) that are non-optimal for the situation. Such impairment has also been associated with an increased risk for antisocial behavior (Patrick *et al.* 2009; Young *et al.* 2009; Miyake & Friedman, 2012).

The current study uses the aST to investigate emotional responding, automatic emotion regulation and response control/inhibition in youth with DBD and high and low callous-unemotional traits (HCU/LCU). Considerable data, including from the aST and related tasks, demonstrate that the performance of a cognitive task reduces the response within the amygdala to an emotional stimulus (Critchley *et al.* 2000; Pessoa *et al.* 2002; Erthal *et al.* 2005; Blair *et al.* 2007; Mitchell *et al.* 2007); i.e. participants undertaking paradigms such as the aST demonstrate automatic emotion regulation. Our goal in using the aST is to elucidate the neurocircuitry dysfunction related to symptom manifestation *across* disorders (in this case CD and ODD), thus departing from diagnosis-based approach to a mechanism-based approach towards the understanding of pathophysiology in DBD (Insel *et al.* 2010; Cuthbert & Insel, 2013).

We predicted: (i) consistent with previous work (White *et al.* 2012; Lozier *et al.* 2014; Baker *et al.* 2015), DBD-HCU youth would show *reduced* amygdala responsiveness to threatening stimuli relative to healthy youth; (ii) consistent with previous work (Viding *et al.* 2012; Sebastian *et al.* 2014, Baker *et al.* 2015), DBD-LCU youth would show *increased* amygdala responsiveness to threatening stimuli relative to healthy youth; (iii) and that amygdala responsiveness would be inversely associated with CU traits in youth with DBD; (iv) on the basis of previous hypotheses (Blair *et al.* 2013), we predicted DBD-LCU youth would show reduced recruitment of attention-based emotion regulation regions (dorsomedial and lateral frontal cortex; Blair *et al.* 2007) relative to healthy youth and DBD-HCU youth; (v) and that DBD youth would show reduced recruitment of regions implicated in response control (anterior insula/inferior frontal and dorsomedial frontal cortex) relative to healthy youth with responsiveness being inversely associated with ADHD symptoms in DBD youth; and (vi) consistent with previous functional connectivity studies (Marsh *et al.* 2008; Herpers *et al.* 2014), we predicted DBD-HCU youth would show *reduced* connectivity between the amygdala and cortical regions to threatening stimuli relative to healthy youth and DBD-LCU youth and that level of connectivity would be inversely associated with CU traits in youth with DBD.

Method

Participants

Sixty-seven youths participated: 29 healthy and 38 with DBD (CD/ODD). Participants were recruited from the community through newspaper adverts, fliers, and referrals from area mental health practitioners. Four participants (healthy $n = 1$, DBD $n = 3$) were excluded (due to, for example, excessive movement). Thus, data from 28 healthy (average age = 13.88 years, 13 females) and 35 DBD (average age = 14.81 years, 13 females) participants were analyzed (see Table 1). Statements of informed assent/consent were obtained from participating children/parents. This study was approved by the NIMH IRB.

https://doi.org/10.1017/S0033291716000118 Published online by Cambridge University Press

Table 1. *Characteristics of healthy youth, and youth with DBD*

	Healthy youth ($n = 28$)	Youth with DBD and LCU ($n = 17$)	Youth with DBD and HCU ($n = 18$)	p value
Age	13.88 (2.03)	14.78 (2.39)	14.56 (1.84)	0.317
IQ	101.18 (10.70)	96.65 (11.46)	95.72 (9.69)	0.182
Gender	15 male, 13 female	12 male, 5 female	10 male, 8 female	0.504
Handedness	6 left, 22 right	3 left, 14 right	3 left, 15 right	0.909
CD	0	10	16	0.145[a]
ODD	0	7	2	0.06[a]
ADHD	0	12	7	0.125[a]
SA[b]	0	1	6	0.002[a]
Mean ICU score	15.58 (6.76)	33.12 (5.68)	48.11 (5.67)	0.000[c]
Conners score	2.31 (3.27)	25.85 (13.45)	28.67 (14.06)	0.000[d]
On medication	0	4[e]	5[f]	0.540[a]

DBD, Disruptive behavioral disorder; LCU, low callous-unemotional; HCU, high callous-unemotional; CD, conduct disorder; ODD, oppositional defiant disorder; ADHD, attention deficit hyperactivity disorder; SA, substance abuse.

[a] Between DBD-LCU and DBD-HCU.

[b] All cannabinoid abuse except one in HCU group (alcohol abuse).

[c] DBD-LCU < DBD + HCU: $t_{33} = 7.817$, $p = 0.000$.

[d] Healthy youth < DBD-LCU: $t_{43} = 9.379$, $p = 0.000$; DBD-LCU = DBD + HCU: $t_{26} = 0.540$, $p = 0.594$.

[e] Atomoxetine ($n = 1$); lamotrigine ($n = 1$); lamotrigine + aripiprazole ($n = 1$); amphetamine, intuitiv, risperidone ($n = 1$).

[f] Amphetamine ($n = 4$); atomoxetine + intuitiv ($n = 1$).

Participants' parents completed the Inventory of Callous-Unemotional Traits – Parent Version (ICU-P). The ICU-P is a 24-item scale assessing CU traits in youth with good construct validity (Frick, 2004; Kimonis *et al.* 2008) and reliability (Cronbach's $\alpha = 0.81$). Following previous studies (Viding *et al.* 2012; Lozier *et al.* 2014), we divided the patients with DBD into two groups on the basis of a median split of the ICU-P scores (median score = 42; LCU/HCU: $n = 17/18$) (see Table 1). Previous community sample studies reveal average ICU scores between, for example, 22 and 31 (standard deviation: 7.88–10.98; Roose *et al.* 2010; Byrd *et al.* 2013). In contrast, clinical samples of patients with DBD and forensic samples reveal average ICU scores of 41 (White *et al.* 2009). As such, all HCU groups showed a level of CU that was above average for patients with DBD and notably greater than that shown by healthy populations.

All youths and their parents completed the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS; Kaufman *et al.* 1997). Assessments were conducted by a doctoral-level clinician and supervised by expert child/adolescent psychiatrists. The K-SADS has demonstrated good validity and inter-rater reliability (Kaufman *et al.* 1997). The parents of 26/28 healthy youths and 28/35 youths with DBD completed the Conners Parent Rating Scale for ADHD – version 2 (Conners *et al.* 1998). IQ was assessed with the Wechsler Abbreviated Scale of Intelligence (2-subtest form; Wechsler, 1999). Exclusion criteria are listed in the Supplementary material, section 1. The groups did not differ significantly in terms of age, sex, handedness or IQ (see Table 1).

Experimental task

We used an adapted version of the aST described previously (Blair *et al.* 2007; Hwang *et al.* 2014) (see Fig. 1). In each trial, participants saw a central fixation point (400 ms), a positive, neutral, or negative image (400 ms), either a numerical array on *task* trials, or a blank screen on *view* trials (400 ms), the same image previously displayed (400 ms), and a second blank screen (1300 ms). For task trials, participants pressed a button corresponding to how many numbers were displayed (numerosity: 3–6). On *congruent* trials, numerosity matched the *actual number values displayed* (e.g. three for 3 s). On *incongruent* trials, numerosity *did not match* the number values displayed (e.g. four for 3 s or six for 3 s). The numerical gap between numerosity and the number values ranged between 1 (e.g. four for 3 s) and 3 (e.g. six for 3 s). Participants were free to respond at any time between the initial numerical presentation and the end of the blank screen display (response window: 1700 ms). Participants made no response for view trials.

The images consisted of 48 positive, 48 negative, and 48 neutral pictures selected from the International Affective Picture System (Lang & Cuthbert, 2005) (see Supplementary material, section 2 for mean valence and arousal values by stimulus class). Participants completed two runs. Each involved 288 trials [32 in each

https://doi.org/10.1017/S0033291716000118 Published online by Cambridge University Press

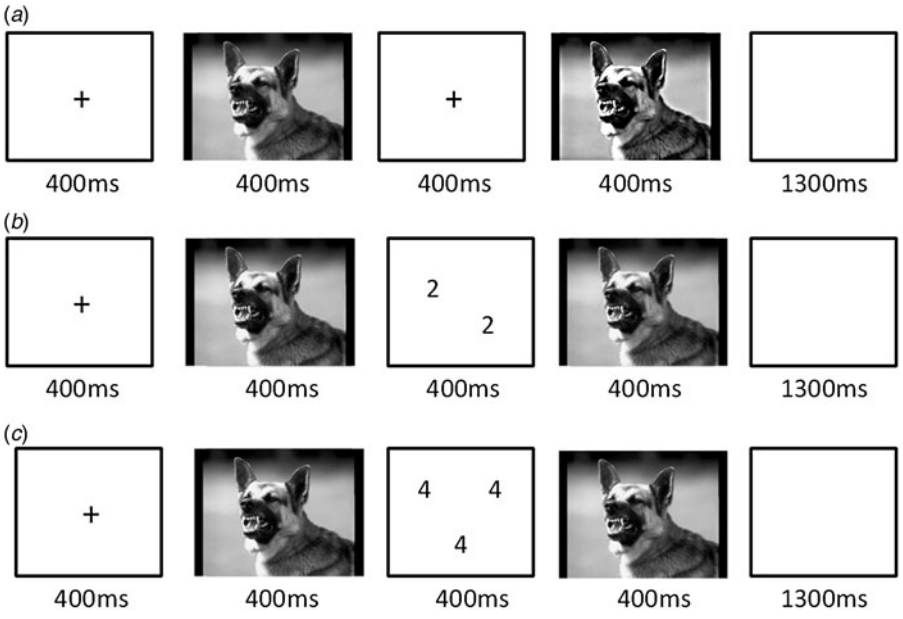

Fig. 1. Example trial sequences. (*a*) Negative view trial; (*b*) negative congruent trial; (*c*) negative incongruent trial.

nine categories (3 image type × 3 task type)] and 96 fixation trials (each of 2500 ms length to generate a baseline). Trial order was randomized across participants.

Image acquisition and analysis

Whole-brain blood oxygen level-dependent (BOLD) fMRI data were acquired using a 3-T GE MRI scanner. Following sagittal localization, functional T2*-weighted images were acquired using an echo-planar single-shot gradient echo pulse sequence with a matrix of 64 × 64 mm^2, repetition time (TR) of 3000 ms, echo time (TE) of 30 ms, field of view (FOV) of 240 mm, and voxels of 3.75 × 3.75 × 4 mm^3. Images were acquired in 30 continuous 4 mm axial slices per brain volume across two runs. The duration of each run was 8 min 13 s. In the same session, a high-resolution T1-weighed anatomical image was acquired to aid with spatial normalization (three-dimensional Spoiled GRASS; TR = 8.1 ms; TE = 3.2 ms, flip angle 20°; FOV = 240 mm, 128 axial slices, thickness = 1.0 mm; 256 × 256 acquisition matrix).

fMRI analysis

Data were analyzed within the framework of a random effects general linear model using Analysis of Functional Neuroimages (AFNI). Both individual- and group-level analyses were conducted. The first five volumes in each scan series, collected before equilibrium magnetization was reached, were discarded. Motion correction was performed by registering all volumes in the EPI dataset to a volume that was collected shortly before acquisition of the high-resolution anatomical dataset.

The EPI datasets for each participant were spatially smoothed (using an isotropic 6 mm Gaussian kernel) to reduce the influence of anatomical variability among the individual maps in generating group maps. Next, the time-series data were normalized by dividing the signal intensity of a voxel at each time point by the mean signal intensity of that voxel for each run and multiplying the result by 100. Resultant regression coefficients represented a percent signal change from the mean. The model involved six motion regressors and the following nine task regressors: negative congruent, negative incongruent, negative view, neutral congruent, neutral incongruent, neutral view, positive congruent, positive incongruent and positive view. A regressor modeling incorrect responses was also included. All regressors were convolved with a canonical hemodynamic response function (HRF) to account for the slow hemodynamic response (with time point commencing at time of first image onset). There was no significant regressor collinearity.

The participants' anatomical scans were individually registered to the Talairach and Tournoux atlas (Talairach & Tournoux, 1988). The individuals' functional EPI data were then registered to their Talairach anatomical scan within AFNI. Linear regression modeling was performed using the 10 regressors (nine task plus incorrect responses) described earlier, plus regressors to model a first-order baseline drift function. This produced β coefficients and associated t statistics for each voxel and regressor.

The BOLD data were analyzed via a 3 (group: healthy youth, youth with DBD-LCU, youth with DBD-HCU) × 3 (emotion: negative, positive, neutral) × 3 (task: congruent, incongruent, view) ANOVA.

https://doi.org/10.1017/S0033291716000118 Published online by Cambridge University Press

Statistical maps were created for each main effect and interaction by thresholding at a single-voxel p value of $p < 0.005$. ClustSim was then applied to these results yielding a minimum cluster size (22 voxels) with a map-wise false-positive probability of $p < 0.05$, corrected for multiple comparisons.

Given our *a priori* hypotheses, regions of interest (ROIs), taken from the AFNI software's anatomical maps (TT_Daemon atlas) were obtained from the amygdala (Talairach & Tournoux, 1988). A small volume-corrected ROI analysis via ClustSim was used on these regions (initial threshold: $p < 0.02$, $k = 13$, corrected $p < 0.05$).

Follow-up analyses were performed to facilitate interpretations. For these analyses, average percent signal change was measured across all voxels within each ROI generated from the functional masks, and data were analyzed using appropriate follow-up independent t tests within SPSS v. 22 (SPSS Inc. USA).

Context-dependent psychophysiological interaction (gPPI) analysis

A gPPI analysis was conducted to examine group differences in functional connectivity following the method described by McLaren and colleagues (2012). Our main goal was to examine group differences in functional connectivity between the amygdala and cortical regions. We took as a seed the region of right amygdala (coordinates: 25.5, −1.5, −12.5) showing a main effect of emotion from the main ANOVA conducted on the BOLD data (see Supplementary Table S2). This seed can be considered relatively unbiased by group membership as it was identified by main effect of emotion (i.e. significant activity to emotion was seen within all groups). The average activation from this seed region was extracted across the time series. Interaction regressors were created by multiplying each of these average time series with nine task time-course vectors (one for each task and emotion condition) which were coded 1 or 0 for task and emotion condition present or absent. The average activation for the seeds was entered into a linear regression model along with the nine interaction regressors and six motion regressors. A 3 (group) ×3 (task) ×3 (emotion) whole-brain repeated-measures ANOVA was then applied to the data, and the regions showing significant group×emotion interaction were reported.

Results

Behavioral data

Two 3 (group: DBD-HCU, DBD-LCU, healthy) ×3 (emotion: positive, neutral, negative) ×2 (task: congruent, incongruent) ANOVAs were applied to the reaction time (RT) and accuracy data (see Supplementary Table S1). With respect to RT, there was a significant main effect of task (incongruent > congruent: $F_{1,60} = 169.349$, $p < 0.001$) and a trend for emotion ($F_{2,59} = 2.898$, $p = 0.059$, negative and positive > neutral, $t_{62} = 1.746$ and 1.924, $p = 0.086$ and 0.059, respectively). With respect to accuracy, there was a significant main effect of task (incongruent < congruent: $F_{1,60} = 22.565$, $p < 0.001$) and group ($F_{2,60} = 4.578$, $p = 0.014$; DBD-LCU < DBD-HCU and healthy youth, $t_{43,33} = 2.352$ and 2.486, $p = 0.023$ and 0.018, respectively). The performance of youth with DBD-HCU and healthy youth did not significantly differ ($t_{44} = 1.056$, $p = 0.297$). No other main effects or interactions for either ANOVA were significant.

Movement data

There were no significant group differences in movement parameters ($F_{1,60} = 1.484$–2.981, $p > 0.1$).

MRI data: main analysis

A whole-brain 3 (group) ×3 (emotion) ×3 (task) ANOVA was applied to the BOLD data. This revealed regions showing significant group × emotion, group × task and group × task × emotion interactions. Regions showing main effects of task and emotion and task × emotion interactions are presented in the Supplementary material, section 3.

Group × emotion interaction

There was a group×emotion interaction within left vmPFC and right (but not left) amygdala ROI (see Table 2, Fig. 2*a, d*). Within both regions, youth with DBD-HCU showed significantly decreased activation to negative relative to neutral stimuli, compared to healthy youth and youth with DBD-LCU who did not significantly differ (vmPFC: $t = 3.573$ and 3.891, $p < 0.001$; right amygdala: $t = 2.491$ and 2.312, $p = 0.017$ and 0.027) (see Fig. 2*b, e*). There were no group differences in either region's response to positive relative to neutral stimuli ($F = 0.827$ and 1.771, $p > 0.05$).

Group × task interaction

There was a group×task interaction within left insula (see Table 2). Within this region, youth with DBD-LCU and youth with DBD-HCU did not differ ($t = 1.542$, $p = 0.133$). However, both showed a significantly decreased differential response to incongruent task trials relative to view trials ($t = 3.471$ and 2.579, $p = 0.001$ and 0.013) and to incongruent relative to congruent task trials ($t = 3.517$ and 3.406, $p = 0.001$) compared to healthy youth (see Fig. 3*d, e*). There were no group differences in differential response to congruent relative to view trials ($t = 0.621$ and 0.118, $p = 0.538$ and 0.907). No other regions

https://doi.org/10.1017/S0033291716000118 Published online by Cambridge University Press

Table 2. *(a) Brain regions showing a significant interaction in comparison between healthy youth, youth with DBD-LCU and youth with DBD-HCU. (b) Brain regions showing a significant interaction of connectivity with right amygdala seed in comparison between healthy youth, youth with DBD-LCU, and youth with DBD-HCU*

Region[a]	Left/right	Coordinates of peak activation				*F*	Voxels
		BA	x	y	z		
(*a*)							
Group × emotion							
Ventro-medial prefrontal cortex	Left	11	−4.5	43.5	−12.5	6.515	30
Amygdala ROI	Right		25.5	−1.5	−21.5	3.306	13
Group × task							
Insula	Left	13	−37.5	7.5	−0.5	5.685	12[b]
Group × task × emotion							
Superior frontal gyrus	Right	9	22.5	37.5	29.5	3.976	24
Caudate	Bilateral		10.5	1.5	20.5	4.682	50
(*b*)							
Right amygdala seed							
Group × emotion							
Inferior frontal gyrus	Left	10	−40.5	40.5	−0.5	6.241	38
Caudate	Left		−4.5	13.5	8.5	6.314	46
Insula	Left	13	−34.5	−22.5	14.5	6.130	24
Posterior cingulate gyrus	Left	24	−4.5	−13.5	38.5	4.696	22

DBD, Disruptive behavioral disorder; LCU, low callous-unemotional; HCU, high callous-unemotional; BA, Brodmann area.
[a] According to the Talairach Daemon Atlas (http://www.nitrc.org/projects/tal-daemon).
[b] Below the ClusterSim cluster size (22 voxels).

showed a significant group × task interaction. While left insula did not survive multiple comparison correction ($k = 22$), this likely reflects a Type II error; the reduced insula activity (as well as left inferior parietal lobule) was seen in both groups of youths with DBD and an exploratory ANOVA contrasting healthy youth with a combined DBD group revealed a highly significant group×task interaction within this region ($k = 57$) (see Fig. 3*a, b*). The only other region showing a significant group×task interaction for this second analysis was the left inferior parietal lobule ($k = 28$; for analysis details, see Supplementary material, section 4).

Group × task × emotion interaction

There was a significant group×emotion×task interaction within right superior frontal gyrus and bilateral caudate (see Table 2). Within both regions, youth with DBD-HCU showed greater activity on negative incongruent trials relative to comparison groups ($t = 2.013$–3.319, $p = 0.002$–0.005), and youth with DBD-LCU showed greater activity on positive incongruent trials than both comparison groups ($t = 2.438$–2.668, $p = 0.011$–0.020). All other contrasts were not significant except within bilateral caudate where healthy youth showed less activity than DBD-LCU for negative congruent trials ($t = 2.146$, $p = 0.038$).

MRI results: gPPI results

A 3 (group) ×3 (emotion) ×3 (task) ANOVA was conducted on the gPPI data using the right amygdala seed. Regions displaying a significant group×emotion interaction included left inferior frontal gyrus, left posterior cingulate gyrus, left caudate, and left insula (see Table 2). Youth with DBD-LCU compared to healthy youth and youth with DBD-HCU showed significantly reduced connectivity between the right amygdala seed and these regions in response to emotional (negative and positive) relative to neutral stimuli ($t = 2.452$–5.355, $p = 0.000$–0.018); although for left posterior cingulate gyrus in response to negative relative to neutral stimuli ($t = 1.916$, $p = 0.062$; see Fig. 2*f, g* for left inferior frontal gyrus). Healthy youth and youth with DBD-HCU showed no significant differences in gPPI connectivity ($t = 0.067$–1.947, $p = 0.058$–0.947), except that youth with DBD-HCU showed significantly increased connectivity between right amygdala and caudate in response to positive relative to neutral stimuli relative to healthy youth ($t = 2.152$, $p = 0.037$).

Correlations with symptom severity

Ten correlations were conducted examining the relationship between BOLD response parameters and

https://doi.org/10.1017/S0033291716000118 Published online by Cambridge University Press

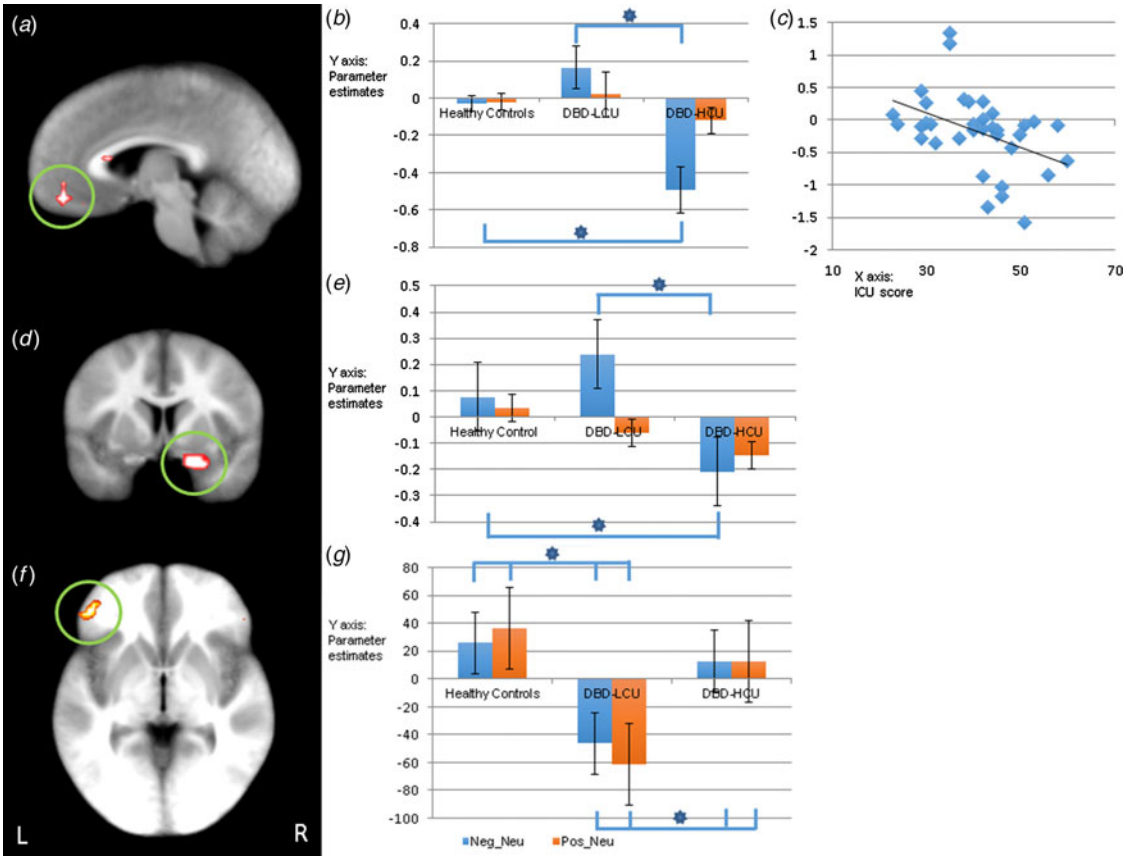

Fig. 2. Regions showing a significant group×emotion interaction: (*a*) blood oxygen level-dependent (BOLD) response data: left ventromedial prefrontal cortex (vmPFC) (coordinates: −4.5, 43.5, −12.5, at = 0.005); (*b*) parameter estimates for left vmPFC; (*c*) negative correlation between symptom severity of callous-unemotional trait measured by the Inventory of Callous-Unemotional Traits (ICU) (x-axis) and BOLD response parameter estimates of negative relative to neutral trials (y-axis) in left vmPFC; (*d*) right amygdala ROI (at $p = 0.05$); (*e*) parameter estimates for this region: context-dependent psychophysiological interaction data with right amygdala seed; (*f*) left inferior frontal gyrus (coordinates: −40.5, 40.5, −0.5 at $p = 0.005$) and; (*g*) parameter estimates for this region. Abbreviations: Neg, negative; Neu, neutral; Pos, positive; Healthy, healthy youth; LCU, youth with DBD-LCU; HCU, youth with DBD-HCU. * Significant contrasts for interaction variables ($p < 0.05$). The results are shown on the Talairach space.

symptom severity in the patients with DBD. CU symptom severity was negatively correlated with differential (negative-neutral) BOLD response for the vmPFC ($r = -0.370$, $p = 0.026$) but not the amygdala ($r = -0.238$, $p > 0.05$) (see Fig. 2*c*). However, it was positively correlated with amygdala-caudate connectivity in response to the negative relative to neutral stimuli ($r = 0.420$, $p = 0.012$). ADHD symptom severity (as indexed by the Conners Parent Rating Scale) was negatively correlated with differential (congruent-view, but not incongruent-view or incongruent-congruent) BOLD response within left insula ($r = -0.477$, $p = 0.010$) (see Fig. 3*c*). Following a reviewer's suggestion and for completion, we also examined the relationship between CU symptom severity and differential (incongruent-view, congruent-view, and incongruent-congruent) BOLD response within left insula. However, these were non-significant ($r = 0.188$, -0.084, 0.105, $p = 0.280$, 0.630, 0.459, respectively). In addition, we examined the relationship between ADHD symptom severity and differential (negative-neutral) BOLD response for the vmPFC and amygdala. However, these were also non-significant (vmPFC: $r = -0.028$, $p = 0.889$; amygdala: $r = -0.174$, $p = 0.377$).

Potential confounds

We conducted analyses excluding youth on psychotropic medications and substance abusers. These analyses revealed similar results to the main analysis reported above (see Supplementary material, sections 5 and 6).

Discussion

We investigated emotional responding, automatic emotion regulation and response control/inhibition in

https://doi.org/10.1017/S0033291716000118 Published online by Cambridge University Press

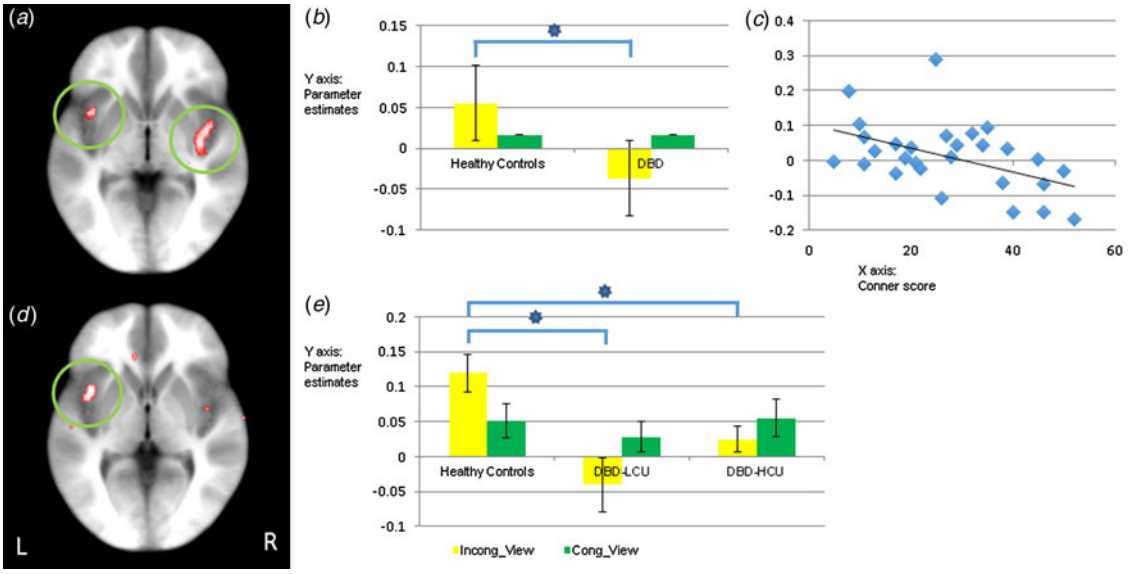

Fig. 3. Regions showing a significant group×task interaction: (*a*) bilateral insula (coordinates: 37.5, −13.5, −6.5; −37.5, 7.5, −0.5 at $p = 0.005$) via Healthy *v*. DBD ANOVA; (*b*) parameter estimates for this region; (*c*) negative correlation between ADHD symptom severity measured by Conners Parent Rating Scale (x-axis) and blood oxygen level-dependent response parameter estimates of congruent relative to view trials (y-axis); (*d*) left insula (coordinates: −37.5, 7.5, −0.5 at $p = 0.005$) via Healthy *v*. DBD-LCU *v*. DBD-HCU ANOVA; (*e*) parameter estimates for this region. Abbreviations: Incong, incongruent trial; Cong, congruent trial; View, view trial; Healthy, healthy youth; DBD, youth with DBD; LCU, youth with DBD-LCU; HCU, youth with DBD-HCU. * Significant contracts for interaction variables ($p < 0.05$). The results are shown on the Talairach space.

youth with DBD and HCU/LCU. There were two main results: first, youth with DBD-HCU showed significantly decreased left vmPFC and right amygdala activation to negative relative to neutral stimuli, compared to healthy youth and youth with DBD-LCU. Moreover, the vmPFC response to negative *v*. neutral stimuli was inversely related to level of CU traits in the patients with DBD. Second, youth with DBD (LCU and HCU) showed decreased activation of bilateral insula on task trials relative to healthy youth. Insula responsiveness was inversely related to ADHD symptomatology in youth with DBD.

In line with our first prediction and previous work (Viding *et al.* 2012; White *et al.* 2012; Lozier *et al.* 2014), youth with DBD-HCU showed reduced amygdala responses to threat stimuli relative to comparison youth. In addition, the current study extends the literature in two ways. First, it indicates that reduced amygdala recruitment is specific for negative relative to positive emotional stimuli (though it remains possible that amygdala responding to happy expressions may be disrupted in youth with DBD-HCU; cf. Fusar-Poli *et al.* 2009). Second, it indicates dysfunction in emotional responding in both the amygdala *and* vmPFC. vmPFC and amygdala responsiveness to negative relative to neutral stimuli were correlated in all three groups (see Supplementary material, section 7) and level of vmPFC response was inversely related to CU traits level in patients with DBD. The relationship between the amygdala and vmPFC is complex. vmPFC may regulate amygdala activity (Milad & Quirk, 2012). However, vmPFC lesions suppress amygdala activity and 'protect' the individual from the development of PTSD/depression (Koenigs & Grafman, 2009). These latter results are consistent with a more interactive role where valence information is provided by the amygdala to vmPFC for representation (Schoenbaum *et al.* 2006). We assume that the current data of decreased activation in vmPFC and amygdala for youth with HCU reflects a failure in this interaction (cf. Marsh *et al.* 2008; Motzkin *et al.* 2011).

In contrast to our second prediction, youth with DBD-LCU did not show significantly increased amygdala responses to threat stimuli relative to healthy youths (only a non-significant trend) though their amygdala responses to threat stimuli were significantly greater than those of youth with HCU. It should be noted that while some previous studies have reported increased amygdala responses to negative stimuli in youth with conduct problems and LCU (Viding *et al.* 2012; Sebastian *et al.* 2014), not all studies have (Lozier *et al.* 2014). However, previous work has consistently shown, as was seen here, that youth with DBD-LCU show increased amygdala responses relative to youth with DBD-HCU [Viding *et al.* 2012; White *et al.* 2012; cf. prediction (iii), Sebastian *et al.* 2014]. Moreover, it is worth noting that while the

https://doi.org/10.1017/S0033291716000118 Published online by Cambridge University Press

group with DBD-HCU was selected for showing elevated CU traits, the group with DBD-LCU was selected for *not* showing CU traits. Selecting a second group of youth with DBD for impairment potentially associated with heightened threat sensitivity (possibly irritability; Thomas *et al.* 2011) might prove beneficial in future research.

Our fourth prediction, that DBD-LCU patients would show reduced recruitment of attention-based emotion regulation regions (dorsomedial and lateral frontal cortex; Blair *et al.* 2007) relative to healthy youth and DBD-HCU patients was not supported. The suggestion had been that increased emotional responsiveness in youth with DBD-LCU might reflect a failure on top-down attention-driven emotion regulation (cf. Blair *et al.* 2007). However, no regions showed significant group×task or group×task×emotion interactions that were consistent with reduced recruitment of systems implicated in top-down attention in patients with DBD-LCU. It should be noted though that youth with DBD-LCU showed decreased connectivity between the amygdala and both (right/left) insula and (right/left) inferior frontal cortex. These regions have been implicated in some accounts of emotion regulation in previous work (Davidson *et al.* 2000 Gold *et al.* 2015). The youth with DBD-LCU thus show some pathology consistent with impaired emotional regulation. However, it is important to note that though they showed significantly increased amygdala and vmPFC responsiveness to negative stimuli relative only to youth with DBD-HCU (there was increased responsiveness relative to healthy youth but this was not statistically significant). As such data from this study did not indicate heightened responsiveness to aversive stimuli (i.e. emotional dysregulation) in youth with DBD-LCU relative to healthy youth though this has been reported in other studies (Viding *et al.* 2012; Sebastian *et al.* 2014).

In line with predictions, youth with DBD (HCU *and* LCU) showed reduced task-related bilateral anterior insula cortex activity, a region implicated in response control (Chambers *et al.* 2009), during incongruent trials relative to healthy youth. This is consistent with previous reports of insula dysfunction in DBD (Crowley *et al.* 2010; Fairchild *et al.* 2014; White *et al.* 2014), and the relationship between dysfunctional response inhibition and externalizing behaviors (Young *et al.* 2009; Patrick *et al.* 2013) particularly impulsivity (Loeber *et al.* 2009). BOLD responses in anterior insula cortex correlated inversely with ADHD symptom severity in youth with DBD. This indicates a second form of pathophysiology in DBD related not to CU but rather impulsiveness and doubtless exacerbating antisocial and risky behavior (such as substance abuse) in these youth (Crowley *et al.* 2010; Blair *et al.* 2013).

In contrast to our final prediction, youth with DBD-HCU did not show *reduced* connectivity between the amygdala and cortical regions to threatening stimuli relative to comparison youth and DBD-LCU youth. Instead, youth with DBD-HCU showed *increased* connectivity between right amygdala and caudate in response to positive relative to neutral stimuli compared to healthy youth. This contrasts with previous functional connectivity findings indicating reduced connectivity between the amygdala and particularly vmPFC in patients with high psychopathic traits (Marsh *et al.* 2008, 2011; Motzkin *et al.* 2011). However, it should be noted that these previous studies reflect connectivity during either resting state (Motzkin *et al.* 2011) or across all task conditions (Marsh *et al.* 2008, 2011). The current study investigated group differences in differential connectivity across specific conditions. It is thus possible that while amygdala-vmPFC global connectivity is reduced in youth with elevated CU traits, any increase in connectivity for emotional relative to neutral stimuli is comparable for youth with DD-HCU and healthy youth.

Implications for treatment

Our results support suggestions that CU traits/emotional responsiveness should be considered when assessing patients with DBD. Youth with DBD-HCU showed decreased activation in the areas of emotional responsiveness including amygdala and vmPFC, which may lead to exercising proactive aggression, whereas youth with DBD-LCU showed decreased connectivity between amygdala and inferior frontal cortex which may lead to difficulty in emotion regulation and in turn exercising more of reactive aggression (Blair *et al.* 2013, 2014). Optimal treatment for patients with hypo-emotionality may differ from patients with hyper-emotionality. Indeed, youth with high CU traits benefit less from current interventions (Frick *et al.* 2014). The current data are not particularly supportive of interventions designed to augment emotional regulation in youth with DBD-LCU but this may reflect patient assessment and/or the form of emotion regulation assessed (Gyurak *et al.* 2011). The current data support suggestions that response control dependent on anterior insula cortex might be deficient in patients with DBD (Young *et al.* 2009; Patrick *et al.* 2013) and it may well be an integral part of assessment for youth with DBD.

Limitations and conclusion

Two caveats should be considered: first, we included youth with substance abuse and those receiving

https://doi.org/10.1017/S0033291716000118 Published online by Cambridge University Press

medication treatment. However, subsequent analyses excluding these subjects yielded similar results to the main analysis (see Supplementary material, sections 5 and 6). Second, there were relatively few group differences in behavioral task performance. The patients with DBD-LCU were less accurate in their responding than both the healthy youth and youth with DBD-HCU who did not differ in performance. However, this was seen for both congruent and incongruent trials and there were no group differences in impact of emotional distracters. This likely reflects the relatively minor differential effect of emotional distracters in this task (there were only trends for trials involving positive or negative emotional distracters to be slower than trials involving neutral distracters). Given the relatively weak impact of these distracters here, it is less surprising that we did not observe, for example, an anticipated reduction in interference from emotional distracters in the youth with DBD-HCU (Mitchell *et al.* 2006). More arousing/negatively valenced distracters might have been more successful in producing group differences in behavior. However, such stimuli are unlikely to be considered ethical for research with adolescents.

In summary, we demonstrated two forms of pathophysiology in youth with DBD that related to different forms of behavioral impairment. One is associated with reduced amygdala and vmPFC responses to negative stimuli and related to increased CU traits. Another with reduced insula responses during response control and related to ADHD symptoms. Appropriate assessment/intervention will need to be individualized according to specific pathophysiology of youth with DBD.

Supplementary material

For supplementary material accompanying this paper visit http://dx.doi.org/10.1017/S0033291716000118.

Acknowledgements

Drs Hwang, White, Sinclair, and Blair are with the Intramural Research Program at the National Institute of Mental Health, National Institutes of Health. This work was supported by the Intramural Research Program at the National Institute of Mental Health, National Institutes of Health under grant number 1-ZIA-MH002860-08 to Dr Blair. Ethics approval for this study was granted by the NIH Combined Neuroscience Institutional Review Board under protocol number 05-M-0105.

References

APA (2013). *Diagnostic and Statistical Manual 5*. American Psychiatric Association: Washington, D.C.

Baker RH, Clanton RL, Rogers JC, De Brito SA (2015). Neuroimaging findings in disruptive behavior disorders. *CNS Spectrums* **20**, 369–381.

Blair RJ (2013). The neurobiology of psychopathic traits in youths. *Nature Reviews Neuroscience* **14**, 786–799.

Blair KS, Smith BW, Mitchell DG, Morton J, Vythilingam M, Pessoa L, Fridberg D, Zametkin A, Sturman D, Nelson EE, Drevets WC, Pine DS, Martin A, Blair RJ (2007). Modulation of emotion by cognition and cognition by emotion. *Neuroimage* **35**, 430–440.

Blair KS, Vythilingam M, Crowe SL, McCaffrey DE, Ng P, Wu CC, Scaramozza M, Mondillo K, Pine DS, Charney DS, Blair RJ (2013). Cognitive control of attention is differentially affected in trauma-exposed individuals with and without post-traumatic stress disorder. *Psychological Medicine* **43**, 85–95.

Blair RJ, Leibenluft E, Pine DS (2014). Conduct disorder and callous-unemotional traits in youth. *New England Journal of Medicine* **371**, 2207–2216.

Buhle JT, Silvers JA, Wager TD, Lopez R, Onyemekwu C, Kober H, Weber J, Ochsner KN (2014). Cognitive reappraisal of emotion: a meta-analysis of human neuroimaging studies. *Cerebral Cortex* **24**, 2981–2990.

Byrd AL, Kahn RE, Pardini DA (2013). A validation of the inventory of callous-unemotional traits in a community sample of young adult males. *Journal of Psychopathology and Behavioral Assessment* **35**, 1–26.

Chambers CD, Garavan H, Bellgrove MA (2009). Insights into the neural basis of response inhibition from cognitive and clinical neuroscience. *Neuroscience & Biobehavioral Reviews* **33**, 631–646.

Conners CK, Sitarenios G, Parker JD, Epstein JN (1998). The revised Conners' Parent Rating Scale (CPRS-R): factor structure, reliability, and criterion validity. *Journal of Abnormal Child Psychology* **26**, 257–268.

Criaud M, Boulinguez P (2013). Have we been asking the right questions when assessing response inhibition in go/no-go tasks with fMRI? A meta-analysis and critical review. *Neuroscience & Biobehavioral Reviews* **37**, 11–23.

Critchley H, Daly E, Phillips M, Brammer M, Bullmore E, Williams S, Van Amelsvoort T, Robertson D, David A, Murphy D (2000). Explicit and implicit neural mechanisms for processing of social information from facial expressions: a functional magnetic resonance imaging study. *Human Brain Mapping* **9**, 93–105.

Crowley TJ, Dalwani MS, Mikulich-Gilbertson SK, Du YP, Lejuez CW, Raymond KM, Banich MT (2010). Risky decisions and their consequences: neural processing by boys with antisocial substance disorder. *PLoS ONE* **5**, e12835.

Cuthbert BN, Insel TR (2013). Toward the future of psychiatric diagnosis: the seven pillars of RDoC. *BMC Medicine* **11**, 126.

Davidson RJ, Putnam KM, Larson CL (2000). Dysfunction in the neural circuitry of emotion regulation – a possible prelude to violence. *Science* **289**, 591–594.

Erthal FS, de Oliveira L, Mocaiber I, Pereira MG, Machado-Pinheiro W, Volchan E, Pessoa L (2005). Load-dependent modulation of affective picture processing. *Cognitive, Affective & Behavioral Neuroscience* **5**, 388–395.

Fairchild G, Hagan CC, Passamonti L, Walsh ND, Goodyer IM, Calder AJ (2014). Atypical neural responses during face processing in female adolescents with conduct disorder. *Journal of the American Academy of Child & Adolescent Psychiatry* **53**, 677–687.

Finger EC, Marsh AA, Blair KS, Reid ME, Sims C, Ng P, Pine DS, Blair RJ (2011). Disrupted reinforcement signaling in the orbitofrontal cortex and caudate in youths with conduct disorder or oppositional defiant disorder and a high level of psychopathic traits. *American Joujrnal of Psychiatry* **168**, 152–162.

Finger EC, Marsh AA, Mitchell DG, Reid ME, Sims C, Budhani S, Kosson DS, Chen G, Towbin KE, Leibenluft E, Pine DS, Blair JR (2008). Abnormal ventromedial prefrontal cortex function in children with psychopathic traits during reversal learning. *Archives of General Psychiatry* **65**, 586–594.

Frick PJ (2004). *The Inventory of Callous-Unemotional Traits*. University of New Orleans: New Orleans.

Frick PJ, Ray JV, Thornton LC, Kahn RE (2014). Annual research review: a developmental psychopathology approach to understanding callous-unemotional traits in children and adolescents with serious conduct problems. *Journal of Child Psychology and Psychiatry* **55**, 532–548.

Fusar-Poli P, Placentino A, Carletti F, Landi P, Allen P, Surguladze S, Benedetti F, Abbamonte M, Gasparotti R, Barale F, Perez J, McGuire P, Politi P (2009). Functional atlas of emotional faces processing: a voxel-based meta-analysis of 105 functional magnetic resonance imaging studies. *Journal of Psychiatry & Neuroscience* **34**, 418–432.

Gold AL, Morey RA, McCarthy G (2015). Amygdala-prefrontal cortex functional connectivity during threat-induced anxiety and goal distraction. *Biological Psychiatry* **77**, 394–403.

Gyurak A, Gross JJ, Etkin A (2011). Explicit and implicit emotion regulation: a dual-process framework. *Cognition and Emotion* **25**, 400–412.

Herpers PC, Scheepers FE, Bons DM, Buitelaar JK, Rommelse NN (2014). The cognitive and neural correlates of psychopathy and especially callous-unemotional traits in youths: a systematic review of the evidence. *Development and Psychopathology* **26**, 245–273.

Hwang S, White SF, Nolan ZT, Sinclair S, Blair RJ (2014). Neurodevelopmental changes in the responsiveness of systems involved in top down attention and emotional responding. *Neuropsychologia* **62**, 277–285.

Insel T, Cuthbert B, Garvey M, Heinssen R, Pine DS, Quinn K, Sanislow C, Wang P (2010). Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. *American Journal of Psychiatry* **167**, 748–751.

Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, Williamson D, Ryan N (1997). Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL): initial reliability and validity data. *Journal of the American Academy of Child & Adolescent Psychiatry* **36**, 980–988.

Kimonis ER, Frick PJ, Skeem JL, Marsee MA, Cruise K, Munoz LC, Aucoin KJ, Morris AS (2008). Assessing callous-unemotional traits in adolescent offenders: validation of the inventory of callous-unemotional traits. *International Journal of Law and Psychiatry* **31**, 241–252.

Koenigs M, Grafman J (2009). Posttraumatic stress disorder: the role of medial prefrontal cortex and amygdala. *Neuroscientist* **15**, 540–548.

Lang PJBM, Cuthbert BN (2005). *International Affective Picture System (IAPS): Affective Ratings of Pictures and Instruction Manual*. University of Florida: Gainesville, FL.

Loeber R, Burke J, Pardini DA (2009). Perspectives on oppositional defiant disorder, conduct disorder, and psychopathic features. *Journal of Child Psychology and Psychiatry* **50**, 133–142.

Lozier LM, Cardinale EM, VanMeter JW, Marsh AA (2014). Mediation of the relationship between callous-unemotional traits and proactive aggression by amygdala response to fear among children with conduct problems. *JAMA Psychiatry* **71**, 627–636.

Marsh AA, Finger EC, Fowler KA, Jurkowitz IT, Schechter JC, Yu HH, Pine DS, Blair RJ (2011). Reduced amygdala-orbitofrontal connectivity during moral judgments in youths with disruptive behavior disorders and psychopathic traits. *Psychiatry Research* **194**, 279–286.

Marsh AA, Finger EC, Mitchell DG, Reid ME, Sims C, Kosson DS, Towbin KE, Leibenluft E, Pine DS, Blair RJ (2008). Reduced amygdala response to fearful expressions in children and adolescents with callous-unemotional traits and disruptive behavior disorders. *American Journal of Psychiatry* **165**, 712–720.

McLaren DG, Ries ML, Xu G, Johnson SC (2012). A generalized form of context-dependent psychophysiological interactions (gPPI): a comparison to standard approaches. *Neuroimage* **61**, 1277–1286.

Milad MR, Quirk GJ (2012). Fear extinction as a model for translational neuroscience: ten years of progress. *Annual Review of Psychology* **63**, 129–151.

Mitchell DG, Nakic M, Fridberg D, Kamel N, Pine DS, Blair RJ (2007). The impact of processing load on emotion. *Neuroimage* **34**, 1299–1309.

Mitchell DG, Richell RA, Leonard A, Blair RJ (2006). Emotion at the expense of cognition: psychopathic individuals outperform controls on an operant response task. *Journal of Abnormal Psychology* **115**, 559–566.

Miyake A, Friedman NP (2012). The nature and organization of individual differences in executive functions: four general conclusions. *Current Directions in Psychological Science* **21**, 8–14.

Motzkin JC, Newman JP, Kiehl KA, Koenigs M (2011). Reduced prefrontal connectivity in psychopathy. *Journal of Neuroscience* **31**, 17348–17357.

Patrick CJ, Fowles DC, Krueger RF (2009). Triarchic conceptualization of psychopathy: developmental origins of disinhibition, boldness, and meanness. *Development and Psychopathology* **21**, 913–938.

Patrick CJ, Venables NC, Yancey JR, Hicks BM, Nelson LD, Kramer MD (2013). A construct-network approach to bridging diagnostic and physiological domains: application to assessment of externalizing psychopathology. *Journal of Abnormal Psychology* **122**, 902–916.

Pessoa L, McKenna M, Gutierrez E, Ungerleider LG (2002). Neural processing of emotional faces requires attention. *Proceedings of the National Academy of Sciences USA* **99**, 11458–11463.

Pessoa L, Padmala S, Morland T (2005). Fate of unattended fearful faces in the amygdala is determined by both attentional resources and cognitive modulation. *Neuroimage* **28**, 249–255.

Roose A, Bijttebier P, Decoene S, Claes L, Frick PJ (2010). Assessing the affective features of psychopathy in adolescence: a further validation of the inventory of callous and unemotional traits. *Assessment* **17**, 44–57.

Schoenbaum G, Roesch MR, Stalnaker TA (2006). Orbitofrontal cortex, decision-making and drug addiction. *Trends in Neuroscience* **29**, 116–124.

Sebastian CL, McCrory EJ, Dadds MR, Cecil CA, Lockwood PL, Hyde ZH, De Brito SA, Viding E (2014). Neural responses to fearful eyes in children with conduct problems and varying levels of callous-unemotional traits. *Psychological Medicine* **44**, 99–109.

Talairach J, Tournoux P (1988). *Co-Planar Stereotaxic Atlas of the Human Brain*. Thieme: Stuttgart.

Thomas LA, Hall JM, Skup M, Jenkins SE, Pine DS, Leibenluft E (2011). A developmental neuroimaging investigation of the change paradigm. *Developmental Science* **14**, 148–161.

Viding E, Sebastian CL, Dadds MR, Lockwood PL, Cecil CA, De Brito SA, McCrory EJ (2012). Amygdala response to preattentive masked fear in children with conduct problems: the role of callous-unemotional traits. *American Journal of Psychiatry* **169**, 1109–1116.

Wechsler D (1999). *Wechsler Abbreviated Scale of Intelligence*. Psychological Corporation: San Antonio, TX.

White SF, Cruise KR, Frick PJ (2009). Differential correlates to self-report and parent-report of callous-unemotional traits in a sample of juvenile sexual offenders. *Behavioral Science & the Law* **27**, 910–928.

White SF, Fowler KA, Sinclair S, Schechter JC, Majestic CM, Pine DS, Blair RJ (2014). Disrupted expected value signaling in youth with disruptive behavior disorders to environmental reinforcers. *Journal of the American Academy of Child and Adolescent Psychiatry* **53**, 579–588 e9.

White SF, Marsh AA, Fowler KA, Schechter JC, Adalio C, Pope K, Sinclair S, Pine DS, Blair RJ (2012). Reduced amygdala response in youths with disruptive behavior disorders and psychopathic traits: decreased emotional response versus increased top-down attention to nonemotional features. *American Journal of Psychiatry* **169**, 750–758.

White SF, Pope K, Sinclair S, Fowler KA, Brislin SJ, Williams WC, Pine DS, Blair RJ (2013). Disrupted expected value and prediction error signaling in youths with disruptive behavior disorders during a passive avoidance task. *American Journal of Psychiatry* **170**, 315–323.

Young SE, Friedman NP, Miyake A, Willcutt EG, Corley RP, Haberstick BC, Hewitt JK (2009). Behavioral disinhibition: liability for externalizing spectrum disorders and its genetic and environmental relation to response inhibition across adolescence. *Journal of Abnormal Psychology* **118**, 117–130.