Title
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Journal
Psychiatry Research, 231(3)

ISSN
0165-1781

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Publication Date
2015-03-01

DOI
10.1016/j.pscychresns.2015.01.017

Peer reviewed

HHS Public Access

Author manuscript

Psychiatry Res. Author manuscript; available in PMC 2016 May 18.

Published in final edited form as:

Psychiatry Res. 2015 March 30; 231(3): 333–340. doi:10.1016/j.pscychresns.2015.01.017.

Frontal and striatal alterations associated with psychopathic traits in adolescents

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Abstract

Neuroimaging research has demonstrated a range of structural deficits in adults with psychopathy, but little is known about structural correlates of psychopathic tendencies in adolescents. Here we examined structural magnetic resonance imaging (sMRI) data obtained from 14-year-old adolescents (n=108) using tensor-based morphometry (TBM) to isolate global and localized differences in brain tissue volumes associated with psychopathic traits in this otherwise healthy developmental population. We found that greater levels of psychopathic traits were correlated with increased brain tissue volumes in the left putamen, left ansa peduncularis, right superiomedial prefrontal cortex, left inferior frontal cortex, right orbitofrontal cortex, and right medial temporal regions and reduced brain tissues volumes in the right middle frontal cortex, left superior parietal lobule, and left inferior parietal lobule. Post hoc analyses of parcellated regional volumes also showed putamen enlargements to correlate with increased psychopathic traits. Consistent with earlier studies, findings suggest poor decision-making and emotional dysregulation associated with psychopathy may be due, in part, to structural anomalies in frontal and temporal regions whereas striatal structural variations may contribute to sensation-seeking and reward-driven behavior in psychopathic individuals. Future studies will help clarify how disturbances in brain maturational

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Financial disclosures

All authors report no potential conflicts of interest, financial or otherwise.

processes might lead to the developmental trajectory from psychopathic tendencies in adolescents to adult psychopathy.

Keywords

Developmental; MRI; Tensor-based morphometry; Putamen

1. Introduction

Psychopathy is a clinical condition defined by a combination of persistent antisocial behavior, marked sensation-seeking, impulsivity, shallow emotion, blunted empathy, and punishment insensitivity that emerges early in life (Hare, 2003). Although a diagnostic level of psychopathy is present in only 1–2% of the general population, it is widely present on a spectrum in otherwise healthy populations. Research on the neural bases of psychopathy has focused largely on the profound emotional deficits and antisocial behavior observed in psychopathic adults, emphasizing the possible contributions of a disturbed frontolimbic circuitry (Gao et al., 2009; Yang and Raine, 2009). To date, findings from several structural imaging studies have supported this argument by showing frontolimbic deficits in adults with high psychopathy scores, with the most robust findings being reduced volumes in frontal and temporal regions including the amygdala (de Oliveira-Souza et al., 2008; Muller et al., 2008; Yang et al., 2009a; Yang et al., 2009b; Ermer et al., 2012; Bertsch et al., 2013). However, conflicting findings have also been presented, particularly for the hippocampus, insula, and the anterior cingulate cortex for psychopathic adults (Laakso et al., 2001; Boccardi et al., 2010; Glenn et al., 2010b; Cope et al., 2012).

More recently, initial evidence has begun to emerge suggesting that deficits in regions densely connected with the frontolimbic circuitry, particularly the striatum, may also contribute to traits associated with psychopathy (Glenn and Yang, 2012; Blair, 2013). The striatum is comprised of the caudate nucleus and the putamen and has been linked to traits such as reward-seeking, stimulus-reinforcement learning, and impulsivity (Barros-Loscertales et al., 2006; Cohen et al., 2009). Studies have linked psychopathy to increased sensitivity to reward and decreased sensitivity to punishment, suggesting potential abnormalities in the striatal regions that contribute to overly focus on the prospect of reward despite signals of potential later punishment (Newman and Kosson, 1986; van Honk and Schutter, 2006; Glenn et al., 2009). To date, *increased* volumes have been found in the striatal in adults with psychopathy (Glenn et al., 2009) and antisocial personality disorder (Barkataki et al., 2006), findings that are in line with the functional imaging findings of abnormal activation or connectivity with the striatum (Osumi et al., 2012; Carre et al., 2013). Therefore, it may be suggested that an overactive reward system (e.g. striatum) may further compromise the weakened regulation system (e.g., prefrontal cortex), leading to heightened psychopathic tendencies.

Despite the accumulating knowledge in the neural basis of psychopathy, studies of psychopathic traits have focused mainly on adults and the examination of psychopathic traits in children and adolescence remains scarce. By revealing structural abnormalities in regions

overlap with those found impaired in adults with psychopathy, findings from studies of conduct disorder (some with comorbid callus-unemotional traits) seem to suggest a neurodevelopmental basis to psychopathy (Blair, 2006a; Gao et al., 2009). For example, reduced volumes in the amygdala, dorsolateral prefrontal cortex and orbitofrontal cortex (Kruesi et al., 2004; Sterzer et al., 2007; Boes et al., 2008; Huebner et al., 2008; Dalwani et al., 2011; Fairchild et al., 2011; Hyatt et al., 2012) have been reported in adolescents with conduct problems. In addition, callous-unemotional traits were found to correlate positively with increased volumes in the orbitofrontal cortex (De Brito et al., 2009; Fairchild et al., 2012), suggesting potential delays in brain maturation in association with certain psychopathic traits. In one study, callous-unemotional traits were also found to correlate negatively with reduced volume in the striatum (Fairchild et al., 2012), but the effect did not survive when controlling for conduct disorder symptoms.

Although findings to date have provided initial evidence suggesting abnormal brain structures associated with psychopathic traits in children and adolescents, there are notable variations among findings. One potential contribution to discrepancy among findings may be that most existing studies have been conducted on relatively small, heterogeneous samples. The aggregation of participants with a wide age range may be particularly alarming because it has been demonstrated that gray matter volumes increase in early childhood and decline in adolescence, but white matter volumes tend to increase well into adulthood (Sowell et al., 2003). The pattern of age-related changes in gray and white matter has also been shown to vary across brain regions during brain maturation (Sowell, 2002). The involvement of substance use in older participants, often co-occurring with antisocial behavior and psychopathic traits, may also complicate the matter by introducing substance-related brain changes. Furthermore, the majority of the findings are from samples with comorbid psychiatric disorders (e.g. conduct disorders, attention deficits hyperactivity disorder), making it difficult to determine to what extent previous findings can be applied to psychopathic traits in the general population.

To address these limitations in the literature, the present study included a community sample of homogeneously aged, healthy adolescents (all aged 14 years old at the time of the scanning) to examine the relationship between psychopathic tendencies and regional brain tissue volumes. We used a recently developed method of tensor-based morphometry (TBM), which allows the illustration of statistical effects on regional volumes of gray matter, white matter, and cerebrospinal fluid (CSF) across the entire brain. Specifically, global and regional differences in brain tissue volume are estimated by applying localized deformations to adjust the anatomy of each individual to match a sample-specific template. By correlating these deformation fields with psychopathic traits across the sample, very subtle morphological changes associated with psychopathic traits in adolescents can be identified, with high accuracy and sensitivity. To date, TBM has been validated and applied to study several disorders (Leow et al., 2009; Yang et al., 2011); however, it has yet to be applied to explore patterns of brain tissue alterations associated with psychopathic traits in adolescents. Based on prior reports, we predicted that psychopathic tendencies would correlate with reduced brain tissue volumes in the fronto-limbic circuitry and increased brain tissue volumes in the striatal regions in this adolescent sample.

2. Methods

2.1. Subjects

The 108 adolescent twins (54 males and 54 females, age 14 years) included in this study were drawn from participants in the University of Southern California (USC) Risk Factors for Antisocial Behavior Twin Study (Baker et al., 2006; Baker et al., 2013), and comprised 27 monozygotic twin pairs (16 male and 11 female twin pairs) and 27 dizygotic twin pairs (5 male, 10 female, and 12 opposite-sex twin pairs). In brief, the USC Twin Study is a longitudinal study assessing the development of antisocial behaviors from childhood to young adulthood, which began in 2000 and now is approaching the end of fifth wave data collection. The adolescents and their families were recruited from Los Angeles County through advertisements, schools, and mothers of twins clubs. The sample is representative of the ethnic and socioeconomic diversity of the Great Los Angeles areas. The present study used data obtained from the third wave of assessment, when the twins were 14 years old, as this was the time point when magnetic resonance imaging (MRI) scans were collected. Participants were excluded if they had a history of significant head injury, major neurological, psychiatric illness, substance abuse, or contraindication to scanning (Yang et al., 2012; Baker et al., 2013). The adolescents and their primary caregivers participated in 6–8 h of laboratory assessment at USC including a 1-h scan. Assessment of psychopathic traits was provided by caregivers, who were predominantly biological mothers (n=50). The remaining were biological father (n=1), grandmother (n=1), foster mother (n=1) and adoptive mother (n=1). Each child's ethnicity was determined by the ethnicity of his/her biological mother and father, as reported by the primary caregiver. The ethnicity breakdown of the sample was as follows: 36.7% Hispanic, 27.4% Caucasian, 14% Black, 4.4% Asian, 0.16% Native American, and 17.3% mixed. Both caregivers and children gave written informed consent/assent prior to the study. The study was approved by the CHLA/USC Institutional Review Boards.

2.2. Behavioral measurements

Psychopathic traits were measured using a slightly extended version of the Child Psychopathy Scale (CPS) – Revised Extended (Lynam, 1997). The CPS is a well-validated instrument for measuring psychopathic traits in children and adolescents and is composed of 14 subscales including glibness, untruthfulness, lack of guilt, callousness, impulsiveness, boredom susceptibility, manipulation, poverty of affect, parasitic lifestyle, behavioral dyscontrol, lack of planning, unreliability, failure to accept responsibility, and grandiosity. The CPS was administered to the caregivers of the adolescents in an interview form. Scores for each item were added to create a total CPS score for each individual. The internal reliabilities for the composite score have been established in previous reports (Baker et al., 2007; Bezdjian et al., 2011), and the frequency of the total CPS scores of this sample is reported in Fig. S1 (see Supplementary Material). To summarize, the parent-report CPS total scores of our sample ranged from 2 to 33 (mean = 12.18, SD = 7.09), with males (mean = 13.96, SD = 7.92, range: 3–33) scoring higher than females (mean = 10.39, SD = 5.68, range: 2–31) (p = 0.008). As a complementary analysis, we also categorized the participants into High-CPS (with CPS total scores in the top 20%) and Low-CPS (with CPS total scores in the low 20%) group, and the TBM results were included in the Supplementary Material

(Fig. S2). For a subset of the sample ($n = 62$), intelligence quotient (IQ) was obtained using Wechsler Intelligence Scale for Children (Wechsler, 2004). For the subsample, the intelligence mean was 100.1 for Full-Scale IQ (range: 77–129), 98.44 for Performance IQ (range 67–124) and 102.15 for Verbal IQ (range: 65–128). Further analysis showed that parent-report CPS total scores did not correlate with Full-Scale, Performance, or Verbal IQ scores (all $p > 0.3$). Post hoc analyses showed that TBM results were unchanged when controlling for IQ, therefore only results controlling for whole brain volume, sex, and subject relatedness were included in this report.

2.3. MRI acquisition and preprocessing

All participants were scanned using a 3 Tesla Siemens Magnetom Trio whole-body scanner at the USC Dornsife Cognitive Neuroscience Imaging Center. Three-dimensional high-resolution T1-weighted images were acquired with a magnetization prepared rapid gradient echo (MP-RAGE) protocol as follows: inversion time (TI)/ repetition time (TR)/echo time (TE) = 800 / 2530/3.09 ms, slice thickness = 1 mm without gap, matrix = 256 × 256, and field of view (FOV) = 256 mm × 256 mm. Image preprocessing (e.g. skull-stripping, correction of signal intensity and inhomogeneity artifacts) was conducted using Freesurfer processing streams where outputs were visually inspected and manually corrected for accuracy (Yang et al., 2011).

TBM relies on matching structures with similar intensity patterns, and measures volumetric differences in a population by analyzing the gradients of the non-linear deformation fields required to align individual images to an anatomical template specific to the population studied (Yang et al., 2011). To detect local differences in brain tissue structure associated with psychopathic traits, TBM processing streams were implemented in the LONI Pipeline environment (Rex et al., 2003) using methods similar to those described in earlier investigations (Leow et al., 2009; Yang et al., 2011). Specifically, TBM processing included optimized non-rigid registration models that quantify the symmetric Kullback-Leibler (KL)-distance between the anatomical template and the transformed individual subject images. Processing steps were as follows: (1) Each preprocessed image volume was first registered to a single image using a nine-parameter registration to adjust for global brain scale, head tilt and alignment. (2) The images were then used to create an anatomical template or minimal deformation target (MDT). This step matches each 3D volume to all other volumes using a mutual information-based inverse-consistent algorithm, followed by applying the inverse of the mean displacement field from all subjects to the MDT. (3) Image volumes from all subjects were each subsequently aligned to the MDT by nonlinearly deforming the anatomy of each individual image to match the anatomical template. The Jacobian operator was then applied to the deformation fields to produce univariate Jacobian determinants (i.e., Jacobian maps) that index the extent of local expansion or contraction required to non-linearly warp each brain to match each subject's anatomy to the MDT. These 3D Jacobian maps represent relative tissue volume differences between each individual and the MDT, and were used to characterize local differences in brain tissue structure associated with the targeted behavioral measure across the sample.

2.4. Statistical analysis

The R statistical package (version 2.9.2; http://www.r-project.org/) was used to compute differences in the deformation fields associated with CPS total scores across the entire brain using the mixed effects model while controlling for sex, whole brain volume, and subject relatedness. Random intercepts were included for each family to account for relatedness within families. The analysis was implemented using the 'nlme' library in the R statistical package (Pinheiro and Bates, 2000). Uncorrected probability values and the corresponding beta (regression coefficient) values from the analyses were mapped onto the MDT. Since comparisons were made at thousands of voxels, results were further thresholded using an enhanced False Discovery Rate (FDR)-control method (Langers et al., 2007). By setting the FDR to 5%, this study was able to control the expected proportion of incorrectly rejected null hypotheses (Benjamini and Hochberg, 1995). In the FDR-corrected maps, 95% of the reported findings reported are expected to be true positives, irrespective of how many contrasts were conducted. FDR-thresholded probability values from each comparison were mapped onto the MDT atlas and color was used to encode the regions and the directions of the FDR-controlled significant correlations between psychopathic traits and brain tissue volume respectively.

For descriptive purposes and to report the location of the observed effects, we extracted MNI atlas coordinate locations for regions showing significant structural volume differences using the Anatomy Toolbox V1.5 (Eickhoff et al., 2005) of the Statistical Parametric Mapping software (SPM8; http://www.fil.ion.ucl.ac.uk/spm/software/spm8) executed in MATLAB (Mathworks, Sherborn, Massachusetts) (Yang et al., 2011). Anatomic locations of clusters with > 2000 voxels are provided in Table S1 (see the Supplementary Material).

2.5. Post hoc analyses

Finally, we applied an independent and widely-used volume quantification method to confirm that local striatum expansions, specifically in the caudate nucleus, putamen and the pallidum, reflect volumetric differences associated with psychopathic traits, as observed in the TBM analyses. The caudate nucleus, putamen and the pallidum volumes were measured by employing the completely independent image segmentation methods of Freesurfer v5.1.0 (http://surfer.nmr.mgh.harvard.edu; (Fischl et al., 2002)). For these procedures, any topographical errors in segmentation were corrected manually on a case-by-case basis (Yang et al., 2011).

3. Results

3.1. TBM analysis across the whole brain

As shown in Fig. 1, parent-reported CPS total scores were significantly correlated with brain tissue volume differences in several frontal, temporal and striatal regions after FDR thresholding. Specifically, higher CPS total scores were correlated with increased brain tissue volumes in the left putamen, including the ansa peduncularis, right superiomedial frontal cortex, right orbitofrontal cortex and right medial temporal cortex across the subjects while controlling for sex, whole brain volume, and subject relatedness (see Supplemental Material, Figs. S3–S4 and Table S1). In addition, higher CPS total scores were found to

correlate with reduced brain tissue volumes in the right middle frontal gyrus, bilateral inferior frontal gyrus, right superior parietal lobule, left inferior parietal gyrus, left supplementary motor area and the occipital cortex (see Supplemental Material, Figs. S3–S4 and Table S1).

As an exploratory measure, we also conducted the analysis separately for males and females and found similar patterns for both sexes. For males, higher CPS total scores were found to correlate with increased volumes in the left putamen, left ansa peduncularis, and left superiomedial frontal gyrus, and reduced volumes in the right middle frontal, right superior parietal lobule, left inferior parietal lobule, left supplementary motor area and the occipital cortex (Fig. 1, b). For females, higher CPS total scores were found to correlate with increased volumes in the left putamen, bilateral gyrus rectus, left inferior frontal gyrus, and left insula and reduced volume in the occipital cortex (Fig. 2, c).

3.2. Post hoc analysis on striatal regions

Post hoc analyses performed to compare subcortical volume estimates obtained independently using Freesurfer confirmed volumetric increases of the left putamen to be correlated with increased parent-reported CPS scores ($p = 0.01$) across the sample of 108 adolescents (Fig. 2), adjusting for whole brain volume and sex. Even so, the associations for the left caudate nucleus and the left pallidum were below the threshold of significance ($p = 0.22, 0.88$, respectively). In addition, Freesurfer showed the volume of the right putamen was also significantly increased ($p = 0.015$). No significant correlation was found for right caudate or pallidum ($p = 0.81, 0.75$, respectively).

For male adolescents, we found increased parent-reported CPS scores to correlate with increased volume in the left putamen ($p = 0.016$) while adjusting for whole brain volume and subject relatedness, but not other striatal structures (all $p > 0.1$). For female adolescents, we found increased parent-reported CPS scores to correlate with increased volume in the right putamen ($p = 0.019$), but below the threshold of significance for the left putamen ($p = 0.08$) and left caudate ($p = 0.065$). No significant correlation was found for other striatal structures for females (all $p > 0.1$).

4. Discussion

Using a homogeneously aged sample of healthy young adolescents, we captured unique patterns of global and local brain dysmorphology associated with psychopathic scores. The principal findings of this study are that abnormal brain tissue volumes in several regions, particularly increased volumes in the putamen, ansa peduncularis, superiomedial prefrontal cortex, inferior frontal cortex, medial temporal regions, and reduced volumes in the middle frontal cortex, superior parietal lobule, and inferior parietal lobule, were significantly correlated with increased psychopathic tendency in adolescents. Interestingly, we observed sex-specific abnormalities associated with psychopathy traits. Particularly, higher psychopathy scores correlate more strongly with enlarged left putamen, reduced right middle frontal volume, and increased right superiomedial frontal volume in males. For females, higher psychopathy scores correlate more prominently with increased volumes in the bilateral gyrus rectus, left inferior frontal cortex, left insula, and right putamen. These

findings support the possibility that psychopathy has a neurodevelopmental basis, with disorder-related brain morphological characteristics detectable in younger populations. In addition, findings of this study further highlight the complexity of brain maturational processes that occur during adolescence with regard to their possible contributions to symptom development such as elevated psychopathic traits.

In line with previous sMRI studies of adults with high psychopathy scores (Yang et al., 2005; Raine et al., 2009; Yang et al., 2010; Ermer et al., 2012), psychopathic tendency in adolescents were found to be associated with brain tissue abnormalities in several frontal regions including reduced middle frontal volume, increased superiomedial and inferior frontal volumes, and increased volume in the gyrus rectus. Findings are in line with those from studies of boys with conduct disorders. For example, De Brito and colleagues showed increased grey matter concentrations in several frontal regions including the medial orbitofrontal cortex in boys with callous-unemotional traits and conduct problems (De Brito et al., 2009). Using the same sample, they also found abnormal white matter concentrations in several frontal regions including decreased white matter concentrations in the right superior frontal cortex and increased white matter concentrations in the bilateral middle frontal gyrus in boys with psychopathic tendency (De Brito et al., 2011). The frontal cortex is centrally involved in functions frequently associated with key impairments of psychopathic individuals, including response inhibition, fear conditioning, and delay of gratification (Patrick, 1994; Dolan and Fullam, 2006; Raine and Yang, 2006). Findings of morphological alterations in these frontal regions may also be supported by previous reports of abnormal activation in these frontal regions in psychopathic individuals (Birbaumer et al., 2005; Rilling et al., 2007; Finger et al., 2008; Veit et al., 2010). For example, psychopathy scores were associated with increased activation in middle frontal gyrus during judgments of fear-evoking moral scenarios in healthy adults (Marsh and Cardinale, 2012). Although any interpretation can only be highly speculative, stronger correlations observed in the middle and superiomedial frontal cortex in males may suggest that poor impulsivity and behavioral control plays a center role in the development of psychopathy in males. On the other hand, stronger correlations observed in the gyrus rectus in females may suggest that impaired emotional regulation and moral cognition is crucial in the development of psychopathy in females. Nonetheless, findings here provide strong support for morphological abnormalities in the frontal cortex to be potential biomarkers for psychopathic tendencies in adolescents.

Another key finding of this study is the correlation between brain tissue contractions in parietal lobe, specifically superior and inferior parietal lobules, and greater psychopathic tendencies in adolescents. Although these brain regions have not received much attention so far, they both play central roles in functions that are closely associated with psychopathic traits. One of the most critical contributions of the parietal lobules is that they are part of the mirror neuron system (Cattaneo and Rizzolatti, 2009). This system is composed of neural circuits activated during the observation of actions, emotions, and sensations - *and* during execution and experiencing of the same actions, emotions and sensations (Gallese, 2003). Therefore, the mirror neuron system is thought to play a role in key aspects of social behavior, such as mentalizing and empathy (Iacoboni et al., 2005; Gazzola et al., 2006). One core feature of psychopathy is the lack of empathy, including impaired recognition and response to sadness, observational learning, and lack of concern about the impact of one's

actions on others (Blair, 2005; Dolan and Fullam, 2006). This is supported by a previous report showing psychopathic traits, specifically coldheartedness, were positively correlated with the level of corticospinal excitability in the motor cortex while watching short videos known to activate the sensorimotor mirror neuron system for pain (Fecteau et al., 2008).

Findings here provide initial evidence suggesting that neuroanatomical disturbances in regions within the mirror neuron network may also be linked to psychopathy. Finding of abnormal insula associated with psychopathic traits in females may be of particular significance. The insula has long been implicated in empathy, the capability to understand and resonate with the affective experience of another, and is crucial in the inhibition of antisocial, aggressive behavior. Abnormal activation in the insula during empathy-related tasks has been linked to higher levels of psychopathy in several adult studies (Decety et al., 2013; Decety et al., 2014; Molenberghs et al., 2014). For developmental populations, prior studies on children with conduct problems have also demonstrated abnormal neural responses to others in pain in the insula (Sterzer et al., 2007). For example, Lockwood and colleagues found children with conduct problems to show reduced activation in the bilateral anterior insula while viewing pictures of others in pain (Lockwood et al., 2013). Furthermore, higher levels of callous traits were associated with reduced responses to others' pain in the anterior insula. Our findings provide further support for the argument that insula plays an important role in the developmental vulnerability to psychopathy, and is a potentially sensitive biomarker for psychopathic tendencies in female adolescents.

In addition to brain tissue abnormalities in the frontal and parietal regions, we also found brain tissue expansions in several subcortical regions, most prominently in the putamen, to be associated with heightened psychopathic tendencies in adolescents. Although the enlargement was more prominent in the left putamen for the males, and right putamen for the females, both sexes show similar positive relationships between increased volumes in the putamen and increase psychopathy scores. Findings are in line with some previous studies (Glenn et al., 2010a; Schiffer et al., 2011), but not the others (Fairchild et al., 2012), which could be due to differences in sample size, age of the cohort studied, and whether the focus was on psychopathy in general or more specific traits (i.e. callous-unemotional).

The striatum, including the putamen, is one of the structures most crucially involved in reward prediction and guiding action selection towards immediate over delayed reward (O'Doherty, 2004; Hariri et al., 2006). Structural brain abnormalities in the putamen may thus contribute to some of the most distinct features of psychopathy such as increased stimulation seeking, perseverative response, and reward-driven and impulsive behavior (Newman et al., 1987; Newman et al., 1992; Hare, 2003). The striatum is also a critical part of the neural circuitry underlying stimulus-reinforcement learning, i.e., learning appropriate behaviors for responding to rewarding stimuli and refraining from responding to those that lead to punishment (Newman and Kosson, 1986; Blair, 2006b). Stimulus-reinforcement learning is a critical component of the passive avoidance in psychopathy, which has been studied extensively (Newman and Kosson, 1986; Blair, 2006b), and is closely linked to decision-making, socialization, and empathy-based learning. Enlarged striatum as observed here may provide neurobiological evidence supporting the theoretical explanation of psychopathy that overactivation by reward leads to impaired ability to modulate the

dominant response for reward in psychopathic individuals (O'Brien and Frick, 1996). Sufficient evidence form animal studies showed that the striatum, particularly the lateral dorsal striatum (i.e. putamen) appears to be involved in habitual stimulus-response associations (Liljeholm and O'Doherty, 2012), which may further explain the response perseveration that is often observed in psychopathic individuals. Furthermore, enlarged ansa peduncularis, which is a main division of the ventral amygdalofugal pathway, was also found to be associated with higher psychopathy scores, particularly in males. The ventral amygdalofugal pathway contains fibers leaving the amygdaloid nucleus to several targets including the hypothalamus, thalamus, septal nuclei and nucleus accumbens, thus enlargement observed in this area may reflect abnormal connection between amygdala and associated structures. This is supported by findings of reduced connectivity with the amygdala (Cohen et al., 2009; Finger et al., 2012; Passamonti et al., 2012; Contreras-Rodriguez et al., 2014) and structural abnormalities in the amygdala (Yang et al., 2009c; Yang et al., 2010; Pardini et al., 2014) in psychopathic individuals.

An important question remains concerning how increased striatal volumes may predispose a person to psychopathic traits. Enlarged putamen has been observed in several other populations including individuals with methamphetamine-dependent (Chang et al., 2005), cocaine-dependent (Jacobsen et al., 2001) and schizophrenia patients with neuroleptic treatment (Gur et al., 1998; Taylor et al., 2005), and was argued to be the result of inflammation and reactive gliosis in the region, possibly assisted by glia-mediated neurotrophic effects to increase striatal sprouting (Song and Haber, 2000). Therefore, one explanation for the association between enlargement of the putamen and psychopathic traits as observed here would be that it represents a compensatory response to maintain function of the striatum. Another explanation for the enlarged putamen and sex-specific changes observed here might come from a developmental perspective. One recent study showed putamen declined in volume with age, and the decreases were more for females than males and greater in the left hemisphere (Dennison et al., 2013). This may be due to sex hormone changes through puberty that induce sex-specific synaptogenesis and synaptic pruning during adolescence. Nonetheless, our findings provide initial evidence suggesting that a delay or disruption in the development of putamen may contribute to the development of psychopathic tendency in adolescents, particularly heightened sensation-seeking and reward-dominated behavior.

Limitations of this study include the use of a twin sample, which may limit the generalizability of findings to the general population. However, our findings are mostly consistent with previous studies of singletons, suggesting structural alterations in frontal, temporal, parietal and striatal regions as critical components underlying early onset psychopathic tendency. Unlike other whole-brain volumetric methods, TBM does not require a segmentation step, which avoids potential partial volume errors associated with tissue classification. As such, results from this current study that point to differences in both gray and white matter structure may be less directly comparable to previous findings concentrating mainly on gray matter. Notably, for subcortical regions, results from the independent FreeSurfer method are complementary to those of TBM, however bilateral instead of unilateral enlargement in putamen and sex-related hemispheric effect was also observed. Nonetheless, both methods are supportive of the argument that striatal

abnormalities may contribute to the development of psychopathic traits in adolescents and future studies are needed to validate the sex- and hemisphere-specific results observed here. Last, there has been some evidence suggesting that pubertal stage may be a better predictor than chronological age for examining developmental changes in brain morphology, particularly subcortical structures (Blanton et al., 2012). Although the potential age-related brain variations among our subjects were limited by using a homogeneously-aged sample, future studies could benefit from further controlling for pubertal stage.

Overall, this study reveals valuable knowledge regarding the neural mechanisms underlying psychopathic traits in adolescents. Future studies examining how genetic predispositions interact with environmental influences in shaping the brain structure and function could help understand the development of psychopathic tendencies throughout the lifespan.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported by grants from National Institute of Mental Health (K99 MH093388 to Y.Y., R01MH58354 to L.A.B., R01MH092301 K.L.N., R01 AG040060 and P41 RR013642 to P.M.T.), and by a grant from the Brain and Creativity Institute, University of Southern California.

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- Structural magnetic resonance imaging data were obtained from 108 adolescents using tensor-based morphometry.
- Higher levels of psychopathic traits correlated with increased volumes in the left putamen, left ansa peduncularis, right superiomedial prefrontal cortex, left inferior frontal cortex, right orbitofrontal cortex, and right medial temporal regions.
- Higher levels of psychopathic traits also correlated with reduced volumes in the right middle frontal cortex, left superior parietal lobule, and left inferior parietal lobule.
- Poor decision-making and emotional dysregulation associated with psychopathy may reflect structural anomalies in frontal and temporal regions whereas striatal structural variations may contribute to sensation-seeking and reward-driven behavior in psychopathic individuals.

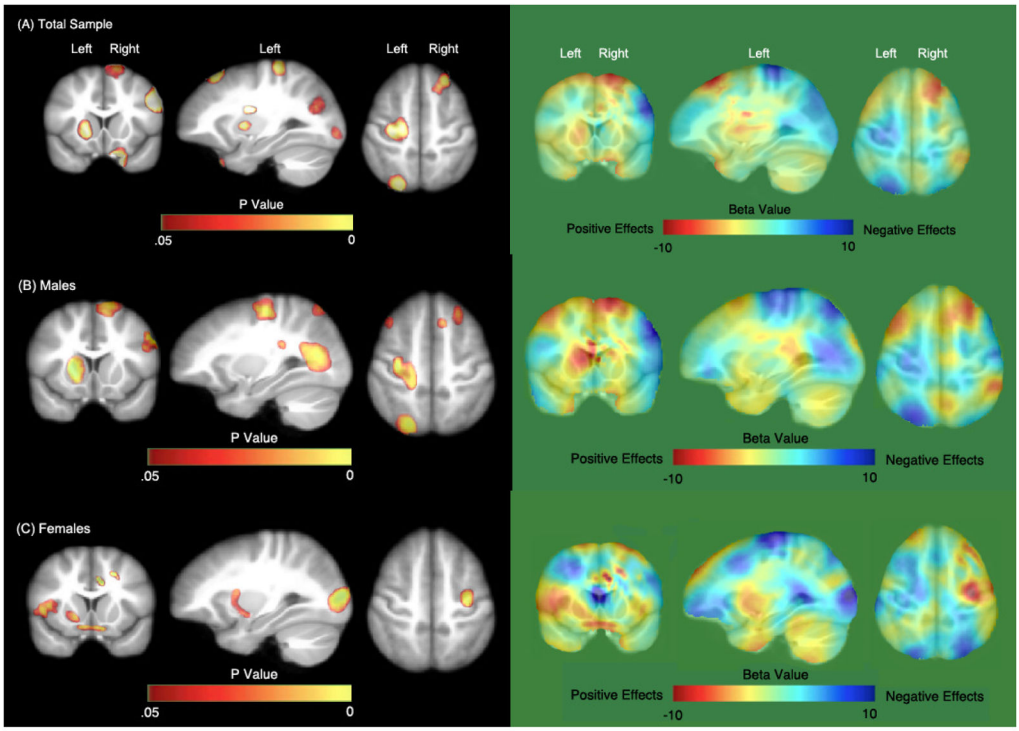

Fig. 1.

The left panel illustrates FDR-corrected ($q = 0.05$) probability maps for (a) total sample, (b) males, and (c) females showing significant correlations between psychopathic tendencies and brain tissue volumes, and the right panel shows the corresponding beta maps indicating the direction of the effects. Cold colors indicate negative and hot colors positive correlations.

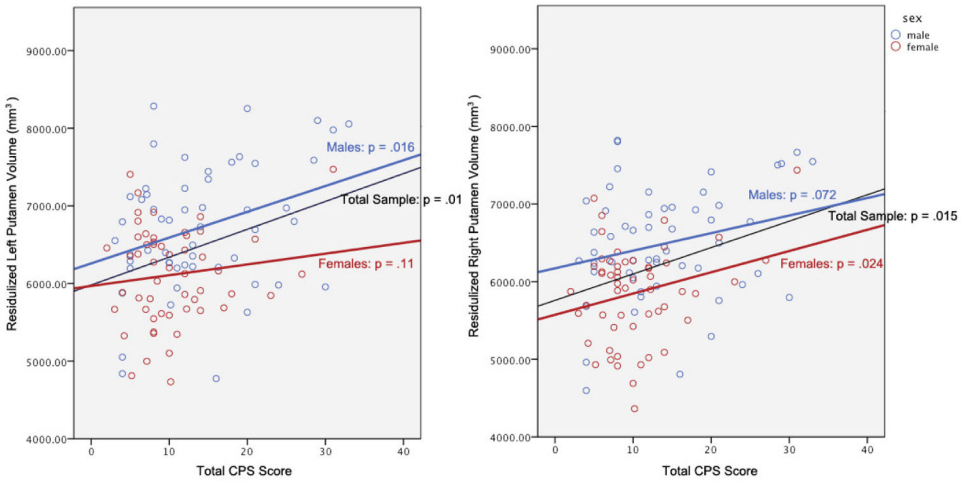

Fig. 2.

Correlations between total Childhood Psychopathy Scale (CPS) scores and gray matter volumes of the left and right putamen, corrected for total brain volumes and subject relatedness.