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Reduced amygdala–orbitofrontal connectivity during moral judgments in youths with disruptive behavior disorders and psychopathic traits

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ABSTRACT

We used functional magnetic resonance imaging (fMRI) to investigate dysfunction in the amygdala and orbitofrontal cortex in adolescents with disruptive behavior disorders and psychopathic traits during a moral judgment task. Fourteen adolescents with psychopathic traits and 14 healthy controls were assessed using fMRI while they categorized illegal and legal behaviors in a moral judgment implicit association task. fMRI data were then analyzed using random-effects analysis of variance and functional connectivity. Youths with psychopathic traits showed reduced amygdala activity when making judgments about legal actions and reduced functional connectivity between the amygdala and orbitofrontal cortex during task performance. These results suggest that psychopathic traits are associated with amygdala and orbitofrontal cortex dysfunction. This dysfunction may relate to previous findings of disrupted moral judgment in this population.

1. Introduction

Psychopathic traits include remorselessness, shallow emotions, lack of empathy, manipulativeness, and irresponsibility. These traits predispose individuals to persistent and severe aggressive and antisocial behaviors and in youths may lead to diagnoses of disruptive behavior disorders such as Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD) (Frick and White, 2008). It has been argued that amygdala and orbitofrontal cortex dysfunction in adolescents with psychopathic traits disrupts emotion-based decision-making, including moral decision making (Blair, 2003; Viding, 2004; Kiehl, 2006; Blair, 2007). On the basis of animal work investigating emotion based decision-making, Schoenbaum and colleagues have stressed the role of the amygdala in stimulus-reinforcement learning and of the orbitofrontal cortex in signaling outcome expectancies (Schoenbaum and Roesch, 2005).

Learning the basics of care-based morality–that some actions harm others and should be avoided and that other actions help others and should be performed–relies on intact functioning of the amygdala and orbitofrontal cortex (Blair, 2007). Specifically, the amygdala's role in stimulus–reinforcement learning may be to allow the individual to learn the goodness or badness of representations of actions. Positively and negatively valenced reinforcement expectancy information provided by the amygdala is then represented as a valenced outcome within the orbitofrontal cortex. Other systems then use this information to allow appropriate decision making, including moral judgments (Blair, 2007).

The functional roles of the amygdala and orbitofrontal cortex may be compromised in youths with psychopathic traits (Blair, 2007). Consistent with this, recent functional magnetic resonance imaging (fMRI) studies have demonstrated that youths with conduct problems and psychopathic traits show atypical amygdala and orbitofrontal cortex activity when viewing fearful or sad expressions and during reversal learning (Finger et al., 2008; Marsh et al., 2008; Jones et al., 2009; Passamonti et al., 2010). Comparable results have been seen in adults with psychopathic traits (Kiehl et al., 2001; Gordon et al., 2004; Birbaumer et al., 2005).

Moreover, both youths with psychopathic traits and adults with psychopathic traits show significant impairment in emotion-based decision making as indexed by both the passive avoidance learning paradigm and the Iowa gambling task (Newman and Kosson, 1986; Blair et al., 2001a; Blair et al., 2004). Youths with psychopathic traits and adults with psychopathic traits are also impaired on some moral judgment tasks (Blair, 1995; Blair et al., 2001b). Consistent with this, psychopathic murderers show a violent implicit association test (IAT) effect for violent actions: they show less of an association between violent actions and unpleasantness and between peaceful actions and pleasantness than do psychopathic non-murderers (Gray et al., 2003).

While fMRI data strongly suggest amygdala and orbitofrontal cortex dysfunction in youths and adults with psychopathic traits (Kiehl et al.,

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2001; Gordon et al., 2004; Birbaumer et al., 2005; Finger et al., 2008; Marsh et al., 2008; Jones et al., 2009), very little of this work has specifically examined decision making. Finger et al. (2008) demonstrated dysfunctional reinforcement outcome signaling in orbitofrontal cortex during reversal learning in youths with psychopathic traits. More critically for this study, a recent fMRI study revealed reduced amygdala activation in adults with high psychopathy scores during a moral decision-making paradigm (Glenn et al., 2009).

In the current study, we examined the neural correlates of moral decision making in youths with psychopathic traits. We used a moral IAT in which participants judged the legality of various actions using button responses that were also associated with either positive or negative judgments (cf. Luo et al., 2006). This task elicits an "IAT effect," whereby participants are slower to judge items as legal (or illegal) when they make their judgments using response buttons associated with opposite-valence items (e.g., making a "legal" judgment with the button used for negative-valence words).

Performance on similar tasks appears to rely on two forms of neuro-computational process (Chee et al., 2000; Phelps et al., 2000; Cunningham et al., 2004; Luo et al., 2006; Beer et al., 2008). The first reflects the representation of the automatic attitude, including its valence, and has been associated with activity within the amygdala and orbitofrontal cortex (Phelps et al., 2000; Cunningham et al., 2004; Luo et al., 2006). The second neuro-computational process reflects mediation of the response conflict that occurs during trials in which the valences of items associated with the same button press are incongruent (e.g., legal actions and negative objects). Such response conflict is typically associated with activity in dorsomedial frontal cortex, dorsal anterior cingulate cortex, and lateral frontal cortex (Chee et al., 2000; Luo et al., 2006; Beer et al., 2008).

The current study tested the hypothesis that youths with psychopathic traits would show decreased amygdala and orbitofrontal cortex activity while performing a moral IAT task. We predicted that these youths would also show reduced amygdala–orbitofrontal cortex connectivity during task performance, as all trial types are hypothesized to be associated with integrated amygdala-orbital frontal cortex activity.

2. Methods

2.1. Participants

Twenty-eight right handed youths participated in this study: 14 youths with ODD or CD and psychopathic traits and 14 healthy comparison youths (Table 1). The youths were recruited from the community through newspaper ads, fliers, and referrals from area mental health practitioners. The study design was reviewed by the Institutional Review Board at the NIMH, and informed assent and consent were obtained from the participants and their parents, respectively, after the nature of the procedures had been fully explained to them.

All youths and parents were administered the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS-PL) (Kaufman et al., 1997) by an experienced clinician trained and supervised by an expert child psychiatrist (D.S. Pine). Clinicians' assessments show good inter-rater reliability (kappa >0.75 for all diagnoses). Exclusion criteria were pervasive developmental disorder, Tourette's syndrome, current or lifetime history of psychosis, depression, bipolar disorder, generalized, social, or separation anxiety disorder, post-traumatic stress disorder, neurologic disorder, history of head trauma, and IQ less than 80. It should be noted that the K-SADS allows for the identification of substance abuse and substance dependence. No children in either group met criteria for substance abuse or dependence. In addition, parents completed the Antisocial Process Screening Device (APSD), which measures psychopathic traits. Youths meeting K-SADS-PL criteria for CD or ODD and who had APSD scores ≥20 or greater returned to complete the Psychopathy Checklist-Youth Version (PCL-YV) assessment. Only youths scoring ≥20 on the PCL-YV were included in the psychopathic traits group. Healthy controls did not meet criteria for any K-SADS-PL diagnosis and scored <20 on the APSD.

Youths with psychopathic traits on medications were included if their qualifying behaviors and traits were present despite medication. Thus, six youths in the psychopathic traits group who were taking psychoactive medication were included in the study. This included four youths taking simple stimulants (methylphenidate, dexmethylphenidate) who withheld medication for 48 h prior to testing, one youth taking an anti-psychotic (aripiprazole), and one youth taking an anti-depressant (bupropion) and an anti-convulsant (oxcarbazepine). The composition of the two groups of youths was not significantly different in terms of age, IQ and gender (Table 1).

2.2. Clinical measures

2.2.1. Antisocial Process Screening Device (ASPD; Frick and Hare, 2001)

A 20 item parent-completed rating of psychopathic traits and conduct and impulsivity problems for the detection of antisocial processes in youths. A three-factor structure has been characterized comprised of the following dimensions: Callous/Unemotional, Narcissism, and Impulsivity (Frick and Hare, 2001). There is no established APSD cutoff score for classification of high psychopathic traits (Edens et al., 2001; Frick and Hare, 2001; Murrie and Cornell, 2002). Consistent

Table 1
Participant characteristics.

Variable	Psychopathic traits ($N=14$)		Healthy controls ($N=14$)		P
Demographics	Mean	S.D.	Mean	S.D.	
Age, y (range)	14.4 (10.9–16.9)	1.9	13.5	1.7	N.s.
IQ (range)	102.6 (85–118)	8.6	106.0 (83–129)	14.5	N.s.
Male sex, no. (%)	8 (57)		11 (79)		N.s.
DSM-IV diagnoses (current), No. (%)					
Conduct disorder	6 (43)		0		–
Oppositional-defiant disorder	8 (57)		0		–
Attention deficit hyperactivity disorder	9 (64)		0		–
Pediatric psychopathic trait rating scale scores (range)					
Antisocial process screening device	29.5 (25–35)	2.9	6.3 (3–14)	3.6	<0.001
Youth psychopathic traits inventory	113.6 (93–154)	21.4	97.4 (71–131)	19.2	<0.05
Psychopathy checklist: youth version	24.0 (20–32)	3.4	–	–	–

with prior studies, (Finger et al., 2008; Marsh et al., 2008), a cutoff score of ≥20/40 was chosen to define the psychopathic group.

2.2.2. Psychopathy Checklist: Youth Version (PCL-YV; Forth et al., 2007)

A 20 item rating scale for assessment of interpersonal, affective and behavioral features related to psychopathic traits in adolescents based on semi-structured interview and collateral information. Consistent with prior studies, (Finger et al., 2008; Marsh et al., 2008), a cutoff score of ≥20/40 was used. Although no set cutoff scores for assessing psychopathy in youths exist, available evidence suggests that both PCL-YV and APSD scores in adolescents are predictive of later increased risks of psychopathy and violent offending (Falkenbach et al., 2003; Corrado et al., 2004). PCL-YV interviews and scoring were conducted by two researchers trained in PCL-YV administration who demonstrated good inter-rater reliability ($R = 0.91$).

2.3. The IAT task

A modified version of the previously reported fMRI morality IAT task was used (Luo, et al., 2006) (Fig. 1). Whereas the previously published tasks presented participants with pictures, the present task presented words to avoid presenting images deemed by the Institutional Review Board to be overly violent for children. In all other respects, this task was similarly constructed. Participants were instructed: "In this task, you're going to be using your response buttons to categorize words. Words are going to appear in the middle of the screen. The two response categories will appear in the upper right and left corners of the screen. For each word, decide if it goes in the left or right category by pressing your left or right response button. There are two kinds of categories: Words that are *good things* (like 'jewel') or *bad things* (like 'cockroach'). Then there will be words that are *legal behaviors* (like 'help') or *illegal behaviors* (like 'steal')."

Sixteen words representing each of four categories–legal and illegal actions and positive and negatively valenced objects (64 words total)–were selected from the Affective Norms for English Words (ANEW) database (Bradley and Lang, 1999). The legal and illegal action words were matched for arousal, length, and frequency.

In each of the four fMRI runs of the task, participants saw 32 words. These words included eight words in each of four categories (illegal and legal actions, negatively and positively valenced objects). Each word appeared for 2000 ms, during which time participants' responses were collected, and was followed by a 500-ms fixation cross. All 32 words were presented three times per run, and the order of words within each block was randomized. Each participant completed two runs in which they responded to legal actions and positively valenced words with one button, and illegal actions and negatively valenced words with the other button (congruent trials). In the other two runs, the illegal actions and positively valenced words shared a button, and the legal actions and negatively valenced words shared a button (incongruent trials). The response categories were visible during every trial and appeared in the upper right and left corners of the screen. Each participant received the runs in one of two orderings (ICCI or CIIC) and the two orderings were distributed equally across groups. Each run contained an additional 48 randomly interspersed 2500 ms fixation trials, and six fixation trials began and concluded each run, making each run 6:30 long. Prior to each run, participants completed a brief unscanned run that presented each word once to familiarize them with the blocks and the task.

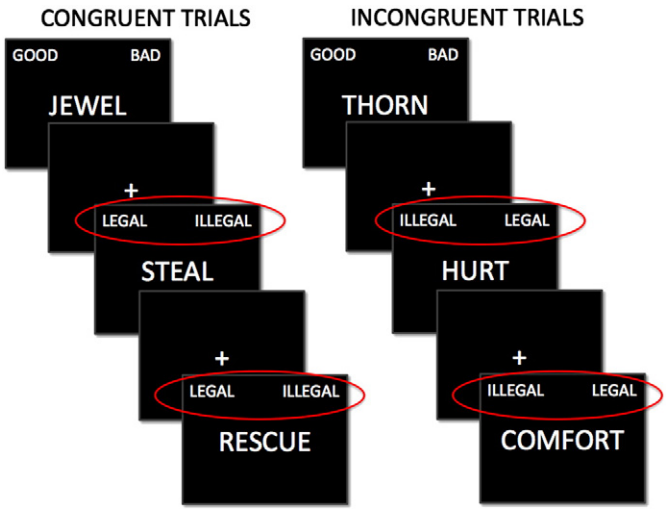

Fig. 1. IAT task design.

2.4. fMRI parameters

T2* weighted images were collected during fMRI scanning using a 1.5 T GE Signa scanner (GE Medical Systems, Milwaukee, WI) (matrix 64×64; repetition time, 2500 ms; echo time, 30 ms; field of view, 240 mm; voxels, 3.75×3.75×4). Functional images were acquired with a gradient echo-planar imaging (EPI) sequence (axial plane, 31 contiguous axial slices). High-resolution T1-weighted anatomical images were also acquired (three-dimension Spoiled GRASS with inversion recovery prep pulse; number of 1.5 mm axial slices, 128; field of view, 240 mm; number of acquisitions, 1; repetition time, 8.1 ms, echo time, 1.8 ms; matrix, 256×256).

2.5. fMRI pre-processing

Imaging data were analyzed in Analysis of Functional Neuroimaging (AFNI) (Cox, 1996). At the individual level, the first 4 functional images from each run were discarded. The remaining functional images were then motion corrected and spatially smoothed with a 6 mm full-width half-maximum Gaussian filter. The time series 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 to create percent signal change coefficients from the mean.

Seven regressors characterizing the trials were then generated: legal items-congruent, legal items-incongruent, illegal items-congruent, illegal items-incongruent, positive (non-moral) objects, negative (non-moral) objects, and incorrect responses. Regressors were created by convolving the train of stimulus events with a gamma-variate hemodynamic response function. Linear regression modeling was performed using the regressors described above plus regressors to model a first order baseline drift function. This produced a beta coefficient and associated *t*-statistic for each voxel and regressor. Following findings that that normalization of brain volumes from age 7–8 years onward does not introduce major age related distortions in localization or time course of the BOLD signal in event related fMRI (Burgund et al., 2002; Kang et al., 2003), participants' anatomical scans were individually registered to the Talaraich and Tourneoux Atlas (Talairach and Tournoux, 1988). The individuals' functional EPI data were then registered to their Talaraiched anatomical scan within AFNI.

2.6. fMRI data analysis

Group analysis of the BOLD data was then performed on regression coefficients from individual subject analyses using two whole brain analyses of variance (ANOVAs) on the BOLD response data: a 2 (group: psychopathic traits, healthy control)×2 (trial type: legal, illegal)×2 (congruence: congruent, incongruent) ANOVA, and a 2 (group: psychopathic traits, healthy control)×2 (trial type: positive objects, negative objects)×2 (congruence: congruent, incongruent) ANOVA. For both ANOVAs, initial thresholding was set at $P<0.005$ with an extent threshold of 10 voxels, a combination that has been demonstrated to

produce a desirable balance between Type I and Type II error rates in fMRI (Lieberman and Cunningham, 2009). We did not employ this threshold when testing amygdala activation, but instead employed small volume correction (SVC). Post–hoc analysis of significant interactions was assessed with planned ANOVAs within SPSS.

Functional connectivity analyses were also performed. These analyses featured correlation analyses of extracted data from specific regions of interest, in other words, we examined covariation across the brain with the activation in the maximally activated voxel in the amygdala cluster created by the original analysis using AFNI. For each participant, voxelwise correlation analyses were conducted between each individual voxel's time series and that of the identified seed. These coefficients were squared, normalized using a Fisher transformation, and compared across groups using *t*-tests. The threshold was set at $P<0.005$ with an extent threshold of 10 voxels.

3. Results

3.1. Behavioral results

A 2 (group: psychopathic traits, healthy controls)×2 (trial type: legal, illegal)×2 (congruence: congruent, incongruent) repeated-measures analysis of variance (ANOVA) was conducted on the percentage of errors and the response latencies for correct responses across groups. The IAT effect was identified: participants showed significantly more errors, $F(1,26)=13.51$, $P<0.001$ (Fig. 2), and slower response latencies for correct responses, $F(1,26)=55.21$, $P<0.001$ (Fig. 3), during incongruent than congruent trials. There was no significant main effect of group or group interactions.

3.2. fMRI results

A 2 (group: psychopathic traits, healthy controls)×2 (trial type: legal, illegal)×2 (congruence: congruent, incongruent) ANOVA was conducted on the whole brain event-related blood oxygen level dependent (BOLD) data using AFNI. This revealed regions showing a significant group-by-trial type interaction, and main effects of group, trial type and congruence (see Table 2).

The only region showing a significant group×trial type effect was within the right amygdala (*xyz* = 17, −1, −22, 6 voxels), $F(1,26)=9.42$, $P<0.005$, ($P<0.05$, SVC) (Fig. 4). Youths with psychopathic traits showed decreased activation in this region when categorizing legal (but not illegal) words relative to healthy youths, $t(26)=2.24$, $P<0.05$. A main effect of group was also seen in bilateral regions of temporal cortex. In both regions, youths with psychopathic traits showed reduced BOLD responses relative to comparison youth.

Notably, dorsomedial frontal cortex and bilateral regions of lateral frontal cortex showed a significant main effect of congruence. In line with previous work (Chee et al., 2000; Luo et al., 2006), these regions showed greater BOLD responses to incongruent relative to congruent trials. However, there was no significant group-by-congruence interaction within these regions.

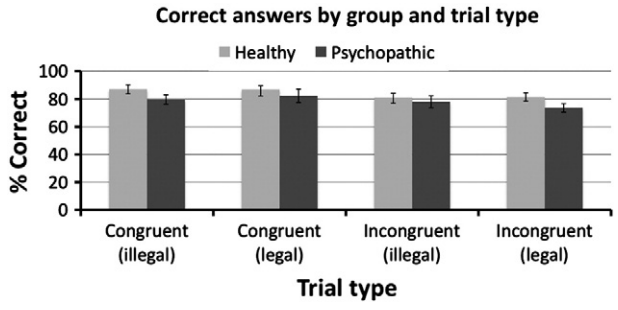

Fig. 2. Percent correct responses by trial type and group. Error bars indicate SEM.

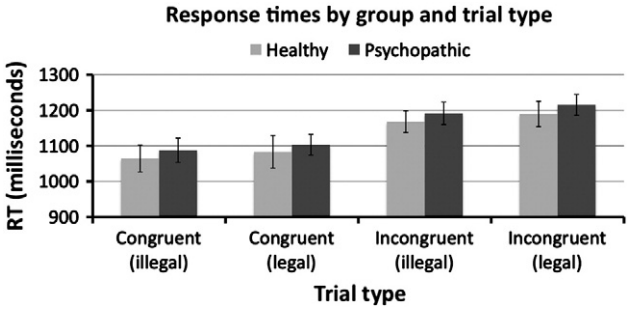

Fig. 3. Response latencies for correct responses by trial type and group. Error bars indicate SEM.

The results of the functional connectivity analysis showed significantly less functional connectivity in youths with psychopathic traits between the amygdala and the orbitofrontal cortex (*xyz* = −15, 41, −4), bilateral regions of temporal cortex and inferior parietal cortex, $t(26)=3.60$, $P<0.005$ (Table 3 and Fig. 4).

Using AFNI, we also conducted a second 2 (group: psychopathic traits, healthy controls)×(trial type: positive object, negative objects)×2 (congruence: congruent or incongruent) ANOVA on the whole brain event-related blood oxygen level dependent (BOLD) data. The results of this ANOVA, $F(1,26)=9.38$, $P<0.005$, were consistent with the results of the analysis of responses to illegal and illegal words.

Four regions showed significant group-by-trial type interaction effects, including two clusters within superior temporal gyrus and one cluster in posterior cingulate cortex, (Table 4). In each of these three regions, no group differences were observed in response to negative objects but in response to positive objects, psychopathic youths showed less activation than healthy youths. These group differences were statistically significant ($P<0.05$), except for one of the clusters in superior temporal gyrus ($P<0.20$).

4. Discussion

In this study, youths with psychopathic traits showed reduced amygdala responsiveness to legal actions relative to healthy youths. Moreover, they showed reduced amygdala–orbitofrontalcortex

Table 2
Regions demonstrating differential BOLD responses during the moral IAT (legal and illegal actions).

Region	L/R	BA	*x*	*y*	*z*	*F*	Voxels
Group×Legality							
Amygdala	R		17	−1	−22	11.4	6
Group (Psychopathic<Controls)							
Middle temporal gyrus	L	37	−55	−64	5	11.1	20
Fusiform gyrus	L	19	−19	−64	−13	11.5	14
Legality (illegal<legal)							
Inferior frontal cortex	L	47	−52	29	−1	10.8	10
Congruence (Congruent<incongruent)							
Cingulate gyrus	R	24	5	−1	47	12.4	30
Precentral gyrus	R	6	32	−10	56	17.6	60
Precentral gyrus	R	6	53	−1	50	13.8	21
Medial frontal gyrus	L	6	−19	−7	53	12.5	16
Cuneus/Posterior cingulate cortex	R	30	11	−64	8	14.3	45
Cuneus	R	17	5	−79	11	13.3	79
Precuneus	L	7	−28	−73	50	12.2	13

Talairach coordinates of peak activation. Regions and Brodmann's areas according to Talairach Daemon Atlas. All regions initially thresholded at $P<0.005$.

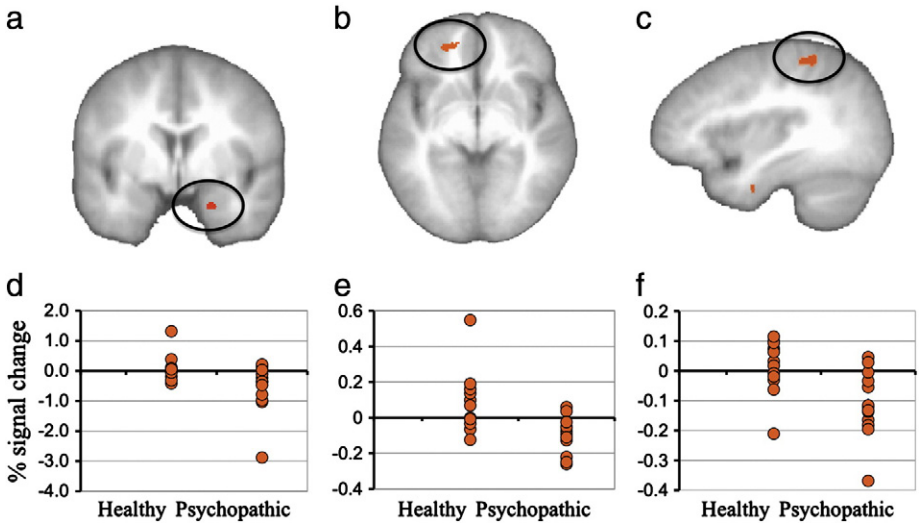

Fig. 4. (A) Region of amygdala where youths with psychopathic traits showed significantly less responsiveness to legal items relative to healthy youths; (B) Region of orbitofrontal cortex showing significantly less functional connectivity with the amygdala in youths with psychopathic traits relative to healthy youths; (C) Region of inferior parietal cortex showing significantly less functional connectivity with the amygdala in youths with psychopathic traits relative to healthy youths; (D) Group differences in amygdala activation during legal-word trials (group differences remain significant following removal of one outlier); (E) Group differences in amygdala–orbitofrontal cortex connectivity (group differences remain significant following removal of one outlier); (F) Group differences in amygdala-parietal cortex connectivity (group differences remain significant following removal of two outliers).

connectivity relative to healthy youths during task performance. They did not, however, differ from healthy youths in terms of dorsomedial or lateral frontal cortex activation during the task.

It has been argued that moral judgments reflect the amygdala's role in stimulus-reinforcement learning. The amygdala's role is thought to involve enabling the individual to learn the goodness or badness of actions and feeding forward reinforcement expectancy information to orbitofrontal cortex to facilitate decision-making (Blair, 2007). These systems are considered dysfunctional in individuals with psychopathic traits, as studies with youths with psychopathic traits (Finger et al., 2008; Marsh et al., 2008; Jones et al., 2009) and adults with psychopathic traits (Kiehl et al., 2001; Gordon et al., 2004; Birbaumer et al., 2005) have demonstrated. Recently, adults with high psychopathy scores have been reported to show reduced amygdala activity during moral decision making (Glenn et al., 2009) and to show reduced correspondence between amygdala activation and judgments of moral severity (Harenski et al., 2010). The current data extend these findings by demonstrating that the region of the amygdala showing reduced responding to legal actions in youths with psychopathic traits showed, as predicted, reduced connectivity with orbitofrontal cortex. The extension of these findings to a youth sample is important because it indicates that the identified pathophysiology is unlikely to reflect a secondary consequence of the disorder (e.g., the increased drug abuse that is prevalent in adult samples) but rather a developmental feature of the pathology.

It should be noted that the moral decision making paradigm used in the study of adults with high psychopathy scores (Glenn et al., 2009) is a more complex task than the moral IAT task used here. The study by Glenn et al. (2009) used variants of what have been termed "trolley problems" (cf. Greene et al., 2001) that force decisions between competing moral objectives. In contrast, the current task involved the participants making simple judgments regarding the legality of items. Importantly, though, both types of task may be reliant on a form of an emotional "automatic moral attitude".

At the neural level, this automatic moral attitude is thought to reflect the amygdala's response to the conditioned stimulus that is the individual's representation of the moral action (whether prosocial or antisocial) and the representation of this valence information within orbitofrontal cortex (Blair, 2007). In the context of "trolley problems", it is argued that this emotional automatic moral attitude is the basis of the distinction between personal dilemmas and impersonal dilemmas, which are distinguished by the salience of the harm to a victim. In the current task, negative and positive emotional automatic moral attitudes may have been activated by reading the antisocial and prosocial actions, respectively.

Table 3
Regions demonstrating significant group differences in functional connectivity with amygdala seed voxel.

Region	L/R	BA	*x*	*y*	*z*	*t*	Voxels
Group (Psychopathic<Controls)							
Rostral anterior cingulate cortex/Orbitofrontal cortex	L	10/32	−15	41	−4	3.6	41
Superior temporal gyrus	R	38	35	−1	−16	3.5	15
Inferior parietal cortex	L	40	−37	−39	52	3.6	36
Middle temporal gyrus	L	21	−63	−23	−10	3.2	12
Lingual gyrus	L	18	−1	−85	−12	3.9	90
Fusiform gyrus	L	18	−27	−91	−14	3.8	12

Talairach coordinates of peak activation. Regions and Brodmann's areas according to Talairach Daemon Atlas. All regions thresholded at $P<0.005$.

Table 4
Regions demonstrating differential BOLD responses during the moral IAT (positive and negative objects).

Region	L/R	BA	*x*	*y*	*z*	*F*	Voxels
Group × Valence							
Superior temporal gyrus	R	22	71	−34	14	20.54	30
Posterior cingulate gyrus	R	31	11	−46	38	17.3	20
Superior temporal gyrus	R	39	53	−58	20	14.1	15
Precuneus	R	7	11	−64	50	16.9	11
Group (Psychopathic<Controls)							
Superior temporal gyrus	L	22	−55	−4	2	14.5	15
Congruence (Congruent<Incongruent)							
Medial frontal gyrus	L	6	−19	−7	53	12.9	11
Paracentral lobule	L	5	−4	−34	53	22.4	17

Talairach coordinates of peak activation. Regions and Brodmann's areas according to Talairach Daemon Atlas. All regions initially thresholded at $P<0.005$.

The claim is not that youths with psychopathic tendencies are selectively impaired in representing the value of legal items. Rather, youths with psychopathic traits are thought to face difficulties associating the appropriate valence with objects and actions generally (Blair, 2007). In the current study, this manifested as a pervasive pattern of atypical activation in response to positively valenced items (legal actions and positive objects). Other work has also identified aberrant neural responses to positively valenced cues in youths with psychopathic tendencies (Finger et al., 2011) or youth with conduct disorder (psychopathy unspecified; Rubia et al., 2009b; Crowley et al., 2010). Currently, it is unclear why the present study, and these previous works, identified particular problems with positively valenced items whereas other work has identified difficulties with negatively valenced items (e.g., Birbaumer et al., 2005; Finger et al., 2008; Marsh et al., 2008; Passamonti et al., 2010). These differences may reflect the computational specifics of the individual tasks used and is a current focus of research in our group.

Three features of the results are worth considering further. First is the apparent selectivity of the result: youths with psychopathic traits showed reduced amygdala responsiveness relative to comparison youths to the legal items but not to the illegal items. We anticipated a significant group difference for illegal items also. The absence of a group difference for illegal actions may reflect a type II error. Previous behavioral work demonstrates significant impairment in the processing of antisocial actions in individuals with psychopathic traits (Blair, 1995; Blair et al., 2001b). And Glenn et al. (2009) found that psychopathy was associated with reduced amygdala activation in response to actions associated with salient harm.

Second, previous IAT imaging studies typically find greater BOLD responses in dorsomedial frontal cortex (including dorsal anterior cingulate cortex) and lateral frontal cortex during incongruent than congruent trials (Chee et al., 2000; Luo et al., 2006; Beer et al., 2008). Dorsomedial frontal cortex is implicated in mediating response conflict (Cohen et al., 2000; Kerns et al., 2004), potentially by recruiting lateral frontal cortex to augment the representation of relevant stimulus features within temporal cortex (MacDonald et al., 2000; Garavan et al., 2002). It has been argued increased dorsomedial frontal and dorsal anterior cingulate cortex activity during the IAT effect reflects increased response conflict during incongruent trials (Luo et al., 2006). In the current study, there was a significant main effect of congruence within dorsomedial frontal cortex that extended into dorsal anterior cingulate cortex and lateral frontal cortex, but no group-by-congruence interaction. This suggests a lack of deficits in anterior cingulate cortex in youths with psychopathic traits during tasks of this type. This finding corroborates similar findings in prior imaging studies in these youths (Finger et al., 2008).

Third, and in line with predictions, healthy comparison youths showed positive connectivity between amygdala and orbitofrontal cortex. This may reflect the amygdala's role in feeding forward reinforcement expectancy information to orbitofrontal cortex to guide decision-making (Blair, 2007). Youths with psychopathic traits showed significantly less positive functional connectivity between these two regions. In fact, in contrast to predictions, the youths with psychopathic traits showed significant negative connectivity between the amygdala and orbitofrontal cortex. This suggests a relationship between amygdala and orbitofrontal cortex activity that is inverse to that of healthy comparison individuals. This may reflect inappropriate interactions between these two regions in youths with psychopathic traits. Alternatively, this might reflect atypical regulatory activity over the amygdala by orbitofrontal cortex in youths with psychopathic traits (cf. Urry et al., 2006). Although we believe that this alternative hypothesis is premature, further research will be conducted to examine emotion regulation in youths with psychopathic traits.

Several additional concerns should be noted regarding the current results. First, no behavioral group differences were observed. This is consistent with the results of prior studies that have measured simple permissibility judgments like those assessed here. One prior behavioral study used a moral-judgments IAT similar to our own, and the authors reported group differences in psychopathic murderers, but not in psychopaths who were not murderers (Gray et al., 2003). In a previous fMRI study of moral reasoning in psychopaths, performance differences were not seen, although higher psychopathic tendencies were associated with reduced amygdala activity (Glenn et al., 2009). By contrast, previous studies testing somewhat more sophisticated moral reasoning have found performance differences in individuals with increased psychopathic traits (Blair, 1995; Blair et al., 2001b). We interpret group differences in neural activation patterns in the absence of behavioral differences as potentially reflecting differences in strategies used by psychopathic and non-psychopathic adolescents during moral judgments. Perhaps some participants relied on semantic knowledge rather than affect-based assessments to perform the task. If prevalent, the use of such a strategy might also help to account for the lack of between-group differences in amygdala activation during illegal-word trials.

Second, one aspect of the functional connectivity analysis approach used here instead of, for example, a psychophysiological interaction (PPI) analysis, is that it does not allow us to distinguish group differences in connectivity related to the performance of the IAT task from group differences in baseline connectivity. However, a PPI analysis would have been less appropriate given our task design. According to our theoretical position, all conditions relied on amygdala–orbitofrontalcortex interaction. Although group differences in amygdala activation may be greatest for legal items, we did not predict that group differences in amygdala–orbitofrontal cortex *connectivity* would vary across conditions. Thus, our analysis, in which functional connectivity was examined across all conditions of the IAT task, was able to test our hypotheses. Future work might, however, include a low-level control condition. This would allow for better examination of whether reduced amygdala–orbitofrontal cortex connectivity reflects group differences in connectivity specific to the task or to particular trials or group differences in baseline connectivity.

Third, the current study contrasted youths with disruptive behavior disorders and psychopathic traits with healthy comparison youths—it did not include a comparison group of youths with disruptive behavior disorders with low levels of psychopathic traits. We assume that the atypical amygdala responsiveness and amygdala–orbitofrontal cortex connectivity observed here are causally related to the emergence of psychopathic traits (Blair, 2007). However, without this second comparison group, we cannot be certain whether the observed pathophysiology relates to youths with disruptive behavior disorders generally or only those with disruptive behavior disorders and psychopathic traits. It will be important for future investigations to compare patterns of neural activation across subgroups of children with conduct problems, given the heterogeneity observed in previous studies of this population (Frick and White, 2008; Passamonti et al., 2010). Moreover, it will be important to determine whether the present results extend to psychopathic adults, who are typically selected using a standard PCL-R cutoff of 30/40 points (higher than the 20/40 points cutoff we employed).

It will be recalled that six children with psychopathic traits in this study were taking psychotropic medications. To rule out the possibility that these medications were the cause of the patterns we observed, we repeated our primary ANOVA excluding these children and observed nearly identical Group × Legality effects in the amygdala as had been identified in the original analysis, ($xyz = 17, -1, -22$, 4 voxels), $F(1,26) = 9.92$, $P < 0.005$. This suggests that group differences we observed were not the result of group differences in medication status. The fact that similar results were obtained after nearly halving our group of adolescents with psychopathic traits supports the stability of the patterns of activation we have identified. However, it should be noted that small sample sizes such as that used in the present study increase the instability of data, thus increasing the risk of identifying patterns of activation that result from chance.

Fourth, disruptive behavior disorders (CD and ODD) are frequently comorbid with Attention Deficit Hyperactivity Disorder (ADHD) (Taylor et al., 1986). In this study, 64% of youths with psychopathic traits also presented with ADHD. It could therefore be argued that group differences reflect ADHD rather than psychopathic traits. Because of this concern, our first phase of studies included two comparison groups of participants: both healthy youths and youths with ADHD (Finger et al., 2008; Marsh et al., 2008). These studies found amygdala or orbitofrontal cortex pathophysiology only in youths with psychopathic traits, not in youths with ADHD. Rubia and colleagues have also demonstrated that youths with CD who do not present with ADHD exhibit orbitofrontal cortex dysfunction whereas youths with ADHD do not (Rubia et al., 2009b). Moreover, they have observed dysfunction in the recruitment of regions of lateral frontal cortex in youths with ADHD that was not seen, as it was not seen in the current study, in youths with pure CD (Rubia et al., 2008, 2009a,b). We therefore considered it unlikely that the group differences hypothesized in the current study would reflect ADHD and did not include this second comparison group.

5. Conclusion

In summary, the results of the present study indicate that psychopathic traits, which include remorselessness, shallow emotions, lack of empathy, and manipulativeness, and which predispose adolescents to severe ongoing antisocial behavior, are associated with atypical patterns of activity in the amygdala and orbitofrontal cortex during a moral decision-making task. We suggest that psychopathic traits may affect adolescents' ability to attach the appropriate affective valence to actions of varying moral permissibility, and from using information about valence to guide their decisions.

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