Journal of Psychiatric Research 149 (2022) 185–193

Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/jpsychires

Larger striatal volume is associated with increased adult psychopathy

Olivia Choy [a,*], Adrian Raine [b], Robert Schug [c]

[a] Department of Psychology, Nanyang Technological University, Singapore
[b] Departments of Criminology, Psychiatry, and Psychology, University of Pennsylvania, USA
[c] School of Criminology, Criminal Justice, and Emergency Management, California State University, Long Beach, USA

ARTICLE INFO

Keywords:
Striatum
Psychopathy
Neuroimaging
Structural MRI
Antisocial

ABSTRACT

Prior studies have inconsistently reported increased volumes of the striatum in adults with psychopathy. A meta-analysis presented here indicates an overall effect size of $d = 0.44$. Nevertheless, variability in findings exist, and questions remain on confounding clinical conditions and generalizability to females. This study tests the hypothesis that striatal volumes are increased in adults with psychopathic traits, and that this relationship is mediated by stimulation-seeking and impulsivity. Striatal volume was assessed using magnetic resonance imaging in 108 adult community-dwelling males alongside psychopathy using the Psychopathy Checklist – Revised. Subsidiary, exploratory analyses were conducted on a small sample of females. Correlational analyses showed that increased striatal volumes were associated with more psychopathic traits ($p = .001$). Effects were observed for all striatal regions, controlling for age, substance dependence and abuse, antisocial personality disorder, attention deficit hyperactivity disorder, social adversity, and total brain volume. An analysis of 18 psychopathic individuals showed that striatal volumes were increased 9.4% compared with 18 matched controls ($p = .01$). Psychopathy in females was also significantly associated with increased striatal volume ($p = .02$). Stimulation-seeking and impulsivity partly mediated the striatal-psychopathy relationship, accounting for 49.4% of this association. Findings from these two samples replicate and build on initial studies indicating striatal enlargement in adults with psychopathy, yielding an updated effect size of $d = 0.48$. Results are consistent with the notion that striatal abnormalities in individuals with psychopathy partly reflect increased sensation-seeking and impulsivity, and support the hypothesis of abnormal reward processing in psychopathy.

1. Introduction

A salient brain imaging correlate of psychopathy is enlargement of the striatum, a subcortical region that is critically involved in the cognitive processing of reward-related information and motivational aspects of behavior (Goto and Grace, 2008; O'doherty et al., 2004; Fairchild et al., 2011; Buckholtz et al., 2010). To date, 9 structural imaging studies have been conducted on striatal volume in adults with psychopathic traits. Findings are informative but inconsistent, both across and within studies. Table 1 provides a summary of structural imaging studies on striatal volume and adult psychopathy. A preliminary meta-analysis conducted on the 7 independent samples which met inclusion criteria yielded an overall effect size of $d = 0.44$, $p = .01$, indicating striatal enlargement in adults with psychopathy (see Supplement for meta-analysis procedures; Fig. S1). Nevertheless, there was significant between-studies heterogeneity ($Q = 13.37$, $p = .04$).

One potential explanation for these heterogeneous findings concerns comorbidity between psychopathy and several psychiatric conditions, including substance dependence (Smith and Newman, 1990), antisocial personality disorder (APD) (Ogloff, 2006), and attention deficit hyperactivity disorder (ADHD) (Eisenbarth et al., 2008). The link between substance use and the striatum is further supported by functional magnetic resonance imaging (MRI) studies, with a recent meta-analysis suggesting that hyperactivation of the striatum is associated with substance use vulnerability (Tervo-Clemmens et al., 2020). Gray matter abnormalities in the caudate nucleus in structural MRI studies of ADHD (Montes et al., 2010; Onnink et al., 2014) suggest that some of the inconsistent findings on the striatum-psychopathy relationship may be attributed to ADHD comorbidity. Only 3 of the 9 studies controlled for psychiatric comorbidity other than substance use (Table 1). Thus, a research gap concerns whether striatal structural abnormalities are specific to psychopathy, or whether in contrast, they are an artefact of psychiatric comorbidity.

Inconsistent findings on the striatum-psychopathy relationship may

* Corresponding author.
E-mail addresses: oliviachoy@ntu.edu.sg (O. Choy), araine@sas.upenn.edu (A. Raine), robert.schug@csulb.edu (R. Schug).

https://doi.org/10.1016/j.jpsychires.2022.03.006
Received 14 September 2021; Received in revised form 31 January 2022; Accepted 4 March 2022
Available online 6 March 2022

Table 1
Summary of structural neuroimaging studies on the striatum and psychopathy in adults.

Study	Sample	Mean age, y (SD)	Sex differences analyzed	Controlled for substance use	Controlled for psychiatric comorbidity other than substance use	Findings reported			
						Caudate	Putamen	Nucleus accumbens	Globus pallidus
Boccardi et al. (2013)	26 male offenders with psychopathy, 25 healthy controls	Offenders: 32.5 (8.4) Controls: 34.6 (10.8)	No	Yes	No	Yes	Yes	Yes	No
Main Findings: Compared with controls, offenders showed a 13% reduction in bilateral nucleus accumbens volume and non-significant enlargements of the caudate nucleus and putamen. Factor 3 of the PCL-R was negatively correlated with caudate and putamen morphology.									
Cope et al. (2012)	66 offenders (36 males, 30 females)	36.9 (7.9)	No	Yes	No	Yes	Yes	No	No
Main Findings: Greater left and right striatal volumes were significantly associated with higher PCL-R scores.									
Glenn et al. (2010)	88 adults (77 males, 9 females; 22 individuals with psychopathy, 22 controls)	Psychopathy group: 31.1 (6.9) Controls: 31.0 (6.6)	No	Yes	Yes	Yes	Yes	Part of the nucleus accumbens was included	Yes
Main Findings: Compared with controls, individuals with PCL-R scores ≥23 showed a 9.6% enlargement in the striatum. Higher total striatal volume was associated with higher levels of psychopathy, and facets 1, 2, and 3 of the PCL-R.									
Korponay et al. (2017)	124 adult male prison inmates	31.6 (7.3)	No	Yes	No	Assessed but not reported	Yes	Yes	Yes
Main Findings: Larger volumes in the nucleus accumbens were associated with higher total PCL-R scores. Higher PCL-R factor 1 scores were associated with reduced right putamen volume. Higher PCL-R factor 2 scores were associated with larger nucleus accumbens, putamen, right globus pallidus, and right caudate volumes.									
Lam et al. (2017)	67 adults (56 males, 11 females)	34.09 (11.85)	No	Yes	Yes	Yes	Yes	No	No
Main Findings: Greater caudate volume correlated with increased total psychopathy and factor 2 scores. Psychopathy moderated the relationship between increased violence and greater putamen and left caudate volume.									
Leutgeb et al. (2015)	40 high-risk male violent offenders, 37 healthy controls	Offenders: 38.1 (12.0) Controls: 36.7 (9.6)	No	No	No	Yes	Yes	No	Yes
Main Findings: Within the offender group, increased right putamen and left pallidum volumes correlated with higher PCL-R factor 2 scores.									
Pujara et al. (2014)	18 male psychopaths, 23 non-psychopaths	Psychopaths: 32.2 (6.5) Non-psychopaths: 32.5 (8.0)	No	No	No	Yes	Yes	Yes	Yes
Main Findings: No group differences in striatal volumes. For individuals with PCL-R scores ≥30, greater nucleus accumbens volumes were associated with higher total psychopathy scores.									
Schiffer et al. (2011)	12 violent men with SUDs (violent offenders), 12 violent men without SUDs, 13 non-violent men with SUDs, 14 non-offenders without SUDs	Violent offenders with SUDs: 36.4 (5.5) Violent offenders without SUDs: 37.4 (10.6) Non-violent men with SUDs: 37.3 (7.9) Non-offenders without SUDs: 36.7 (11.4)	No	Yes	No	Yes	No	Yes	No
Main Findings: Greater left nucleus accumbens volumes were associated with greater factor 1 and factor 2 psychopathy scores. Greater right caudate volumes were correlated with higher scores for facets 2 and 4.									
Vieira et al. (2015)	35 healthy adults (15 males, 20 females)	21.06 (1.80)	No	Yes	Yes	Yes	Yes	No	Assessed but not reported
Main Findings: Psychopathy scores were negatively associated with left striatal volume. Increased psychopathy was associated with increased left caudate volume, but not left putamen volume. Higher levels of meanness were associated with increased striatal volumes.									

Note: SUD = substance use disorder; PCL-R = Psychopathy Checklist-Revised.

also be partly attributed to methodological issues. In addition to small sample sizes in many studies, subject populations vary. Most studies recruited participants from institutional settings, with only 2 studies examining this association in general community samples (Glenn et al., 2010; Vieira et al., 2015). Furthermore, only 4 of the 9 studies include mixed-sex samples of adults. Few controlled for sex, and the moderating effect of sex was not tested in any study (Glenn et al., 2010; Vieira et al., 2015; Cope et al., 2012; Lam et al., 2017). Thus, one question that has not been addressed in any prior study is whether striatal enlargement is observed in adult females with psychopathic traits. This limitation has recently been highlighted in a study noting the lack of psychopathy research in women in the community compared to studies on male prisoner and inpatient samples (Thomson et al., 2019).

A further issue concerns inconsistency in the regions of the striatum that are assessed. Volumetric analyses of different striatal subregions are reported across studies, rendering a fair comparison of results challenging. Regions of the striatum include the caudate, putamen, nucleus accumbens, and globus pallidus (Báez-Mendoza and Schultz, 2013; Glenn and Yang, 2012). Many studies do not assess or report findings on specific striatal subregions in psychopathy. Furthermore, it remains unclear whether different dimensions of psychopathy are associated with structural abnormalities in the striatum, and what findings have been reported are mixed. While some studies document associations between increased striatal volumes and higher scores on factor 1 (Interpersonal/Affective) and factor 2 (Lifestyle/Antisocial) of the Psychopathy Checklist-Revised (PCL-R) (Korponay et al., 2017; Schiffer et al., 2011), others report *negative* correlations between striatum morphology and PCL-R factors (Boccardi et al., 2013). Discrepancies in research findings may also be accounted for by the type of analyses (group vs. correlational) conducted. For example, one study reported no significant group difference in striatal volumes between psychopathic and non-psychopathic offenders, but nevertheless found higher psychopathy scores to be associated with greater nucleus accumbens volume among individuals with high levels of psychopathy (Pujara et al., 2014).

Individual laboratories to date have not attempted to replicate their prior findings, and investigation of the striatum-psychopathy relationship in the same population (e.g., clinical, community) using the same assessments of psychopathy is lacking. Although two structural imaging studies have examined the role of the striatum in psychopathy in community-recruited participants, one study employed a self-report measure based on the triarchic conceptualization of psychopathy (Vieira et al., 2015), while the other used the interview-based PCL-R employing a four-factor model (Glenn et al., 2010). Overall, while prior studies have made advances, the inevitable limitations of initial studies preclude firm conclusions about the relationship between striatal volume and psychopathy.

1.1. Current study

We have previously reported higher striatal volumes in adults with psychopathy drawn from the community (Glenn et al., 2010). The current study now aims to replicate, for the first time, this same finding using equivalent measures. We recruited a new sample of community participants using the same population sampling strategy and the same psychopathy rating scale. We also attempted to extend the initial informative imaging studies on psychopathy and the striatum by addressing the inevitable methodological gaps noted above at six levels. First, this study controls for a number of demographic and psychiatric variables in order to clarify the neurobiological basis of psychopathy. Second, we assess multiple striatal regions in relation to psychopathy. Third, associations between striatal volumes and PCL-R facets are tested. Fourth, a preliminary exploratory analysis on a small sample of females is conducted to examine potential sex differences in the striatum-psychopathy relationship. Fifth, two potential mechanisms underlying this association, impulsivity and stimulation-seeking, are examined in a formal mediation model. Sixth, in addition to controlling for whole brain volume, we conducted tests of anatomical specificity using the cerebellum and using the thalamus, an analogous subcortical region that lies close to the striatum with intimate connections via the cortico-striatal-thalamic loop (Peters et al., 2016) and yet does not play a primary role in reward processing.

2. Method

2.1. Participants

Following the sampling strategy of our prior study (Glenn et al., 2010), participants were recruited from temporary employment agencies in the Greater Los Angeles area. Data on study variables were obtained for 108 males (mean age = 31.36 years, SD = 8.01; Table 2 and Fig. 1). 40.74% of participants were Caucasian and 59.26% of participants were of other ethnicities. For supplemental analysis only, data on a small sample of 12 females were available (mean age = 29.83 years, SD = 10.86; 16.66% Caucasian, 83.33% Others). Written informed consent was provided by participants. A certificate of confidentiality was obtained from the Secretary of Health and Human Services, while study protocols were approved by the Institutional Review Boards of the University of Southern California and the University of Pennsylvania.

2.2. MRI acquisition and image processing

MRI scanning was performed on a Siemens 3T Trio scanner. An 8-min T1-weighted magnetization prepared rapid gradient echo (MPRAGE) structural scan was performed (echo time (TE) = 4.77 ms, repetition time (TR) = 2500 ms, flip angle = 7°, 256 × 256 × 176 matrix, 1 × 1 × 1 mm voxel size). FreeSurfer 5.1.0 (Fischl, 2012) was used to process the T1 images obtained through MRI scans and compute striatal volumes for all participants. Pre-processing steps included skull-stripping to remove non-brain tissue from images, correction of signal intensity, motion and inhomogeneity artifacts, spatial registration to Talairach space, and tissue segmentation to classify gray and white matter (Dale et al., 1999; Fischl and Dale, 2000). Images were manually inspected on a slice-by-slice basis following previously established procedures (Yang et al., 2009, 2010) to ensure that non-brain material had been properly removed and gray and white matter were accurately

Table 2
Descriptive statistics (n = 108).

	Mean (SD)/%	Range
Age	31.36 (8.01)	19–61
Race		
Caucasian, %	40.74	
Other, %	59.26	
Social adversity	3.04 (1.94)	0–10
Psychopathy		
Total score	18.30 (8.90)	0–35
Facet 1 (Interpersonal)	3.85 (1.98)	0–8
Facet 2 (Affective)	4.34 (2.50)	0–8
Facet 3 (Lifestyle)	5.19 (2.85)	0–10
Facet 4 (Antisocial)	3.61 (2.44)	0–9
APD, %	21.30	
Substance dependence/abuse, %	58.33	
ADHD	5.43 (5.04)	0–23.17
Number of head injuries	1.64 (2.77)	0–20
Total brain volume (mm^3)	1044204.11 (99694.22)	808906–1337530
Total striatum (mm^3)	23439.88 (2712.35)	17477-31923
Caudate (mm^3)	7183.20 (979.79)	5024–9582
Putamen (mm^3)	11437.37 (1512.41)	6729–16969
Nucleus accumbens (mm^3)	1255.34 (254.34)	837–2060
Globus pallidus (mm^3)	3563.96 (487.44)	2376–4822
Thalamus (mm^3)	15801.18 (1819.75)	12120-20138

Note: APD = antisocial personality disorder; ADHD = attention deficit hyperactivity disorder.

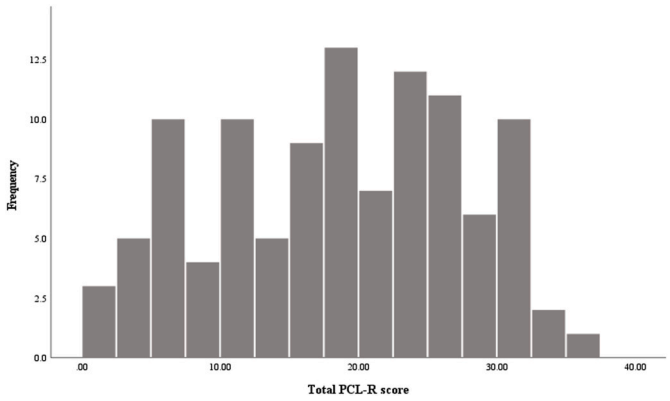

Fig. 1. Histogram of PCL-R scores (n = 108).

segmented. Manual inspection was conducted by a research assistant blind to psychopathy scores and other participant characteristics. Consistent with the subregions of the striatum investigated in prior studies on the striatum and psychopathy (Pujara et al., 2014; Glenn et al., 2010), segmentation of the caudate, putamen, nucleus accumbens, and globus pallidus was conducted together with the thalamus and cerebellum using standard FreeSurfer parcellation (Fig. 2). Total striatal volumes were defined as the sum of the volumes of the four striatal subregions.

2.3. Psychopathy

Psychopathy was assessed using the PCL-R, which consists of 20 items rated by interviewers on a 3-point scale (0 = does not apply, 1 = applies somewhat, 2 = definitely applies) (Hare, 2003). Ratings were made by one of the authors (R.S.), who was supervised by the second author and received intensive, systematic training on the administration and scoring of the PCL-R from Dr. Robert D. Hare and Dr. Adelle Forth. Seven collateral data sources were used including 1) information from the Interpersonal Measure of Psychopathy (IM-P) (Kosson et al., 1997) during the session, 2) independent IM-P ratings made by different laboratory assistants during other phases of testing, 3) self-reported theft, drug offenses, and violent crime as assessed by an adult extension of the National Youth Survey self-report delinquency measure (Elliott et al., 1983), 4) official state Department of Justice criminal records, 5) professional nationwide criminal and court record database searches, 6) data derived from, and behavioral observations made during, the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First et al., 1997b), and 7) the SCID Axis II Personality Disorders (SCID-II) (First et al., 1997a). These information were used to score items according to the PCL-R manual (Hare, 2003). Internal reliability of the PCL-R in the current study was r = 0.86. For completeness, 4 facet scores were also evaluated (see Supplement for details).

2.4. Covariates

APD was assessed in participants using the SCID II (First et al., 1997a). Past or current substance dependence and abuse were also assessed using the SCID II, reflecting participants' use of multiple classes of substances, which include alcohol, marijuana, sedatives/anxiolytics/hypnotics, stimulants, opiates, cocaine/methamphetamine, and hallucinogens/PCP (1 = yes, 0 = no). A total adult ADHD score was also obtained from participants (Barkley, 2011), with missing values dealt with using regression imputation. Head injury was assessed from self-reports on the number of times participants had suffered a head injury.

Total brain volume was used as a covariate, while thalamic and cerebellar volumes were employed as controls in supplemental analyses. Demographic variables considered as covariates include age and race (1 = non-Caucasian, 0 = Caucasian). Furthermore, as exposure to childhood family adversity and abuse have been associated with alterations in both the structure and function of the striatum (Gheorghe et al., 2021; Holz et al., 2017) and higher levels of psychopathic traits in adulthood (Gao et al., 2010), an index of social adversity was calculated based on the sum of responses to 13 items (Choy et al., 2015) (see Supplement for details). Higher scores reflected greater social adversity.

To test whether total brain volume, APD, substance dependence and

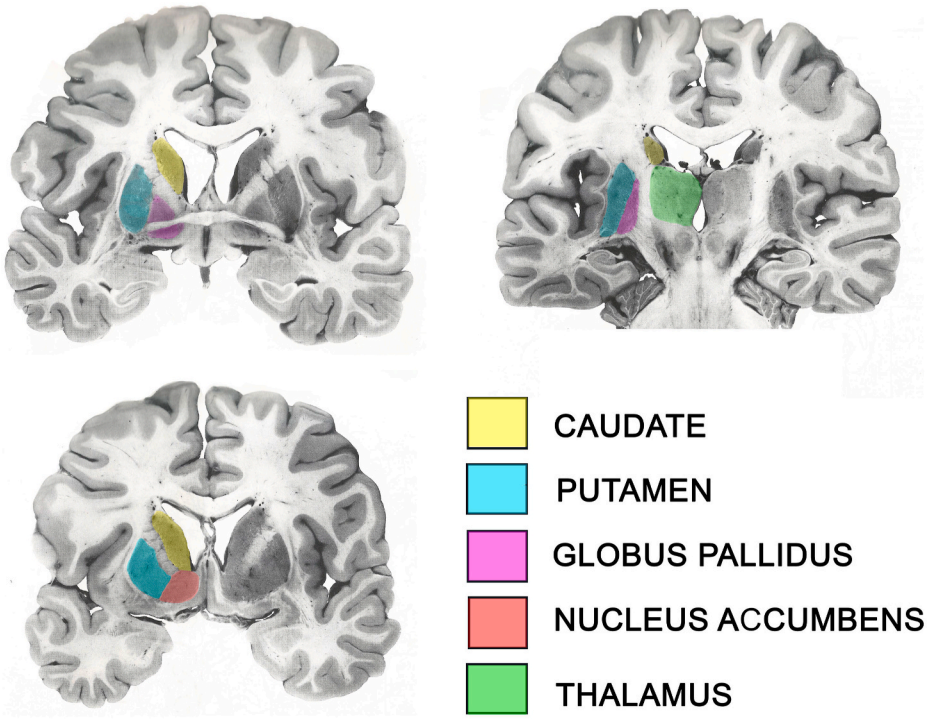

Fig. 2. Anatomical locations of the key regions of interest: caudate, putamen, globus pallidus (top left), nucleus accumbens (bottom left), and thalamus (top right).

abuse, ADHD symptoms, number of head injuries, age, race, and social adversity were possible confounders of the relationship between striatal structure and psychopathy, the bivariate relationships between striatal volume, psychopathy, and the hypothesized confounders were examined using correlational analyses. Variables that were significantly associated with the independent variable (psychopathy) or the dependent variable (striatum) were included in the regression analyses as covariates.

2.5. Statistical analyses

Regressions were conducted on the total sample to evaluate the relationship between striatal volumes and psychopathy, and to enhance statistical power. As four subregions of the striatum were examined, to account for multiple testing, the p values for striatal subregions were adjusted using the false discovery rate (FDR) method with a $q = .05$ (Benjamini and Hochberg, 1995). Separate regressions were performed for total PCL-R and the four PCL-R facets.

To test the robustness of the findings, in addition to the dimensional approach employed, between-group analyses were conducted. In an attempt to replicate prior findings, a cut-off score of 23 and above on the PCL-R was used for membership into the psychopathic group. This lower cut-off score was adopted as it has been suggested to be more appropriate for community samples and because this same cut-off score was employed in our prior study on psychopathy and the striatum (Glenn et al., 2010), the findings of which we were aiming to replicate in the current study. A propensity score-matched analysis was performed to create two groups consisting of 18 male psychopathic individuals and 18 controls matched on age, race, APD, substance dependence and abuse, and ADHD symptoms (see Supplement for procedure).

Differences between the two groups with respect to demographic variables and comorbidities were examined using independent samples t tests and χ^2 tests. No significant difference in age, race, number of APD symptoms, ADHD symptoms, and substance dependence or abuse were observed between groups (Table 3). Group differences in striatal volumes were assessed using ANOVA. All analyses were performed using SPSS statistical software (IBM SPSS Statistics Version 26.0). Tests were two-tailed. Effect sizes were computed using Cohen's d.

Table 3
Comparisons between the psychopathic and control groups.

	Control Group (n = 18)	Psychopathic Group (n = 18)	Statistic	p-value
Matched variables				
Age	30.44 (7.39)	29.94 (10.53)	$t = .17$	.87
Race, % Caucasian	55.6	50.0	$\chi^2 = .11$	.74
Substance dependence/ abuse, %	72.2	55.6	$\chi^2 = 1.08$	.30
APD, %	33.3	33.3	$\chi^2 = .00$	1.00
ADHD	4.17 (4.36)	4.43 (5.34)	$t = -.16$	.88
Psychopathy				
Total score	12.58 (5.75)	26.72 (2.95)	$t = -9.27$	<.001
Factor 1 Affective-Interpersonal	5.67 (3.03)	12.06 (1.39)	$t = -8.13$	<.001
Factor 2 Impulsive-Antisocial	6.23 (3.21)	12.39 (2.36)	$t = -6.57$	<.001
Head injuries	1.50 (1.20)	2.67 (4.55)	$t = -1.05$	.30
Social adversity	3.08 (2.00)	3.84 (1.98)	$t = -1.14$	.26
Total brain volume (mm^3)	1049597.17 (99828.58)	1061832.00 (72746.73)	$t = -.42$	.68

Note: Data for continuous variables are presented as mean (SD).

2.6. Supplemental analysis

Three additional sets of supplemental analysis were conducted. Pearson correlations were conducted to examine the association between striatal volume and psychopathy in the smaller female sample. Mediation analyses were also conducted. Using the PROCESS macro, a bootstrapping approach was employed to test the significance of the indirect effect of striatal volume on psychopathy through impulsivity and sensation-seeking (Hayes, 2013) (see Supplement for details). The magnitude of the mediation effect was expressed as the ratio of the indirect to total effect of striatal volume on psychopathy. To further test the anatomical specificity of our findings, regressions were conducted, predicting striatal volume from psychopathy while controlling for thalamic volume in one model, and for cerebellar volume in another (see Supplement).

3. Results

3.1. Bivariate associations between study variables and potential confounds

As part of a preliminary analysis, bivariate relationships between the key study variables and hypothesized confounders were analyzed to assess candidacy as a covariate in the regressions. Race and number of head injuries were not significantly associated with total striatal volumes or PCL-R scores (Table 4). As age, APD, substance dependence and abuse, ADHD scores, social adversity, and total brain volume were statistically significantly associated with either the volume in the striatum or with psychopathy, they were included in the regression models as covariates.

3.2. Associations between striatal volumes and psychopathy

A preliminary regression analysis without including statistical controls showed a statistically significant positive association between striatal volume and psychopathy (standardized beta $\beta = 0.28$, $t = 3.00$, $p < .01$; Fig. 3). After controlling for covariates, regression analysis predicting striatal volume using psychopathy scores indicated that greater total psychopathy scores were associated with increased volumes in the striatum ($\beta = 0.31$, $t = 3.46$, $p = .001$, $d = 0.67$). This association was found for both the right and left striatum ($p = .001$).

Relationships between striatal subregions and psychopathy were also investigated. Higher levels of psychopathy were associated with greater volumes in all subregions, namely the caudate ($\beta = 0.26$, $t = 2.66$, $p = .01$, $d = 0.52$), putamen ($\beta = 0.25$, $t = 2.59$, $p = .01$, $d = 0.50$), nucleus accumbens ($\beta = 0.22$, $t = 2.03$, $p < .05$, $d = 0.39$), and globus pallidus ($\beta = 0.33$, $t = 3.37$, $p = .001$, $d = 0.66$). These findings survived FDR correction. Controlling for age, substance dependence and abuse, APD,

Table 4
Correlations between key study variables and hypothesized confounders.

	Total PCL-R score	Striatal volume
Age	.01	-.50**
Race	.17	-.02
APD	.44**	.04
Substance dependence/abuse	.24*	.15
ADHD	.24*	.22*
Number of head injuries	.17	.13
Social adversity	.26**	-.05
Total brain volume	-.06	.37**

Note: APD = antisocial personality disorder; ADHD = attention deficit hyperactivity disorder.
*$p < .05$; **$p < .01$.

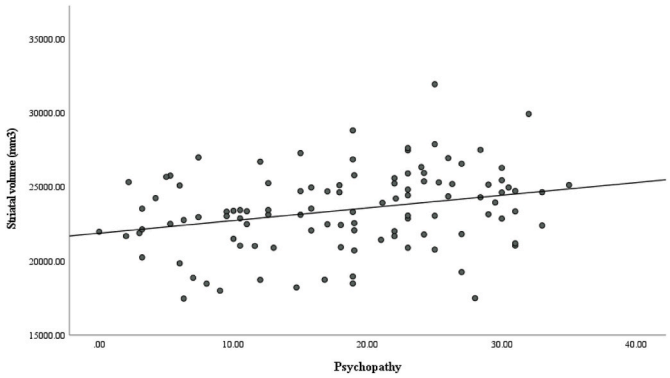

Fig. 3. Association between striatal volumes and psychopathy in the total sample (n = 108).

ADHD symptoms, social adversity, and total brain volume, total striatal volume was significantly positively associated with all four psychopathy facets ($p < .05$; Tables S2 and S3).

3.3. Striatal volumes in psychopathic and non-psychopathic groups

Compared with controls, individuals in the psychopathic group showed a 9.4% increase in striatal volume [$F(1, 34) = 6.93$, $p = .01$, $d = 0.88$] (Fig. 4; Table S1). The psychopathic group exhibited larger volumes in the caudate [$F(1, 34) = 5.54$, $p = .03$, $d = 0.78$], putamen [$F(1, 34) = 4.32$, $p < .05$, $d = 0.69$], and nucleus accumbens [$F(1, 34) = 4.33$, $p < .05$, $d = 0.69$]. Although a similar pattern of findings was observed in the globus pallidus, the group difference showed a trend towards statistical significance [$F(1, 34) = 3.10$, $p = .09$, $d = 0.59$]. However, these results did not survive FDR correction.

3.4. Supplemental analysis

3.4.1. Female sample

To supplement the results obtained, data from a sample of 12 females who were recruited in the same study were assessed. None of the hypothesized confounders were significantly associated with volumes in the striatum or psychopathy ($p > .05$). Zero-order correlations showed that higher psychopathy scores were associated with larger volumes of the striatum ($r = 0.66$, $p = .02$, $d = 1.75$).

3.4.2. Mediation effects

Results from mediation analyses indicate that impulsivity and need for stimulation partly mediate the striatal-psychopathy association (total indirect effect: $\beta = 0.14$, $p < .05$; Figs. S2 and S3), accounting for 49.41% of this relationship.

3.4.3. Anatomical specificity

The association between increased striatal volumes and higher psychopathy scores remained statistically significant even when thalamus ($\beta = 0.25$, $t = 2.92$, $p < .01$) and cerebellum volumes were controlled for ($\beta = 0.29$, $t = 3.36$, $p = .001$; see Supplement).

4. Discussion

We had previously observed a 9.6% increase in the striatum in psychopathic individuals (Glenn et al., 2010). The primary aim of the current study was to evaluate whether these findings were replicated after controlling for confounds, to place findings in the context of a meta-analysis, and to make a step towards understanding the mechanism of action. We found that compared with controls, psychopathic individuals had a 9.4% increase in striatal volume. Analyses using a dimensional approach and examining all psychopathy facets yielded a consistent pattern of results. Volumetric increases were observed in all subregions of the striatum in psychopathic individuals. Results are consistent with the findings of two other studies on general community samples (Glenn et al., 2010; Vieira et al., 2015). In addition, supplementary analyses provided preliminary evidence that a similar pattern of findings may extend to females, suggesting generalizability of findings. The inclusion of the results from these 2 independent samples of males and females yields an overall effect size of $d = 0.48$ (see Supplement). Mediation analyses indicated that need for stimulation and impulsivity are potential mechanisms-of-action.

The most influential accounts of striatal involvement in psychopathy have focused on reward processing. The dorsal and ventral striatum in psychopathy have been highlighted in facilitating appetitive behaviors (Glenn and Yang, 2012). This perspective converges with prior findings indicating that psychopathic individuals exhibit reward dominance – an attentional bias toward rewarding stimuli (Frick et al., 2003; Scerbo et al., 1990) – a perspective receiving support from more recent reviews of psychopathy and reward processing (Reidy et al., 2017). Abnormalities in regions of the striatum have been suggested to result in a failure to signal when behaviors are no longer rewarding (Glenn and Yang, 2012). One systematic review of imaging studies concluded that psychopathic and antisocial behavior is associated with increased ventral striatal activity when anticipating rewards (Murray et al., 2018). Others have presented evidence that psychopathic individuals are not so much characterized by abnormal reward expectation as by enhanced communication between the striatum and the dorsomedial prefrontal cortex (Geurts et al., 2016). In contrast, one study has documented psychopathic offenders to have white matter deficits in a striato-thalamo-frontal network connecting the nucleus accumbens, thalamus, and prefrontal cortex (Hoppenbrouwers et al., 2013). Despite interpretive differences, the field is coalescing to the view that psychopaths are characterized by aberrations in reward processing that result in pathological reward-seeking and that striatal abnormalities partly contribute to this pathology.

We sought to move beyond assessing striatal-psychopathy relations to examine possible processes whereby striatal enlargement predisposes to psychopathy. We found that stimulation-seeking and impulsivity partly mediated the striatum-psychopathy relationship, accounting for approximately half of that relationship. Findings support the perspective that impulsive antisocial traits are associated with hypersensitivity of the ventral striatum to the anticipation of rewards (Murray et al., 2018) and are consistent with child imaging research arguing that early enlargement of the nucleus accumbens can predispose to later adolescent risk-taking (Galvan et al., 2006). Relatedly, in adults, hypersensitivity to rewards may predispose individuals to seek stimulating and rewarding experiences, including criminal activities that encapsulate property, drugs, and sex. We caution however that mediation analyses, while testing a causal model, cannot document causality, and that longitudinal research is required to further elucidate mechanisms underlying the striatum-psychopathy relationship. Consideration should also be given to other theoretical perspectives particularly because stimulation-seeking and impulsivity only partly mediated this relationship. For example, the striatum has been implicated in moral decision-making (Darby et al., 2018) and morality is significantly compromised in psychopaths (Fumagalli and Priori, 2012).

What causes enlargement of the striatum in individuals with psychopathy is an unresolved issue. While not the sole cause, this morphological abnormality may be neurodevelopmental in nature. Brain imaging studies have shown that in healthy individuals, striatal volumes decline between adolescence and young adulthood (Sowell et al., 1999). Striatal enlargement may therefore represent neuroanatomical immaturity in psychopathic individuals. Developmental arrest can potentially result in a lack of neural pruning, leading to an increase in synaptic and neuronal density and an increase in striatal volume (Barkataki et al., 2006). Increased gray matter volume in striatal regions may also be reflective of increased neuronal connectivity. Given that the

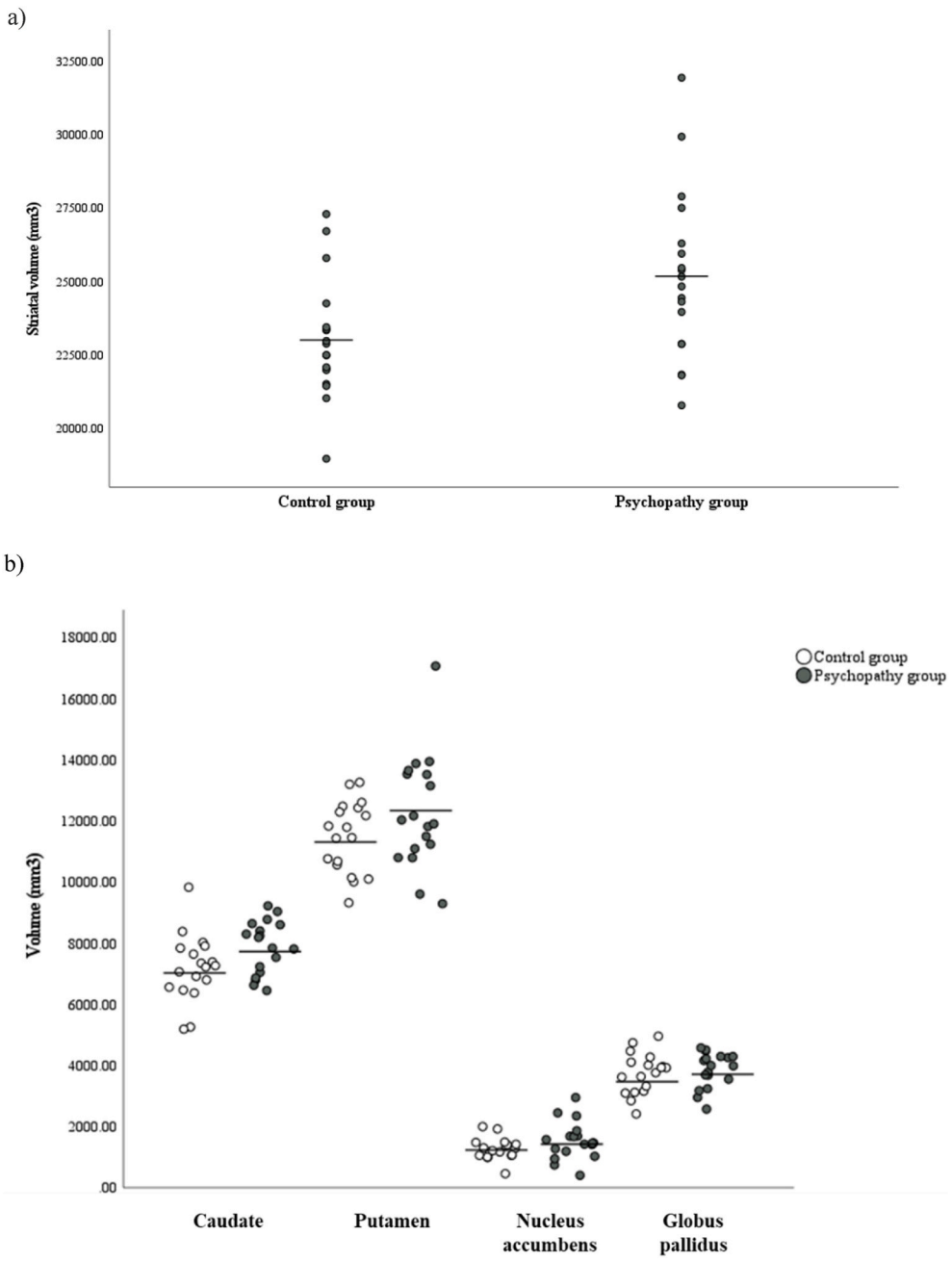

Fig. 4. Scatterplots and means of a) total striatal volumes and b) volumes of striatal subregions in the psychopathic (n = 18) and control (n = 18) groups.

volume of the striatal areas delineated in the current study have been shown to have high heritabilities ranging from 53% to 86% (Gillespie et al., 2017; Kremen et al., 2010), striatal enlargement in psychopathic individuals could be genetic in origin.

Alternatives to a genetic viewpoint should also be considered. Striatal enlargement may have experiential origins that occur later than childhood and beyond the early neurodevelopmental years. Recent radiocarbon-14 dating research has documented that neurogenesis originating in the subventricular zone takes place in the striatum in adulthood, with GABAergic interneurons increasing 10% in humans compared to 0.5% in rodents (Inta et al., 2016). A well-established finding is that environmental influences that include exploratory behavior, exercise, and social experience can stimulate neurogenesis (Moreno-Jiménez et al., 2019). A classic perspective on psychopaths is that they are "on-the-move" and engage in a wide variety of social and behavioral experiences (Cleckley, 1976). This is borne out in the current study as psychopathy scores were positively associated with number and variations in sexual experiences, varied job experiences, increased family size, home and school moves, and more children (Table S4). While environmental influences on striatal enlargement are sparse, basketball training has been associated with an 8.1% increase in striatal volume compared to height-matched controls and controlling for whole brain volume (Park et al., 2011), suggesting that environmental experience can increase striatal size independent of genetic influences. As such, environmental influences on neurogenesis associated with psychopathy could in part account for increased striatal volume in individuals with psychopathic traits – a counter to a genetic perspective.

Several limitations exist. Using structural MRI, this study only examined the anatomical structure of the striatum. Functional processes are not assessed. It is also unknown whether any motion artifacts may have reduced image quality. In addition, the present study was cross-sectional and does not make causal claims about the role of the

striatum on psychopathy. Moreover, although this study expands on prior findings by documenting that enlarged striatal volumes are observed in females with increased psychopathic traits, the sample size is too small to unequivocally address the issue of sex differences in the striatum-antisocial behavior relationship. Further structural MRI studies on larger samples of females are needed.

5. Conclusion

The meta-analytic and new study findings aimed to address limitations of prior investigations, including the lack of attention to females and failure to control for psychiatric confounds. Results indicate striatal enlargement in adults with psychopathic traits. Partial mediation of this relationship through stimulation-seeking and impulsivity suggest that striatal enlargement may predispose to basic personality processes which in turn predispose to psychopathy. Findings provide some support for a reward processing theoretical perspective on the etiology of psychopathy. Delineating the cause of striatal enlargement represents a future research challenge, with neurodevelopmental, genetic, and environmentally-initiated neurogenesis perspectives requiring further resolution. As neurodevelopmental perspectives on psychopathic and antisocial behavior are gaining traction (Wakschlag et al., 2018; Fairchild et al., 2013; Raine, 2018), longitudinal brain imaging alongside assessment of callous-unemotional traits throughout childhood and adolescence could provide much-needed insights (Craig et al., 2019; Ducharme et al., 2011).

Author statement

Olivia Choy: Analysis, Writing, Visualization.

Adrian Raine: Conceptualization, Methodology, Analysis, Writing, Supervision, Funding Acquisition.

Robert Schug: Investigation.

Acknowledgments

This study was supported in part by a grant to the second author from NIH (K02MH01114).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychires.2022.03.006.

References

Báez-Mendoza, R., Schultz, W., 2013. The role of the striatum in social behavior. Front. Neurosci. 7, 233.
Barkataki, I., Kumari, V., Das, M., Taylor, P., Sharma, T., 2006. Volumetric structural brain abnormalities in men with schizophrenia or antisocial personality disorder. Behav. Brain Res. 169, 239–247.
Barkley, R.A., 2011. Barkley Adult ADHD Rating Scale-IV (BAARS-IV). Guilford Press.
Benjamini, Y., Hochberg, Y., 1995. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J. Roy. Stat. Soc. B 57, 289–300.
Boccardi, M., Bocchetta, M., Aronen, H.J., Repo-Tiihonen, E., Vaurio, O., Thompson, P. M., Tiihonen, J., Frisoni, G.B., 2013. Atypical nucleus accumbens morphology in psychopathy: another limbic piece in the puzzle. Int. J. Law Psychiatr. 36, 157–167.
Buckholtz, J.W., Treadway, M.T., Cowan, R.L., Woodward, N.D., Benning, S.D., Li, R., Ansari, M.S., Baldwin, R.M., Schwartzman, A.N., Shelby, E.S., 2010. Mesolimbic dopamine reward system hypersensitivity in individuals with psychopathic traits. Nat. Neurosci. 13, 419–421.
Choy, O., Raine, A., Portnoy, J., Rudo-Hutt, A., Gao, Y., Soyfer, L., 2015. The mediating role of heart rate on the social adversity-antisocial behavior relationship: a social neurocriminology perspective. J. Res. Crime Delinquen. 52, 303–341.
Cleckley, H., 1976. The Mask of Sanity, fifth ed. Mosby, St. Louis, MO, p. 346.
Cope, L.M., Shane, M.S., Segall, J.M., Nyalakanti, P.K., Stevens, M.C., Pearlson, G.D., Calhoun, V.D., Kiehl, K.A., 2012. Examining the effect of psychopathic traits on gray matter volume in a community substance abuse sample. Psychiatr. Res. Neuroimaging 204, 91–100.
Craig, M.C., Mulder, L.M., Zwiers, M.P., Sethi, A., Hoekstra, P.J., Dietrich, A., Baumeister, S., Aggensteiner, P.M., Banaschewski, T., Brandeis, D., 2019. Distinct associations between fronto-striatal glutamate concentrations and callous-unemotional traits and proactive aggression in disruptive behavior. Cortex 121, 135–146.
Dale, A.M., Fischl, B., Sereno, M.I., 1999. Cortical surface-based analysis: I. Segmentation and surface reconstruction. Neuroimage 9, 179–194.
Darby, R.R., Horn, A., Cushman, F., Fox, M.D., 2018. Lesion network localization of criminal behavior. Proc. Natl. Acad. Sci. Unit. States Am. 115, 601–606.
Ducharme, S., Hudziak, J.J., Botteron, K.N., Ganjavi, H., Lepage, C., Collins, D.L., Albaugh, M.D., Evans, A.C., Karama, S., Group, B.D.C., 2011. Right anterior cingulate cortical thickness and bilateral striatal volume correlate with child behavior checklist aggressive behavior scores in healthy children. Biol. Psychiatr. 70, 283–290.
Eisenbarth, H., Alpers, G.W., Conzelmann, A., Jacob, C.P., Weyers, P., Pauli, P., 2008. Psychopathic traits in adult ADHD patients. Pers. Indiv. Differ. 45, 468–472.
Elliott, D.S., Ageton, S.S., Huizinga, D., Knowles, B.A., Canter, R.J., 1983. The Prevalence and Incidence of Delinquent Behavior: 1976-1980. National Estimates of Delinquent Behavior by Sex, Race, Social Class, and Other Selected Variables. Behavioral Research Institute, Boulder, CO.
Fairchild, G., Passamonti, L., Hurford, G., Hagan, C.C., Von Dem Hagen, E.A., Van Goozen, S.H., Goodyer, I.M., Calder, A.J., 2011. Brain structure abnormalities in early-onset and adolescent-onset conduct disorder. Am. J. Psychiatr. 168, 624–633.
Fairchild, G., Van Goozen, S.H., Calder, A.J., Goodyer, I.M., 2013. Research review: evaluating and reformulating the developmental taxonomic theory of antisocial behaviour. JCPP (J. Child Psychol. Psychiatry) 54, 924–940.
First, M.B., Gibbon, M., Spitzer, R.L., Benjamin, L.S., Williams, J.B., 1997a. Structured Clinical Interview for DSM-IV® axis Ii Personality Disorders SCID-II. American Psychiatric Pub.
First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B., 1997b. User's Guide for the Structured Clinical Interview for DSM-IV axis I Disorders SCID-I: Clinician Version. American Psychiatric Pub.
Fischl, B., 2012. FreeSurfer. *Neuroimage* 62, 774–781.
Fischl, B., Dale, A.M., 2000. Measuring the thickness of the human cerebral cortex from magnetic resonance images. Proc. Natl. Acad. Sci. Unit. States Am. 97, 11050–11055.
Frick, P.J., Cornell, A.H., Bodin, S.D., Dane, H.E., Barry, C.T., Loney, B.R., 2003. Callous-unemotional traits and developmental pathways to severe conduct problems. Dev. Psychol. 39, 246.
Fumagalli, M., Priori, A., 2012. Functional and clinical neuroanatomy of morality. Brain 135, 2006–2021.
Galvan, A., Hare, T.A., Parra, C.E., Penn, J., Voss, H., Glover, G., Casey, B., 2006. Earlier development of the accumbens relative to orbitofrontal cortex might underlie risk-taking behavior in adolescents. J. Neurosci. 26, 6885–6892.
Gao, Y., Raine, A., Chan, F., Venables, P.H., Mednick, S.A., 2010. Early maternal and paternal bonding, childhood physical abuse and adult psychopathic personality. Psychol. Med. 40, 1007.
Geurts, D.E., Von Borries, K., Volman, I., Bulten, B.H., Cools, R., Verkes, R.-J., 2016. Neural connectivity during reward expectation dissociates psychopathic criminals from non-criminal individuals with high impulsive/antisocial psychopathic traits. Soc. Cognit. Affect Neurosci. 11, 1326–1334.
Gheorghe, D.A., Li, C., Gallacher, J., Bauermeister, S., 2021. Associations of perceived adverse lifetime experiences with brain structure in UK Biobank participants. JCPP (J. Child Psychol. Psychiatry) 62, 822–830.
Gillespie, N.A., Neale, M.C., Hagler Jr., D.J., Eyler, L.T., Fennema-Notestine, C., Franz, C. E., Lyons, M.J., Mcevoy, L.K., Dale, A.M., Panizzon, M.S., 2017. Genetic and environmental influences on mean diffusivity and volume in subcortical brain regions. Hum. Brain Mapp. 38, 2589–2598.
Glenn, A.L., Raine, A., Yaralian, P.S., Yang, Y., 2010. Increased volume of the striatum in psychopathic individuals. Biol. Psychiatr. 67, 52–58.
Glenn, A.L., Yang, Y., 2012. The potential role of the striatum in antisocial behavior and psychopathy. Biol. Psychiatr. 72, 817–822.
Goto, Y., Grace, A.A., 2008. Limbic and cortical information processing in the nucleus accumbens. Trends Neurosci. 31, 552–558.
Hare, R.D., 2003. The Psychopathy Checklist–Revised. Toronto, ON, 2003.
Hayes, A.F., 2013. Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach. Guilford Press, New York.
Holz, N.E., Boecker-Schlier, R., Buchmann, A.F., Blomeyer, D., Jennen-Steinmetz, C., Baumeister, S., Plichta, M.M., Cattrell, A., Schumann, G., Esser, G., 2017. Ventral striatum and amygdala activity as convergence sites for early adversity and conduct disorder. Soc. Cognit. Affect Neurosci. 12, 261–272.
Hoppenbrouwers, S.S., Nazeri, A., De Jesus, D.R., Stirpe, T., Felsky, D., Schutter, D., Daskalakis, Z.J., Voineskos, A.N., 2013. White matter deficits in psychopathic offenders and correlation with factor structure. PLoS One 8.
Inta, D., Lang, U., Borgwardt, S., Meyer-Lindenberg, A., Gass, P., 2016. Adult Neurogenesis in the Human Striatum: Possible Implications for Psychiatric Disorders. Nature Publishing Group.
Korponay, C., Pujara, M., Deming, P., Philippi, C., Decety, J., Kosson, D.S., Kiehl, K.A., Koenigs, M., 2017. Impulsive-antisocial dimension of psychopathy linked to enlargement and abnormal functional connectivity of the striatum. Biol. Psychiatr.: Cognitive Neuroscience and Neuroimaging 2, 149–157.
Kosson, D.S., Steuerwald, B.L., Forth, A.E., Kirkhart, K.J., 1997. A new method for assessing the interpersonal behavior of psychopathic individuals: preliminary validation studies. Psychol. Assess. 9, 89.
Kremen, W.S., Prom-Wormley, E., Panizzon, M.S., Eyler, L.T., Fischl, B., Neale, M.C., Franz, C.E., Lyons, M.J., Pacheco, J., Perry, M.E., 2010. Genetic and environmental influences on the size of specific brain regions in midlife: the VETSA MRI study. Neuroimage 49, 1213–1223.

Lam, B.Y.H., Yang, Y., Schug, R.A., Han, C., Liu, J., Lee, T.M.C., 2017. Psychopathy moderates the relationship between orbitofrontal and striatal alterations and violence: the investigation of individuals accused of homicide. Front. Hum. Neurosci. 11.
Leutgeb, V., Leitner, M., Wabnegger, A., Klug, D., Scharmüller, W., Zussner, T., Schienle, A., 2015. Brain abnormalities in high-risk violent offenders and their association with psychopathic traits and criminal recidivism. Neuroscience 308, 194–201.
Montes, L.G.A., Ricardo-Garcell, J., De La Torre, L.B., Alcántara, H.P., García, R.B.M., Fernandez-Bouzas, A., Acosta, D.A., 2010. Clinical correlations of grey matter reductions in the caudate nucleus of adults with attention deficit hyperactivity disorder. J. Psychiatr. Neurosci.: JPN 35, 238.
Moreno-Jiménez, E.P., Jurado-Arjona, J., Ávila, J., Llorens-Martín, M., 2019. The social component of environmental enrichment is a pro-neurogenic stimulus in adult c57BL6 female mice. Front. Cell Dev. Biol. 7, 62.
Murray, L., Waller, R., Hyde, L.W., 2018. A systematic review examining the link between psychopathic personality traits, antisocial behavior, and neural reactivity during reward and loss processing. Personality Disorders: Theory, Research, and Treatment 9, 497.
O'doherty, J., Dayan, P., Schultz, J., Deichmann, R., Friston, K., Dolan, R.J., 2004. Dissociable roles of ventral and dorsal striatum in instrumental conditioning. Science 304, 452–454.
Ogloff, J.R., 2006. Psychopathy/antisocial personality disorder conundrum. Aust. N. Z. J. Psychiatr. 40, 519–528.
Onnink, A.M.H., Zwiers, M.P., Hoogman, M., Mostert, J.C., Kan, C.C., Buitelaar, J., Franke, B., 2014. Brain alterations in adult ADHD: effects of gender, treatment and comorbid depression. Eur. Neuropsychopharmacol 24, 397–409.
Park, I.S., Lee, K.J., Han, J.W., Lee, N.J., Lee, W.T., Park, K.A., 2011. Basketball training increases striatum volume. Hum. Mov. Sci. 30, 56–62.
Peters, S.K., Dunlop, K., Downar, J., 2016. Cortico-striatal-thalamic loop circuits of the salience network: a central pathway in psychiatric disease and treatment. Front. Syst. Neurosci. 10, 104.
Pujara, M., Motzkin, J.C., Newman, J.P., Kiehl, K.A., Koenigs, M., 2014. Neural correlates of reward and loss sensitivity in psychopathy. Soc. Cognit. Affect Neurosci. 9, 794–801.
Raine, A., 2018. Antisocial personality as a neurodevelopmental disorder. Annu. Rev. Clin. Psychol. 14, 259–289.
Reidy, D.E., Krusemark, E., Kosson, D.S., Kearns, M.C., Smith-Darden, J., Kiehl, K.A., 2017. The development of severe and chronic violence among youth: the role of psychopathic traits and reward processing. Child Psychiatr. Hum. Dev. 48, 967–982.
Scerbo, A., Raine, A., O'brien, M., Chan, C.-J., Rhee, C., Smiley, N., 1990. Reward dominance and passive avoidance learning in adolescent psychopaths. J. Abnorm. Child Psychol. 18, 451–463.
Schiffer, B., Müller, B.W., Scherbaum, N., Hodgins, S., Forsting, M., Wiltfang, J., Gizewski, E.R., Leygraf, N., 2011. Disentangling structural brain alterations associated with violent behavior from those associated with substance use disorders. Arch. Gen. Psychiatr. 68, 1039–1049.
Smith, S.S., Newman, J.P., 1990. Alcohol and drug abuse-dependence disorders in psychopathic and nonpsychopathic criminal offenders. J. Abnorm. Psychol. 99, 430.
Sowell, E.R., Thompson, P.M., Holmes, C.J., Jernigan, T.L., Toga, A.W., 1999. In vivo evidence for post-adolescent brain maturation in frontal and striatal regions. Nat. Neurosci. 2, 859–861.
Tervo-Clemmens, B., Quach, A., Calabro, F.J., Foran, W., Luna, B., 2020. Meta-analysis and review of functional neuroimaging differences underlying adolescent vulnerability to substance use. Neuroimage 209, 116476.
Thomson, N.D., Kiehl, K.A., Bjork, J.M., 2019. Violence and aggression in young women: the importance of psychopathy and neurobiological function. Physiol. Behav. 201, 130–138.
Vieira, J.B., Ferreira-Santos, F., Almeida, P.R., Barbosa, F., Marques-Teixeira, J., Marsh, A.A., 2015. Psychopathic traits are associated with cortical and subcortical volume alterations in healthy individuals. Soc. Cognit. Affect Neurosci. 10, 1693–1704.
Wakschlag, L.S., Perlman, S.B., Blair, R.J., Leibenluft, E., Briggs-Gowan, M.J., Pine, D.S., 2018. The neurodevelopmental basis of early childhood disruptive behavior: irritable and callous phenotypes as exemplars. Am. J. Psychiatr. 175, 114–130.
Yang, Y., Raine, A., Colletti, P., Toga, A.W., Narr, K.L., 2010. Morphological alterations in the prefrontal cortex and the amygdala in unsuccessful psychopaths. J. Abnorm. Psychol. 119, 546.
Yang, Y., Raine, A., Narr, K.L., Colletti, P., Toga, A.W., 2009. Localization of deformations within the amygdala in individuals with psychopathy. Arch. Gen. Psychiatr. 66, 986–994.