

PSYCHOPATHY, MORALITY, AND BRAIN FUNCTION
IN ADOLESCENCE: A PILOT STUDY

by

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ABSTRACT

Psychopathy is a serious psychological condition that has been associated with deficits in brain structure and functioning in adults, including altered functioning during the process of moral decision-making. Whether these same brain deficits are present in adolescents with psychopathic traits is not well understood. Using fMRI, the neural correlates of moral decision-making were examined in relation to psychopathic traits in youth. Whole brain analyses show that activity in a number of regions, including the temporal pole, postcentral gyrus, anterior cingulate, and middle frontal gyrus, while viewing moral images, was positively correlated with psychopathy scores measured using the Youth Psychopathic Traits Inventory. These results contradict previous findings in adults which have found decreased functioning in individuals with psychopathic traits in the orbitofrontal cortex and amygdala. These results suggest that there may be important differences in the neural correlates of psychopathy in adults and adolescents, and that it may be essential to consider the developmental changes that occur in the brain during adolescence to better understand the development of psychopathic traits.

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CHAPTER 1

INTRODUCTION

Psychopathy is a serious psychological disorder which imposes a substantial burden on society, as it is associated with higher levels of interpersonal violence and crime. It is typically considered a personality disorder, and has also been described as a developmental disorder in which individuals exhibit a lack of emotion, manipulative behavior, irresponsible interpersonal relationships, impulsivity, and possibly violence (Wu and Barnes, 2013). Although psychopathy is not present as a diagnosis in the DSM-5 (American Psychiatric Association, 2013), it is considered to be a distinct disorder by many psychologists. It is most similar to antisocial personality disorder (ASPD), a disorder characterized by stable and persistent impulsive, dishonest, and sometimes criminal behavior. Consistent with the characterization of psychopathy as a developmental disorder, experts agree that some youth exhibit psychopathic-like traits (Frick et al., 1994; Lynam, 1996) and that these youth might be more likely than others to become chronic offenders (Salekin, 2008). Previous research has established that psychopathic traits, when present, tend to be stable across adolescence and into early adulthood (Lynam et al, 2009; Neumann et al., 2011), but developmental trends have only been studied with behavioral methods and never with neuroimaging.

There are specific structural and functional brain deficits which have been associated with adult psychopathy. The most commonly implicated regions are the prefrontal cortex (PFC; Yang & Raine, 2009) and amygdala (Ermer, Cope, Nyalakanti, Calhoun & Kiehl, 2012). The prefrontal cortex is important in higher-order thought including inhibition and emotion appraisal

and regulation, while the amygdala is crucial for emotion processing, fear conditioning, and moral reasoning. One particular region of the prefrontal cortex, the orbitofrontal cortex/ventromedial prefrontal cortex (OFC), has been found to be important in the process of moral decision-making because of its role in emotional appraisal and regulation (Ochsner et al., 2002) and in recognizing the emotions of others (Shamay-Tsoory et al., 2005). Moll and colleagues (2002) found that the OFC is active in response to moral compared to non-moral stimuli, particularly when a social-emotional component is involved. In a behavioral study of patients with OFC lesions (Koenigs et al., 2007), patients showed typical patterns of responding when moral dilemmas did not feature competing considerations between aggregate welfare and harm to others. When moral dilemmas did feature these competing considerations, however, OFC lesion patients showed higher rates of utilitarian judgments (choosing to save the many over the few, even when the dilemma entailed an action as emotionally aversive as killing a child) than controls. The authors therefore assert that the OFC is vital in resolving moral dilemmas when social emotions are involved. These results illustrate the importance of the OFC in processes of emotional moral decision making, and how the functional deficits in the OFC, leading to reduced social emotions, might result in the immoral behavior shown by psychopaths. In a study using the Prisoner's Dilemma, for example, psychopathy level was negatively correlated with activity in the OFC when individuals chose to cooperate (Rilling et al., 2007) – cooperation in the context of a moral dilemma produced different levels of activity for high- and low-psychopathy individuals. This result suggests one function of the OFC is to activate the emotional states necessary for normal decision making. Cooperation, being the prepotent emotional response, was associated with normal OFC activity only for individuals low in psychopathy. Therefore, low OFC activity, seen in individuals with higher levels of psychopathy,

may be associated with cooperating for reasons of personal gain, rather than an emotional tendency toward cooperation with others.

The amygdala is part of the neural circuitry responsible for emotional responding (van Harmelen et al., 2013), fear conditioning, stimulus-reinforcement learning, and processing facial expressions such as fear (Davis and Whalen, 2001). Individuals with psychopathic traits have been found to have structural (Yang et al., 2009) and functional (Glenn, Raine and Schug, 2009; Harenski, Harenski, Shane and Kiehl, 2010) deficits in this region. Failure to effectively learn that immoral acts result in unpleasant consequences (stimulus-reinforcement learning) could explain why psychopathic individuals commit immoral acts regardless of the negative consequences. The functioning of the amygdala is important in a practical context because previous research has shown that adolescents' emotions in the context of moral decision-making (Should I steal this? Should I lie to my friend?) are predictive of their actual behavior in such situations (Malti and Krennauer, 2013). If abnormalities in amygdala functioning result in altered fear perception, emotional responding, or learning for adolescents, then they may act in antisocial or other undesirable ways.

Additional research using moral reasoning paradigms confirms this. Using a task similar to the current study, Harenski, Harenski, Shane and Kiehl (2010) found that psychopathic prisoners showed significantly less activation in the anterior temporal cortex and the OFC while viewing moral compared to nonmoral or neutral stimuli than non-psychopathic prisoners. In addition, the right amygdala was found to be an important modulator of moral violation severity ratings in non-psychopaths – increased activity in the right amygdala during picture viewing was associated with higher severity ratings. This effect was not present in the psychopathic offenders. These results suggest that psychopaths process moral violations differently than non-

psychopaths. Specifically, they suggest that while the amygdala is crucial in modulating the perception of the severity of a moral violation in non-psychopaths, it is not involved in this process for psychopaths. All together, the results from these studies of morality show that in adults, the amygdala and the OFC respond differently to moral reasoning tasks in psychopaths compared to non-psychopaths.

A small number of studies have used a moral reasoning task to extend these results to adolescents. Harenski, Harenski, and Kiehl (2014) saw different associations in adolescents than they had observed previously in adults; they did not find the same reduction in OFC activity as in adults, nor did they find a negative correlation between psychopathy scores and OFC activity in the moral compared to nonmoral condition. They did find that activity in the anterior temporal cortex was negatively associated with symptoms of conduct disorder, and also found that callous and unemotional traits mediated the relationship between amygdala activity and severity ratings of moral violation stimuli. Callous and unemotional traits, while similar to psychopathic traits, are a distinct construct and embody the interpersonal and affective symptoms demonstrated in the adult conceptualization of psychopathy (Frick & White, 2008). Like in adults, incarcerated adolescent offenders who endorsed low levels of callous and unemotional traits showed a positive relationship between severity ratings and amygdala activity, where adolescents with high levels of callous and unemotional traits showed a negative relationship between amygdala activity and severity ratings. Additionally, as in adults, activity in the anterior temporal cortex was negatively related to psychopathy in the moral > nonmoral condition.

Other previous studies using MRI to examine structural and functional characteristics of the brains of adolescents with callous-unemotional traits have found several kinds of deficits on related tasks. Viding and colleagues (2012) found that adolescents aged 10-16 with conduct

problems and high levels of callous-unemotional traits showed the lowest level of right amygdala activity in response to fearful faces, compared to typically developing adolescents and adolescents with conduct problems but low levels of callous-unemotional traits. These results indicate that adolescents with conduct problems and high levels of callous-unemotionality show deficits in affective processing compared to their peers with low callous-unemotionality. This, in turn, may influence their behavior in a negative way. Similar results were found when participants were directed to look either at either fearful faces or fearful eyes specifically (Sebastian et al., 2014).

Jones, Laurens, Herba, Barker and Viding (2009) found similar results in a sample of boys aged 10-12 on a task comparing reactivity to fearful versus neutral faces. Typically developing adolescents showed significant bilateral amygdala activation when processing fearful faces, while adolescents with high levels of callous-unemotional traits showed activation only in the left amygdala. These results again suggest that the affective processing deficits are accompanied by reduced right amygdala reactivity to others' fear.

In an implicit association task asking adolescents to categorize illegal and legal behaviors, Marsh and colleagues found that psychopathic traits were associated with reduced amygdala activity while categorizing legal tasks, as well as reduced functional connectivity between the amygdala and orbitofrontal cortex (Marsh et al., 2011). However, the psychopathy/non-psychopathy groups did not differ in amygdala activity when categorizing the illegal tasks. The authors suggest that this may be the result of participants utilizing semantic knowledge, not emotionally driven knowledge, in order to make categorizations of illegal tasks. Additionally, the groups did not show differing activation in any regions of the prefrontal cortex, even though they found reduced functional connectivity between the amygdala and the OFC.

Structural abnormalities have also been observed in imaging studies of children and adolescents with conduct problems. One study found that boys aged 12-17 with diagnoses of childhood-onset CD had a 6% reduction in total gray matter volume compared to healthy controls (Huebner et al., 2008), including significant reduction in the left amygdala, left hippocampus, and orbitofrontal cortex/ventromedial prefrontal cortex. Gray matter volumes in these limbic and prefrontal areas, including the left hippocampus and the bilateral amygdala, were negatively associated with CD symptomatology (*ibid.*). A second study of boys aged 10-12 did not find any differences in gray matter volume, but did see increased gray matter concentration in the posterior medial orbitofrontal cortex in boys with high levels of callous-unemotional traits (De Brito, 2009). And although structural deficits have been observed in the OFC in adolescents, it is still unclear whether and to what extent functional deficits might exist in this region.

The results from imaging studies of adult psychopaths and adolescents with high levels of psychopathy or callous-unemotionality show that there appear to be several deficits shared between these groups. The amygdala, first and foremost, has repeatedly been found to be deficient, and these deficiencies have been related to fear responses in adolescents, as well as moral reasoning, CD symptom severity, and categorizing legal, but not illegal, tasks. Second, structural deficits in the orbitofrontal cortex have been associated with CD symptom severity, and functional deficits have been associated with impaired moral reasoning in adult psychopathic samples.

Several studies have identified differences in brain structure and functioning in adolescents with conduct problems and psychopathic traits, yet the relationship between these differences and moral reasoning has not been widely explored. One study (Harenski, Harenski &

Kiehl, 2014) focusing specifically on the neural correlates of moral reasoning in adolescents examined brain functioning in a sample of adolescents incarcerated in a maximum-security correctional facility, and therefore may only be representative of youth at the extreme end of the spectrum in terms of psychopathic traits and behavioral problems. Additionally, the sample was nearing adulthood, with a mean age of approximately 17 years. The current study examines a sample of younger adolescents recruited from the community who show varying levels of psychopathic traits, with a mean age of approximately 13 years. It is the first step in elucidating the development of moral reasoning in the typically developing brain. Based on the literature reviewed above, the following hypotheses were tested:

1) Similar to adults, there will be a negative relationship between amygdala activity and psychopathic traits when viewing moral violation compared to nonmoral violation images in adolescents.

2) Similar to adults, there will be a negative relationship between OFC activity and psychopathic traits when viewing moral violation compared to nonmoral violation images in adolescents.

CHAPTER 2

METHOD

Participants

Participants were 16 adolescent males recruited from local middle and high schools and community buildings such as YMCAs and libraries, and from a radio ad targeting parents of adolescents with behavior problems. The sample ranged in age from 11 – 17 ($M = 13.69$, $SD = 1.448$). The racial/ethnic breakdown of the sample was 68.8% African-American, 18.8% Caucasian, and 12.5% Hispanic. One participant met criteria for ODD/CD; the remainder of the participants endorsed few symptoms of ODD or CD. Participants were excluded if they were nonfluent in English; had a history of psychiatric diagnoses such as autism spectrum disorder or bipolar disorder; were claustrophobic, or had any metal implants which could not be easily removed. Participants and their parents were informed of the nature of the study and of its potential risks and benefits. Each participant and each parent gave verbal and written consent/assent to participate in the study.

Stimuli and Design

A correlational design was used to examine the relationship between psychopathic traits and brain activity while adolescents viewed photographs of moral violations, negatively valenced images without moral content (nonmoral), or neutral scenes. An example of each type of image can be found in Figure 1. Images of the three types were matched according to number of faces shown in the image. Twenty-five of each type of image was shown in randomized order. Before entering the scanner, adolescents were asked if they knew what it means for something to be

morally right or wrong. They were told that they would see some pictures, and some of the pictures might go against the rules they have in their heads about what is right and what is wrong, and those are called moral violations. Participants were instructed to decide if a picture showed a moral violation, and to rate the severity of the violation with a rating of 1 indicating no violation was present, 2 or 3 indicating that some moral violation was present, and 4 indicating that a severe violation was present. Stimuli were presented using back-projection with an LCD projector onto a screen at the end of the patient table. Each image was presented for four seconds, followed by four seconds for participants to rate the severity of the violation. A fixation period ranging from zero to four seconds followed each rating period.

Measures

Descriptive statistics for the measures used in this study can be found in Table 1.

Youth Psychopathic Traits Inventory: The Youth Psychopathic Traits Inventory (YPI; Andershed et al., 2002) is a 50-item self-report measure based on an adult model of psychopathy. It was developed to identify youths who engage in frequent antisocial behavior into adulthood. This measure has 10 scales meant to measure core psychopathy traits: dishonest charm, grandiosity, lying, manipulation, remorselessness, callousness, unemotionality, impulsiveness, irresponsibility, and thrill seeking. Each item is answered on a 4-point Likert scale, where higher scores indicate more psychopathic traits. The total psychopathy score was used in analyses. This measure was chosen because it shows adequately strong relationships to other measures of youth psychopathy (Cauffman, Kimonis, Dmitrieva, and Monahan, 2009). It has shown internal consistency of approximately .90 in past studies (Campbell, Doucette and French, 2009). In the current study, the internal consistency was acceptable ($\alpha = .785$). The mean YPI Total Score of this sample fell between one previously reported in a non-selected community sample ($M =$

106.3, SD = 13.12; Campbell, Doucette & French, 2009) and one reported in a sample of incarcerated youths (M = 120.4, SD = 20.8; Dolan & Rennie, 2006). Total scores in the current study ranged from 79-128.

Kaufmann Brief Intelligence Test – 2: The Kaufman Brief Intelligence Test – 2 (KBIT-2; Kaufmann and Kaufmann, 2004) is a brief standardized intelligence test appropriate for individuals aged 4-90 years old. It has been well validated and has three subtests: verbal knowledge, riddles, and matrices. The KBIT-2 shows good internal reliability (scores between scales range from .86 to .92) and good test-retest reliability (range from .76 to .88). Scores on the KBIT-2 have been shown to correlate strongly (.77) with scores on the WISC-IV (Kaufmann and Kaufmann, 2004), the “gold-standard” IQ test for children. Full-scale IQ was used as a screening criteria; only adolescents with full-scale IQs of 70 or above were included in the study.

Schedule for Affective Disorders and Schizophrenia for School Aged Children: The Schedule for Affective Disorders and Schizophrenia for School Aged Children (K-SADS) is a well-standardized semi-structured clinical interview which is used to assess for symptoms of DSM-IV-TR Axis 1 disorders that may be diagnosed in children and adolescents, including ODD and CD. Symptom ratings are secured by interviewing the child and the parent, and creating summary ratings of each symptom. The K-SADS shows excellent inter-rater reliability, ranging from 93-100% agreement, and adequate test-retest reliability for ODD and CD diagnoses ($\kappa = .74 - .83$ for present and lifetime diagnoses). It shows good concurrent validity with other diagnostic interviews including the Diagnostic Interview for Children and Adolescents (DICA) and the Diagnostic Interview Schedule for Children (DISC). It shows improved test-retest reliability over the DISC for diagnoses of ODD (Kaufman et al., 1997). This measure was used to determine whether participants from the sample had a diagnosis of ODD or CD.

MRI Data Acquisition

MRI scans were conducted on a 3T Siemens Allegra short-bore scanner (Siemens Medical Inc., Erlangen, Germany) at the Civitan International Research Center of the University of Alabama at Birmingham. For structural imaging, initial high-resolution T1-weighted scans were acquired using a 160-slice three-dimensional (3D) MPRAGE volume scan with TR = 200 ms, TE = 3.34 ms, flip angle 7, FOV = 25.6 cm, 256 × 256 matrix size and 1-mm slice thickness. The stimuli were rear-projected onto a translucent plastic screen and participants viewed the screen through a mirror attached to the head coil. For functional imaging, data were acquired with a slice thickness of 3 mm and gap 0mm, with 32 slices, flip angle 90°, and a TR of 2.00s, FOV 192x192 and 64x64 matrix. Head movement was minimized by placing padding around the participant's head and instructing them not to move.

MRI Image Analysis

Image preprocessing was conducted using Statistical Parametric Mapping (SPM12b) software (Wellcome Department of Cognitive Neurology, London, UK) and involved image realignment, coregistration with anatomical image, segmentation, normalization into a standard stereotactic space using the Montreal Neurological Institute (MNI) template, and spatial smoothing with an 8 mm full width at half maximum Gaussian kernel to decrease spatial noise. Data from one participant was excluded because of movement greater than 5 mm, and data from another was excluded because of dental hardware resulting in signal dropout. See Table 2 for complete information on the number of volumes included in analyses for each participant.

A fixed effects model was used to analyze individual participant data. A separate general linear model (GLM) as implemented in SPM12b (Friston et al., 1995) was defined for each subject with the 4 second viewing period for moral, nonmoral, and neutral images entered as

regressors. Each regressor was convolved with a standardized model of the hemodynamic response. To identify regions that differed when viewing moral compared to nonmoral or neutral scenes, three within-subject contrasts were examined: (i) moral > nonmoral, (ii) moral > neutral, (iii) moral + nonmoral > neutral.

The second-level (group) data were analyzed using a random effects model. First, my goal was to explore which areas of activation differed between the conditions. Whole-brain analyses were performed by using the GLM as implemented in SPM12b, and significant voxels were identified using a paired t-statistic on a voxel-by-voxel basis. Statistical maps were superimposed on normalized T1-weighted images. Due to the exploratory nature of the pilot study, statistical significance of activation was determined and reported at an uncorrected voxel-wise threshold of $p < .001$ with an extent threshold of 50 continuous voxels. In cases where this yielded no suprathreshold clusters, a statistical threshold of $p < .005$ with an extent threshold of 10 continuous voxels was used (see Table 4, Table 5, and Table 6). This has previously been discussed as a statistical threshold that provides a desirable balance between Type I and Type II errors (Lieberman & Cunningham, 2009).

To identify regions in which activity during viewing moral violations compared to nonmoral or neutral images was correlated with psychopathy scores, I used SPM12b multiple regression analyses to examine activation in the same contrasts specified above as a function of YPI total scores. Age was also entered as a covariate of no interest. Statistical significance of activation was determined and reported at an uncorrected height threshold of $p < .005$ with an extent threshold of 10 voxels.

Anatomical regions of interest (ROIs) were isolated using WFU Pickatlas (Maldjian, Laurienti, Burdette & Kraft, 2003) and data extracted using MarsBaR (Brett, Anton, Valabregue & Poline, 2002). Mean activation was utilized in correlations with behavioral data.

CHAPTER 3

RESULTS

Paired sample t-tests indicated that participants rated moral violations as more severe than nonmoral violations ($t = 6.226, p < .001$) and moral violations as more severe than neutral images ($t = 5.262, p < .001$). Participants also rated nonmoral violations as more severe than neutral images ($t = 3.410, p = .004$). Correlations between behavioral variables can be found in Table 3. Psychopathy scores were not related to age, IQ, or severity ratings. Neither age nor IQ were related to moral or nonmoral severity ratings, but IQ was negatively related to neutral stimuli severity ratings, indicating that adolescents with lower full-scale IQs rated neutral stimuli as more severe violations.

Regions found to be active in the whole group analysis for all contrasts of interest can be found in Table 4. No suprathreshold clusters were observed at the statistical threshold of $p < .001$, so analysis was performed at threshold $p < .005$. The superior frontal gyrus, temporal pole, and supplementary motor areas showed greater activity while viewing moral violation stimuli than nonmoral violation stimuli. The middle frontal gyrus showed greater activity when viewing moral violation stimuli compared to neutral stimuli. There were no suprathreshold clusters when comparing nonmoral violation stimuli to neutral stimuli, nor were there any when comparing either moral or nonmoral stimuli to neutral stimuli.

Activity in several regions correlated significantly with YPI total scores (Table 5). Controlling for age, total psychopathy scores were positively associated with activity in several regions, including the anterior cingulate. Analyses were also performed at a lower statistical

threshold of $p < .005$, revealing positive associations between YPI total scores and activity in the orbitofrontal cortex, temporal pole, and the frontopolar cortex when participants viewed moral violation compared to nonmoral violation images. No negative associations were observed between psychopathy scores and brain activity.

When comparing viewing moral images to neutral images, YPI total scores were positively associated with activity in the temporal pole, superior temporal gyrus, anterior cingulate, inferior frontal gyrus, insula, and fusiform gyrus, controlling for age.

In order to test the positive relationship previously reported between amygdala activity and perceived severity of moral violations in non-psychopaths (Harenski, Harenski, Shane & Kiehl, 2010; Harenski, Harenski & Kiehl, 2014), mean data were extracted from the right and left amygdala independently, and correlated with severity rating data. Correlations were non-significant (right amygdala, $r = .198$, $p = .48$; left amygdala, $r = .332$, $p = .227$). In order to remove variability associated with psychopathy scores, regression analyses were conducted with YPI total score as a covariate of no interest. Severity rating did not account for a significant amount of variance in either right or left amygdala activity (all $p > .28$).

Additionally, a regression was performed with severity ratings of moral violations as the covariate of interest, in order to determine which regions were active when viewing moral violations that are perceived as more severe or wrong. No suprathreshold clusters were seen at the $p < .001$ statistical threshold so analyses were performed with a statistical threshold of $p < .005$. Positive relationships between activity in the moral compared to nonmoral condition and moral severity ratings were observed in the anterior cingulate, OFC, temporal pole, superior temporal gyrus, middle frontal gyrus, and parahippocampal gyrus.

Because psychopathy is not a unitary construct and has multiple dimensions, exploratory analyses were performed separately on the Callousness and Impulsivity subscales of the YPI. Callousness was positively correlated with activity in the precuneus, angular gyrus, and the posterior cingulate cortex during the moral > nonmoral condition. Impulsivity was positively correlated with activity in the ACC, the orbitofrontal cortex, the insula, and the superior temporal gyrus during the moral > nonmoral condition.

CHAPTER 4

DISCUSSION

This pilot study examined brain activity in response to viewing moral versus nonmoral or neutral stimuli in a community sample of adolescents with varying levels of psychopathic traits. In the group as a whole, the superior temporal gyrus and temporal pole, areas previously implicated in moral processing, were more active when viewing moral compared to nonmoral stimuli. Although I hypothesized that psychopathy would be associated with reductions in brain functioning during the task, a number of areas showed positive relationships with psychopathy when viewing moral compared to nonmoral stimuli, including the orbitofrontal cortex, temporal pole, anterior cingulate, and dorsolateral prefrontal cortex. These results suggest that the patterns of brain functioning observed in adults with psychopathic traits may be quite different from those of adolescents.

Main Effects

Areas that showed a main effect of condition (moral > nonmoral) included the superior temporal gyrus and the temporal pole. In adults, the superior temporal sulcus (adjacent to the superior temporal gyrus) has been implicated in distinguishing moral violations from other unpleasant stimuli in an adult sample (Moll et al., 2002; Harenski, Harenski, Shane & Kiehl, 2010). This area has also been implicated in distinguishing personal moral dilemmas from impersonal ones (Greene, Sommerville, Nystrom, Darley, & Cohen, 2001), as illustrated by the classic trolley dilemmas. Increased activity in the temporal poles has also previously been associated with viewing morally salient stimuli – specifically, in determining whether a harmful

action is intentional or not (Decety, Michalska & Kinzler, 2012). The current results reinforce the idea that the superior temporal gyrus and temporal poles are key in distinguishing whether an unpleasant image is morally wrong or not, and are in line with previous research findings in adults.

No activity was observed in the amygdala when distinguishing moral from nonmoral or neutral images. This is in line with the results of a previous study including adolescents recruited from the community, which found that the amygdala was not active when comparing viewing moral images to viewing nonmoral images (Harenski, Harenski, Shane & Kiehl, 2012).

However, in a sample of incarcerated male adolescents, Harenski and colleagues (2014) found increased left amygdala activity when viewing moral compared to nonmoral stimuli.

One potential reason for the differences in results among these studies is the sample makeup.

Two studies (Harenski, Harenski, Shane & Kiehl, 2012), including the current study, recruited participants from the community and included small sample sizes. The third study (Harenski, Harenski, & Kiehl, 2014) recruited from a maximum security detention facility and included a large sample size. The sample size in the current study, as well as in the previous study using a community sample (Harenski, Harenski, Shane & Kiehl, 2012), may be too small to see differences in amygdala activity during the moral compared to nonmoral condition. Amygdala activation in response to moral compared to nonmoral stimuli may have a relatively small effect size. However, similar studies of youth with psychopathic traits have found activity differences in the amygdala with sample sizes equal to or smaller than the ones reported in this and the above studies (Marsh et al., 2011; Jones, Laurens, Herba, Barker & Viding, 2009).

Another potential explanation is that the stimuli in the studies that found no amygdala activity were not emotionally salient enough to the current sample. The amygdala is crucially

involved in emotion processing, and amygdala lesions produce a general reduction in emotional responses (Aggleton, 1992). The amygdala also has a crucial role in detecting and responding to threatening situations (Morris et al., 1998). If the amygdala is not responding to the stimuli presented in the current study, which include but are not limited to images of an individual holding a knife to someone's neck, an individual in a car surrounded by four men bearing weapons, and an individual preparing to punch another person, then perhaps the sample failed to find these stimuli emotionally arousing or fear-inducing.

Relationships with Psychopathy

Contrary to Hypothesis 1, amygdala activity when viewing moral compared to nonmoral stimuli did not appear to have a relationship to psychopathy level. See Figure 2 and Figure 3 for plots of amygdala activity in relation to YPI total score. This may be due to an overall low level of amygdala activity; if, as previously stated, the sample did not find the stimuli to be fear-provoking, then amygdala activity may be low overall and any correlation therefore not apparent. Correlations may also not be apparent if the effect size of amygdala activity in response to moral stimuli is small.

Alternately, any correlations may not be apparent because they vary depending on the level of psychopathy. Harenski and colleagues (2014) found that in high-callous and unemotional adolescents, the correlation between psychopathy and amygdala activity was negative, while in low-callous and unemotional adolescents the correlation was positive. Due to the small sample size of the current study, the sample was not divided into high- and low-psychopathy groups. However, if correlations are different at high and low ends of the spectrum of psychopathic traits, then in the whole sample an overall correlation may not be apparent.

In contrast to hypothesis 2, activity in the OFC while viewing moral compared to nonmoral images was *positively* correlated with psychopathy scores (Fig. 4c). Given that psychopathy has repeatedly been associated with impaired function in the OFC (Yang & Raine, 2009; Blair et al., 2006), this result is unexpected. One potential explanation is that the age of the participants influences relationships, as previous studies have shown that age is positively related to vmPFC/OFC activity while viewing moral stimuli (Decety, Michalska & Kinzler, 2012). Based on such findings, there may be less variability in OFC functioning in youth. If the majority of adolescent participants show low levels of activity in the OFC, it may be more difficult to detect any relationships with psychopathic traits.

In the exploratory whole brain analyses, when comparing both moral to nonmoral images, and moral to neutral images, we also found that individuals scoring higher in psychopathy demonstrated more activity in the anterior cingulate (Fig. 4a). The ACC is involved in error detection and performance monitoring, including evaluating competing responses (Carter et al., 1998; in this case, competing responses would be whether or not the image viewed contains a moral violation). This is in contrast to previous results in adult samples, which have shown negative relationships between psychopathy scores and activity in the cingulate cortex when viewing negative images (Müller et al., 2003) and also a relationship between structural abnormalities of the cingulate and emotional detachment in psychopathy (Sethi et al., 2014), though other studies have found no evidence of structural deficits in the anterior cingulate in individuals scoring higher in psychopathy (Glenn, Yang, Raine & Colletti, 2010). In a meta-analysis, Yang and Raine (2009) found that adult antisocial populations showed a significant decrease in functioning in the ACC, but this did not appear to be moderated by PCL-R score. And another study found that ACC activity in adolescents was negatively correlated with

psychopathic traits when viewing images of painful injuries to others and the self (Marsh et al., 2013).

As can be seen, some previous studies have found negative relationships between psychopathy and activity in the cingulate cortex, while others have found that activity in the ACC has no relationship to psychopathy. One potential confound is the relationship between ACC activity and perceived severity of the moral violations being viewed. Decety and colleagues found that activity in the anterior cingulate cortex (ACC) was positively correlated with how “wrong” participants found a moral action to be (Decety, Michalska & Kinzler, 2012). In order to determine whether this may be the case, a regression analysis was conducted with average severity rating for the moral violation condition as a covariate of interest.

Activity in the anterior cingulate cortex was, in fact, positively related to severity ratings of moral violations. However, in the current sample, moral severity ratings were not correlated with total psychopathy score, suggesting that severity ratings do not mediate the relationship between psychopathy and ACC activity. Harenski and colleagues (2014) did not find any correlations between severity ratings and ACC activity, and the adult literature is mixed. These findings suggest that the ACC may function differently in adolescents who have higher levels of psychopathic traits. Longitudinal studies may help to determine whether the increases in functioning in adolescents develop into reductions in functioning in adulthood.

The age of the sample might be key to understanding the positive relationship between ACC activity and level of psychopathic traits. With a mean age of approximately 13 years, the sample in the current study is not yet mature. Previous studies have shown that adolescents show higher levels of activity in the ACC compared to adults (Eshel, Nelson, Blair, Pine & Ernst, 2007) during the process of decision-making, thus indicating that the ACC continues to develop

into adulthood. Because of the ACC's involvement in evaluating competing responses, this suggests that adolescents who show more psychopathic traits may have a more difficult time determining whether something is a moral violation or not. By adulthood, they may be desensitized to such stimuli. Therefore, as the sample ages, the relationship between ACC activity and moral processing may change.

We also found a positive correlation between psychopathy scores and activity in the lateral frontopolar cortex (lFPC), or frontal pole (Fig. 4b). Previous research has found that the FPC is consistently engaged when community subjects make judgments about moral stimuli (Moll, Eslinger & de Oliveira-Souza, 2001), and Harenski and colleagues (Harenski, Harenski and Kiehl, 2014) also found a main effect in the medial frontal gyrus, part of the FPC, when participants viewed moral compared to nonmoral stimuli. Such results show that the FPC is part of the network of brain regions that distinguish moral from nonmoral stimuli. Other studies have shown a connection between the FPC and psychopathy; de Oliveira-Souza and colleagues (de Oliveira-Souza et al., 2008) found a significant link between psychopathy and gray matter reduction in the FPC. Like the OFC, the FPC plays a crucial role in decision making (Koechlin & Hyafil, 2007). However, the FPC seems to be uniquely attuned to ambiguous scenarios; for example, patients with FPC lesions show no deficits on standard neuropsychological tests of prefrontal function, but do show impairment in making decisions in open-ended and poorly-defined situations (Burgess, Dumontheil & Gilbert, 2007).

While a number of the stimuli presented to participants in the current study required little context to understand (a knife being held to someone's neck, for example), other stimuli may be more ambiguous (such as a hand reaching into a purse). Without context, participants with higher levels of psychopathic traits may have more difficulty determining the context and deciding

whether the image represented a moral violation or not. If this is the case, it may explain why participants with higher levels of psychopathic traits showed greater activation in the FPC during moral compared to nonmoral trials.

Where the current results differ from previous results, one possible explanation is simply that the adolescent brain processes moral stimuli differently than does the adult brain. Possibly, the deficits associated with psychopathic traits do not emerge until later adolescence or early adulthood. Decety and colleagues found that areas involved in processing moral stimuli develop with age, including the amygdala, insula, and vmPFC (Decety, Michalska and Kinzler, 2012). Specifically, amygdala and insula activity were negatively related to age, while vmPFC activity were positively related to age. However, participants of all ages (ranging 4-37 years old) rated violations equally “wrong.” This indicates that children, adults and adolescents are able to distinguish behaviorally in similar ways between morally “wrong” actions and morally permissible ones; however, the brains of children, adolescents, and adults process such stimuli differently. Although we can see that the adolescents in the current sample can distinguish between a moral violation and a negative but nonmoral image (rating moral violations as more severe) in their behavioral ratings, the brain regions involved in making these distinctions are still developing. The patterns of activity may continue to change as the sample ages. Specifically, as participants age, baseline activity in the OFC may increase, which could reveal a negative rather than positive relationship with psychopathy. Similar results may occur with amygdala activity.

CHAPTER 5

IMPLICATIONS

The implications of the current study, as a pilot, are limited. However, these preliminary results suggest that the functional deficits present in adults with psychopathic traits may not be present early in adolescence. This suggests that interventions implemented at this time, for adolescents who show antisocial behaviors, have the potential to change behavior before the brain deficits develop, and thus may be more effective than interventions later in life. Therefore, we can say that efforts should be focused on preventing antisocial and criminal behavior in middle- and high-school-aged children who are exhibiting psychopathic traits. Interventions at even earlier ages may be even more effective in heading off maladaptive changes in the brain.

This study is also an initial step in a longitudinal MRI study, with the aim of describing how the neural correlates of psychopathic traits in adolescents might change with age. These future data may reveal whether brain deficits associated with psychopathic traits do indeed develop later in adolescence, in the absence of intervention. One main focus of future study will be to see whether the increased activity currently observed in adolescents with higher psychopathic traits persists as they age.

CHAPTER 6

LIMITATIONS

One of the main limitations of this study is the relatively small sample size. Effects may be less robust because of the small sample. However, we view this as an initial step in understanding the development of brain abnormalities associated with psychopathy. Another limitation is the correlational nature of the study. A between-groups design, sampling from individuals who have disruptive behavior disorders or histories of delinquency, may have provided a sample more easily compared to the samples studied in the adult literature. Due to difficulties in recruiting at-risk or behaviorally challenged adolescents, the current sample represents a limited range of antisocial traits and behaviors. Scores on our psychopathy measure therefore fall within a restricted range. It is likely that a sample which includes a wider range of psychopathy scores would yield slightly different results. However, because the current sample showed a mean YPI score higher than in previous unselected community samples (Campbell, Doucette & French, 2009), the sample is not entirely unrepresentative of an antisocial sample.

Additionally, participant movement within the scanner limited the amount of useable data from each participant. In future scans with this cohort, more explicit instructions will be provided to reduce movement within the scanner, so as to maximize useable data.

FIGURE 1. Images of moral violations (a) involved physical assault, stealing, cheating, or drug use. Nonmoral images (b) were designed to elicit or depict negative emotions, such as verbal arguments, or pictures of cuts, injections, or injuries, but did not contain moral content. Neutral images (c) were not emotion-provoking.



FIGURE 2. YPI total score is not correlated with mean right amygdala activity during moral > nonmoral conditions.

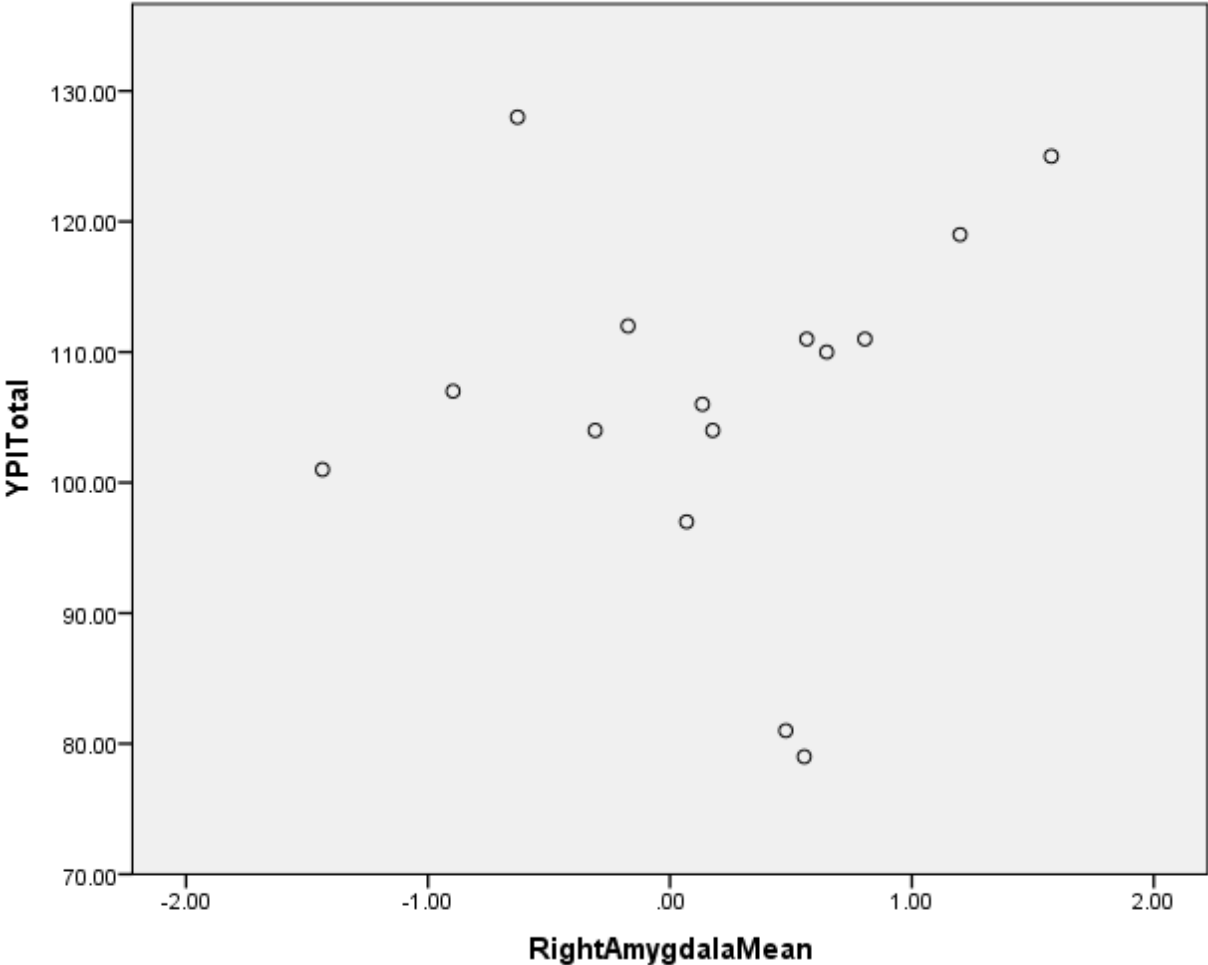


FIGURE 3. YPI total score is not correlated with mean left amygdala activity during moral > nonmoral conditions.

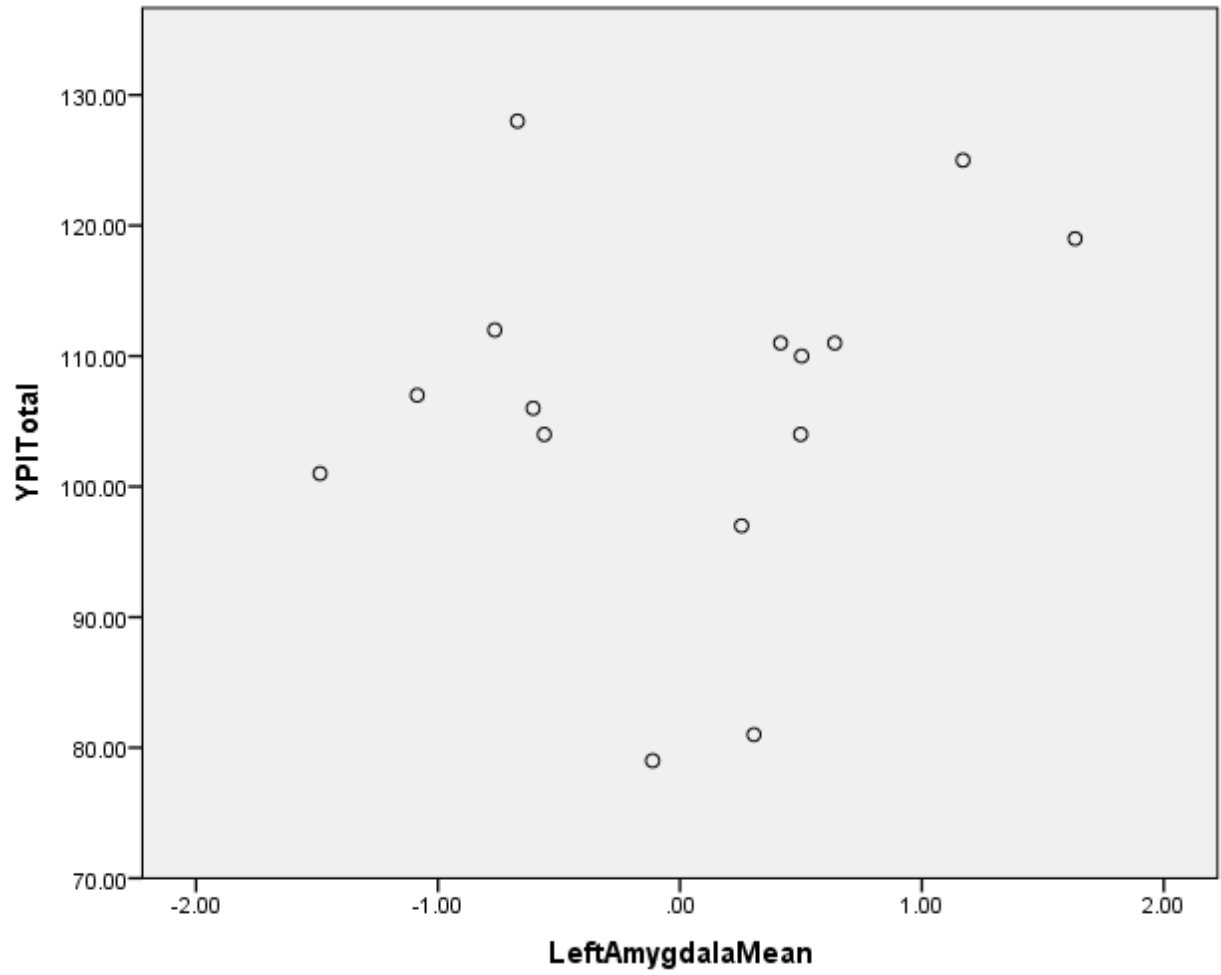
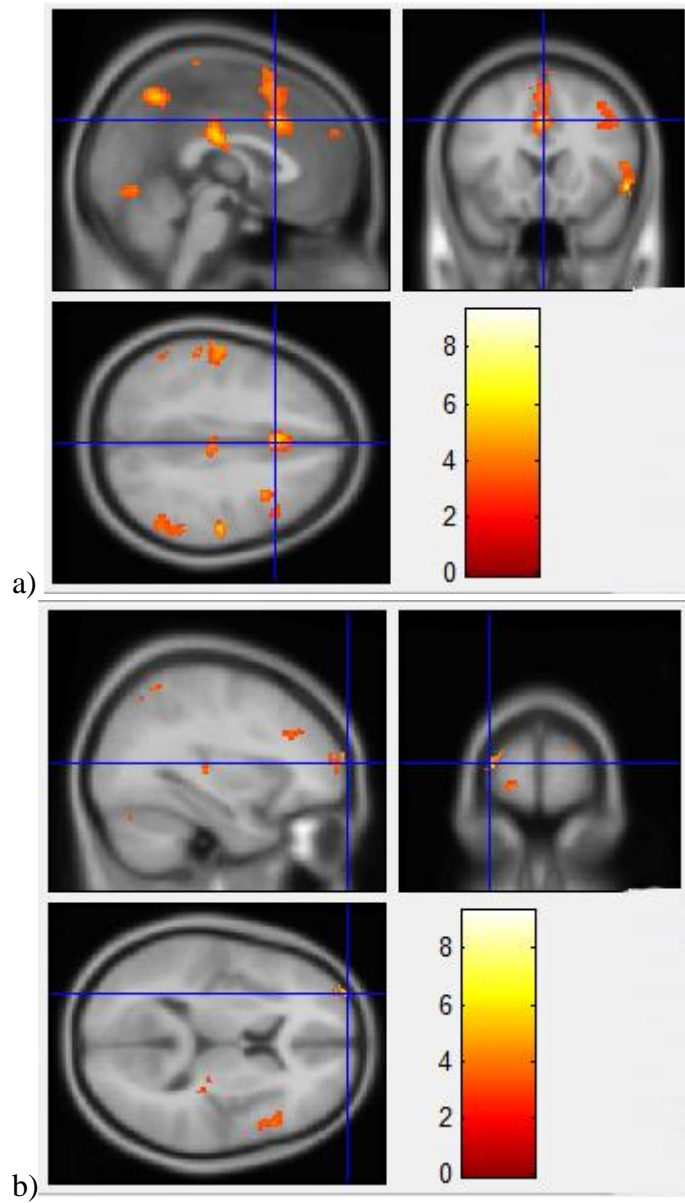


FIGURE 4. YPI Total score is positively associated with activity in the a) anterior cingulate cortex; b) frontal pole; c) orbitofrontal cortex; and d) temporal pole during moral > nonmoral conditions.



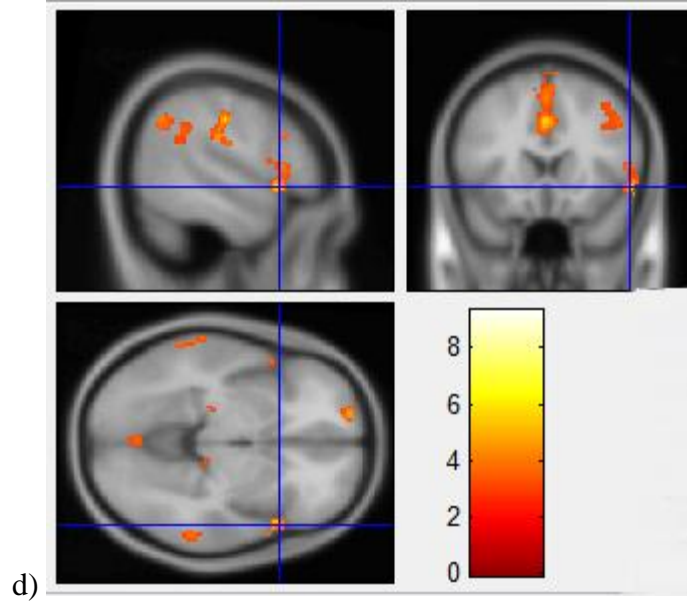
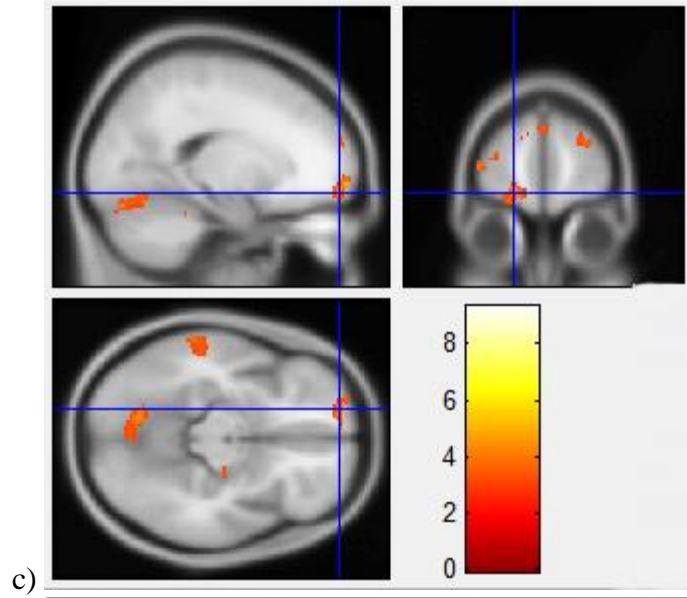


Table 1. Descriptive statistics

Variable	Mean (SD)
Age	13.69 (1.448)
YPI Total	106.3125 (13.1236)
Dishonest Charm	11.125 (2.872)
Grandiosity	10.563 (2.732)
Lying	9.813 (2.482)
Manipulation	9.688 (3.092)
Remorselessness	9.563 (1.999)
Unemotionality	11.563 (2.632)
Callousness	9.313 (2.983)
Thrill Seeking	13.875 (2.802)
Impulsiveness	12.188 (2.287)
Irresponsibility	8.625 (2.419)
K-BIT 2	
Full-Scale IQ	98.375 (11.735)
Verbal IQ	98.688 (11.528)
Nonverbal IQ	98.000 (11.255)

Table 2. Volumes included for each participant

Participant Number	Useable TRs	Total # of Volumes
102 [^]	41-147; 149-227	185
103	1-240	240
105	0; excess movement	Data not used
106	37-127	90
107	76-265	190
108	0; signal dropout	Data not used
109	1-97; 108-183	172
110*	1-405	405
111*	1-405	405
112	1-166; 170-382	379
113	1-107	107
114*	1-386	386
115*	1-405	405
117	13-382	370
119*	1-390	390
120*	1-381	381
122*	1-379	379
123	1-284	284

*Indicates full scan data was used for the participant; no volumes missing

[^]Indicates data were not used in analyses specific to the amygdala, due to missing amygdala data

Table 3. Correlations in behavioral data

	Age	YPI Total	Avg. Moral Severity Rating	Avg. Nomoral Severity Rating	Avg. Neutral Severity Rating	KBIT Full- Scale IQ	KBIT Verbal IQ	KBIT Nonverbal IQ
Age	1							
YPI Total	-.061	1						
Avg. Moral Severity Rating	-.019	.151	1					
Avg. Nonmoral Severity Rating	-.306	.136	.161	1				
Avg. Neutral Severity Rating	.130	-.340	-.711**	.231	1			
KBIT Full- Scale IQ	-.350	-.072	.260	-.356	-.582*	1		
KBIT Verbal IQ	-.366	-.183	.048	-.346	-.449	.884**	1	
KBIT Nonverbal IQ	-.254	.050	.416	-.276	-.582*	.879**	.555*	1

*p < .05

**p < .01

Table 4. Brain regions active at the group level in contrasts of interest.

Anatomical region	MNI coordinates	Cluster size (k)
Moral > nonmoral*		
Supplementary motor area	10, 14, 66 12, 22, 56 22, 4, 58	96
Superior temporal gyrus	-30, 12, 24	20
Temporal pole	34, 22, -28	20
Moral > neutral*		
Middle frontal gyrus	30, 50, 32	17
Nonmoral > neutral*		
No suprathreshold clusters		
Moral/nonmoral > neutral*		
No suprathreshold clusters		
Moral > fixation*		
Supplementary motor area	-6, 2, 64	36
Precentral gyrus	40, -20, 52	15
Condition > fixation*		
Supplementary motor area	-14, -10, 66	15

**Analysis performed with statistical threshold $p < .005$ and an extent threshold of 10 continuous voxels.*

Table 5. Brain regions significantly positively correlated with YPI total scores in contrasts of interest.

Anatomical region	MNI coordinates	Cluster size (k)
Moral > nonmoral		
Corpus callosum	4, -16, 24 5, -24, 38	154
Anterior cingulate cortex	-2, 20, 36	100
Precuneus	-2, -60, 52 6, -66, 56	84
Precentral gyrus	-42, 6, 46	64
Postcentral gyrus	65, -18, 38 54, -24, 26	60
Cerebellum/Declive	40, -66, -24 32, -74, -22	58
Postcentral gyrus	-58, -18, 38	50
Temporal pole*	54, 18, -6	260
Inferior frontal gyrus*	52, 20, 8	
Rolandic operculum*	62, 8, 4	
Superior frontal gyrus/OFC*	-18, 64, -6	153
Frontal pole*	-32, 66, 10 -40, 50, 12 -32, 58, 12	79

**Analysis performed with statistical threshold $p < .005$ and an extent threshold of 10 continuous voxels.*

Moral > neutral		
Cerebellum	-6, -36, -14 22, -36, -32 16, -40, -26	262
Postcentral gyrus	-56, -18, 36 -62, -14, 32	178
Supramarginal gyrus	-64, -22, 36	
Anterior cingulate cortex	8, 18, 36 -6, 24, 32 -6, 16, 34	174
Inferior frontal gyrus	-42, 24, 6	119
Insula	-34, 22, 8 -30, 18, 2	
Temporal pole	54, 12, -6	97
Superior temporal gyrus	62, 10, -4	
Lingual gyrus	6, -72, -2	85

Parahippocampal gyrus	-24, -24, -20 -20, -36, -22	69
Corpus callosum	4, -20, 22	59
Inferior frontal gyrus	44, 20, 8	56
Supplemental motor area	0, 6, 44 2, 2, 52	53

Table 6. Brain regions significantly positively correlated with severity ratings in the moral > nonmoral condition (statistical threshold $p < .005$, extent threshold 10 voxels)

Anatomical region	MNI coordinates	Cluster size (k)
Cuneus	-22, -72, 4 -14, -84, 2	518
Anterior cingulate	-12, 24, -6 -8, 36, -8	244
Cuneus	16, -80, 18 -6, -74, 22 2, -80, 28	199
Middle temporal gyrus	-50, -12, -16 -45, 10, -10 -50, -4, -10	177
Dorsolateral prefrontal cortex	-22, 52, 14	100
Precuneus	28, -48, 4	67
Inferior occipital gyrus	32, -92, -14 30, -100, -6 38, -94, 2	63
L. Calcarine	-2, -102, 2 -2, -98, 18	62
Cerebellum	-46, -48, -30	54
Superior temporal gyrus	-46, -14, 0	52
Orbitofrontal cortex	40, 64, -4 34, 64, -14 44, 58, -12	45
Superior parietal lobule	-20, -50, 60 -14, -56, 64	44
Parahippocampal gyrus	-20, -2, -34	
Inferior temporal gyrus	64, -48, -12 68, -44, -5	41
Temporal pole	-46, 20, -30	24
Superior temporal gyrus	-68, -40, 12	14

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APPENDIX: IRB

Office for Research
Institutional Review Board for the
Protection of Human Subjects

February 13, 2014



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College of Arts & Sciences
The University of Alabama

Re: IRB Protocol # 14-003-ME "Brain and Behavior Development Study"

Dr. Glenn:

The University of Alabama Medical IRB has granted initial approval of the above application for a one-year period. Please be advised that your protocol will expire one year from the date of approval, 2/13/14.

If your research will continue beyond this date, complete the Renewal Application Form. If you need to modify the study, please submit the Modification of An Approved Protocol Form. Changes in this study cannot be initiated without IRB approval, except when necessary to eliminate apparent immediate hazards to participants. When the study closes, please complete the Request for Study Closure Form.

Should you need to submit any further correspondence regarding this proposal, please include the assigned IRB application number. Please use reproductions of the IRB approved stamped consent/assent forms to obtain consent from your participants.

Good luck with your research.

Sincerely,



John C. Higginbotham, Ph.D., MPH
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