Discover Mental Health

RESEARCH Open Access

Real-time aggression in youth and its connection to region-specific structural brain alterations

Melissa Hatch[1,2], Ahria Dominguez[1,3], Johannah Bashford-Largo[1,4,5], R. James R. Blair[6], Karina S. Blair[7], Matthew Dobbertin[8], Patrick Tyler[4] and Sahil Bajaj[1,9*]

*Correspondence:
Sahil Bajaj
sbajaj@mdanderson.org

Full list of author information is available at the end of the article

Abstract

Aggression is expressed across psychiatric diagnoses. Literature displays associations between aggression and grey matter volume (GMV) in frontal, limbic, and striatal areas. Aggression is commonly assessed using self-report. Real-time aggressive incidents may provide a distinctive representation of the neural correlates of aggression. Structural MRI data were collected from 185 youth: 97 (32F/65 M) in the aggression group (AG) [mean age: 16.22 (SD = 1.10)] and 88 (36F/52 M) in the non-aggressive group (NG) [mean age: 16.29 (SD = 1.31)]. Data were acquired through the Boys Town National Database. Youth were included in AG if they had at least one aggressive incident within the first three months of residential care at Boys Town. FreeSurfer was used to estimate region-specific volumetric parameters following whole brain parcellation into 68 cortical and 14 sub-cortical regions. A multivariate analysis of covariance (MANCOVA) was conducted on pre-hypothesized bilateral brain regions of interest (ROIs) [i.e., middle frontal cortex, orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), pericalcarine, insula, amygdala, and striatum], including age and intracranial volume as covariates. Our MANCOVA showed significant differences in GMV [$F(24,158) = 1.61$, $p \leq 0.05$]. AG showed lower GMV relative to NG in left lateral OFC [$F(1,183) = 4.54$, $p \leq 0.05$], bilateral caudal ACC [$F(1,183) = 5.21–6.37$, $ps \leq 0.05$], bilateral rostral ACC [$F(1,183) = 3.80–5.54$, $ps \leq 0.05$], and bilateral caudate [$F(1,183) = 4.60–5.61$, $ps < 0.05$]. Remaining ROIs had no significant differences in GMV. Our results provide insight regarding the structural brain biomarkers of real-time aggression in youth. These findings provide consistent evidence for region-specific structural alterations in the adolescent brain that may aid in clinical applications across diagnoses.

1 Introduction

Aggression is common in youth and poses a significant burden on both the individual and society [1, 2]. Consistent aggressive behavior in adolescence is associated with an increased probability for low socioeconomic status and unemployment, violence, social isolation, and criminal behavior in adulthood [3]. In addition, the surrounding

environment of aggressive individuals is negatively affected by factors such as increased expenses and impaired daily functioning among caregivers [4]. These factors are likely to escalate as age increases, possibly leading to much higher costs and criminal behavior [4]. Aggression is a trans-diagnostic symptom and is expressed across various psychopathologies [1, 2]. To better understand the relationship between aggressive behavior and its corresponding neural biomarkers, neuroimaging can be a useful tool. The combination of information on underlying psychiatric diagnoses paired with brain biomarkers of aggression may aid in developing individualized treatment strategies [2]. Furthermore, the goal of the current study is to examine real-time aggression, collected through staff observations, as opposed to self-reported aggression. This approach is unique in that it has seldom been explored in previous neuroimaging literature.

A number of studies have examined associations between aggression and brain structure [5–11]. Prior work suggests that higher levels of aggression are associated with structural alterations in cortical regions [5, 10, 12, 13]. For instance, reduced grey matter volume (GMV) within the middle frontal cortex (MFC) and prefrontal regions have been discovered in adults and adolescents who self-report aggression [12, 14–16]. Similarly, the anterior cingulate cortex (ACC) has continually been identified as a region that may play a part in aggressive behavior. Specifically, high aggression scores were associated with cortical thinning of ACC in children and adolescents [13, 17]. In addition, negative associations have been found between dorsal ACC GMV and aggression in children, adolescents, and young adults [5, 7]. Another study found cortical thinning in visual regions (e.g., pericalcarine) in individuals who experienced repeated assaultive trauma and showed higher physical aggression [10, 18]. With respect to the insula, decreases in GMV are prevalent throughout aggression literature [8, 9]. Specifically, negative relationships have been found between aggression subtypes and insular volume in adults and adolescents [12, 19].

Prior work has also identified reduced GMV associated with higher levels of aggression in subcortical regions [17, 20, 21]. Particularly, there are a substantial number of studies linking GMV alterations with limbic brain areas including the amygdala [19, 20, 22, 23]. For example, lower amygdala volume in men has been associated with higher levels of aggression and psychopathic features across the lifespan [20]. In addition, striatal GMV alterations associated with aggression are prevalent throughout literature, however, directionality of these relationships have shown somewhat mixed results [17, 24]

There have been structural inconsistencies throughout the literature in striatal regions including the caudate, nucleus accumbens, and putamen, regarding aggression [13, 17]. While some studies indicate *positive* correlations with caudate volume [13, 17], others indicate the opposite [6, 21, 24, 25]. Likewise, in adults, aggression has been associated with GMV *decreases* and cortical thinning of the orbitofrontal cortex (OFC) [11, 18], though *increases* in the OFC GMV have also been found to be associated with higher levels of aggression in adolescents [13, 26].

To date, most neuroimaging studies assess aggression using either a self-report or a parent/teacher-report questionnaire [7, 9, 11, 13, 17, 27]. These questionnaires focus on evaluating specific disorders and their respective subtypes. Although self-report is a widely used method to collect data, there is always room for skewed responses based on variables such as time constraints and motivational decline [28–30]. Assessing aggressive behavior based on incidents in real time may provide a more expansive view of

aggression that is not self-biased [31] and may provide insight into the neural correlates of aggression that cannot be captured by self-report alone [32]. To address issues such as motivational decline and time constraints, the current study will utilize real-time data collection methods, differentiating it from previous neuroimaging studies assessing aggression using self-report.

The present study looks at volumetric group differences between non-aggressive and aggressive adolescents. Behavioral data were collected through real-time observation, reporting on adolescents who exhibit verbal aggression, physical aggression, property damage, physical assault on adult, and/or physical assault on other youth. These observations were collected over the span of three months. Based on prior published/cited work on aggression, we hypothesized that lower GMV within the MFC, OFC, ACC, pericalcarine, insula, amygdala, and striatum would be observed in adolescents with aggressive behavior compared to non-aggressive adolescents. This study was not preregistered. The analyses were conducted on data that had already been collected prior to the development of specific hypotheses and analytic plans. We recognize the importance of preregistration in promoting transparency and scientific rigor, and we are committed to incorporating preregistration practices in our future prospective research.

2 Methods

2.1 Participants

Of the 185 participants included in this study 97 youth (32F/65 M) were in the aggression group (AG) [mean age: 16.22 (SD = 1.10), mean IQ: 97.67 (SD = 12.33)] and 88 youth (36F/52 M) in the non-aggressive group (NG) [mean age: 16.29 (SD = 1.31), mean IQ: 99.70 (SD = 12.14)]. Youth were included in AG if they had at least one reported aggressive incident across the first three months of residential treatment on Boys Town campus [33]. All participants were recruited from a residential treatment facility, referred for behavioral and/or mental health issues. Exclusion criteria for these participants included active substance dependence, Tourette's syndrome, neurological disorders, claustrophobia, pervasive developmental disorders, head trauma, lifetime history of psychosis, braces, presence of active safety concerns, non-English speaking, and an IQ < 75 [33, 34]. Psychiatric diagnoses were obtained through detailed clinical interviews conducted by an on-site licensed and board-certified child psychiatrist from Boys Town National Research Hospital (BTNRH) [33, 34]. Clinical interviews were conducted with the adolescents, as well as with their legal guardian. Official Institutional Review Board approval at BTNRH was obtained before all data collection. Additionally, each adolescent and parent/legal guardian provided written informed assent/consent prior to participating [33, 34].

2.2 Data collection

2.2.1 Neuroanatomical data

High-resolution structural MRI data (T1-weighted) were obtained at BTNRH using a 3 T Siemens MRI scanner. A 3D magnetization-prepared rapid acquisition gradient echo (MPRAGE) sequence, consisting of 176 axial slices (slice thickness = 1 mm, voxel resolution = $0.9 \times 0.9 \times 1$ mm^3, repetition time = 2200 ms; echo time = 2.48 ms; matrix size = 256×208; field of view (FOV) = 230 mm, and flip angle = 8°), was acquired for

whole-brain anatomical data. Participant head movement in the scanner was reduced to a minimum through close monitoring and instruction from research assistants [34].

2.2.2 General intelligence (IQ)

All estimates of the IQ were derived from the Wechsler Abbreviated Scale of Intelligence II (WASI-II) [35]. IQ was estimated from the matrix reasoning and verbal comprehension subtests. The combined matrix reasoning and verbal comprehension T-scores were used to calculate the Full-Scale IQ (FSIQ). FSIQ scores have previously been found to be strongly correlated ($r = 0.92$) with scores on the full Wechsler Adult Intelligence Scale (WAIS)-III and highly reliable (α = 0.98) [36, 37].

2.2.3 Real-time aggression data

Aggression data were obtained from the Boys Town National Database [38] which consisted of a report of serious aggressive incidents. These data were collected daily based on staff observations, reported to a program supervisor, and documented within 24 h. Incident reports made by staff members included five aggression codes: verbal aggression, physical aggression, property damage, physical assault on adult, and physical assault on youth [33]. Each code had specific criteria, adhering to the training manual. The codes are as follows [38]:

Verbal Aggression "Program participant engages in verbally threatening, harassing, and/or aggressive behavior towards another person(s) with an attempt to intimidate. Behaviors could include threatening stares, body movements, gestures, swearing aggressively, etc. (This does not include complaining or teasing, unless it is coupled with other threatening comments or gestures and intimidation occurs)."

Physical Aggression: "Program participant engages in physically aggressive behaviors such as throwing objects, slamming doors, overturning furniture, or slamming fists. There is an attempt at intimidation, but there is no physical contact between people. This code should not be used for physical assault unless the above behaviors were also displayed."

Property Damage:

"Program participant has damaged property intentionally."

Physical Assault on Adult: "Program participant assaults a staff member or other adult. Injury may or may not have resulted, but intentional aggressive physical contact occurred (e.g., biting, choking, jumping on, kicking, punching, scratching, pushing, spitting at)."

Physical Assault on Youth: "Program participant assaults a youth. Injury may or may not have resulted, but intentional aggressive physical contact occurred (e.g. biting, choking, jumping on, kicking, punching, scratching, pushing, spitting at)."

Along with incident details, reports included the date and time of the incident. The total number of aggressive incidents within the first three months of program placement was collected and calculated towards the participant's aggression level.

2.3 Image preprocessing

To estimate volumetric parameters and process anatomical brain images, the "recon-all" pipeline from the FreeSurfer (RRID:SCR_001847) toolbox (Version 6.0; https://surfer.nmr.mgh.harvard.edu) was used [39, 40]. The structural image processing steps included

head motion-correction, brain extraction, automated transformation to the standard MINI template space, volumetric segmentation into cortical and sub-cortical matter, intensity correction, and parcellation of the cerebral cortex into gyral and sulcal matter [41]. For full details, see [39, 40, 42]. Standard quality control steps were performed in FreeSurfer (RRID:SCR_001847) to ensure accuracy. This included head motion correction, normalization, and skull stripping [43]. Surface boundaries on the white and grey matter interface and the edge of the grey matter (pial surface) were generated, where surface estimation defects were automatically refined. Each of these steps was completed using FreeSurfer's (RRID:SCR_001847) "recon-all" pipeline [39, 40]. It is important to note that although head motion is not explicitly corrected for as a covariate in our analyses, "recon-all" preprocessing steps are robust to motion including robust registration and skull stripping using mri_robust_register, which is designed to be tolerant to motion artifacts in T1-weighted images [44]. In addition, brain extraction (skullstrip) has adaptive techniques that fail under high motion [45]. Lastly, visual quality control steps to rate motion artifacts [45] were conducted, where the subset of 185 participants that were included in the current study (out of 616 total participants), passed.

Additional quality control measures adhered to the ENIGMA (RRID:SCR_005515) cortical surface segmentations protocol (for full details and scripts, http://enigma.usc.edu/). This protocol includes the detection of outliers, plotting cortical surface segmentations, and checking external views of segmentations via different angles. If subjects had structural outliers, they were inspected for segmentation issues prior to moving forward with the protocol. To ensure that all lobes were present and that labeling was correct, surface reconstructions were checked. Subjects were rated as either "pass" (no issues with QC), "moderate" (failure of some regions), or "fail" (severe concerns) (all steps developed by the ENIGMA consortium [RRID:SCR_005515]) [46].

2.4 Data analysis

2.4.1 Demographics characteristics and covariates

Group differences for age, IQ, and intracranial volume (ICV) were examined through independent sample *t*-tests, and those for sex, medication status, and psychiatric diagnoses were examined via x^2 test. See Table 1 for more details.

2.4.2 Aggression group

The two groups of participants included AG with an aggression mean greater than zero, and NG with an aggression mean of zero. Their aggression mean was derived from their total number of aggressive incidents across all five incident categories within the first three months of treatment. For descriptive information on each incident category, mean and standard deviation of each category was calculated. For more detailed insight into the composition of AG, we calculated the percentage of participants within AG that had more than one aggressive incident. Self-reported aggression scores from the Reactive-Proactive Aggression Questionnaire (RPQ) were available for 144 of the 185 adolescents in the current study, which reflected pre-admission aggression levels, as it was administered shortly after admission to Boys Town. To evaluate the validity of our group classifications, we conducted a Pearson's correlation between RPQ total scores, and continuous real-time aggression means.

Table 1 Demographic Characteristics

Characteristics	AG (N = 97)	NG (N = 88)	*p*-value (Chi-squared/two-sample t-test)
Sex (F/M)	32/65	36/52	0.27
Mean Age (SD)	16.22 (1.10)	16.29 (1.31)	0.69
Mean IQ (SD)	97.67 (12.33)	99.70 (12.14)	0.26
ICV ($\times 10^6$) in mm^3 (SD)	1.51 (0.15)	1.50 (0.15)	0.69
Psychiatric Disorders (N)			
MDD (%)	12 (12.37)	12 (13.64)	0.80
SAD (%)	20 (20.62)	25 (28.41)	0.22
GAD (%)	24 (24.74)	25 (28.41)	0.57
PTSD (%)	18 (18.56)	10 (11.36)	0.17
CD (%)	65 (67.01)	57 (64.77)	0.75
ADHD (%)	70 (72.16)	65 (73.86)	0.80
ODD (%)	76 (78.35)	64 (72.73)	0.37
Medications (N)			
Antipsychotic (%)	10 (10.31)	7 (7.95)	0.58
Stimulants (%)	24 (24.74)	16 (18.18)	0.28
SSRIs (%)	15 (15.46)	16 (18.18)	0.62

AG = Aggression Group; NG = Non-Aggressive Group; SD = Standard Deviation; IQ = Intelligent Quotient; ICV = Intracranial Volume; MDD = Major Depressive Disorder; SAD = Social Anxiety Disorder; GAD = Generalized Anxiety Disorder; PTSD = Post-Traumatic Stress Disorder; CD = Conduct Disorder; ADHD = Attention-Deficit/Hyperactivity Disorder; ODD = Oppositional Defiant Disorder; SSRIs = Selective Serotonin Reuptake Inhibitors

2.4.3 Region-specific group differences in GMV

The pipelines *aparc.annot* and *mri_segstats* in FreeSurfer (RRID:SCR_001847) were used to estimate region-specific volume parameters. FreeSurfer (RRID:SCR_001847) was used to parcellate the whole brain into 68 (34R/34L) cortical [41], and 14 (7R/7L) sub-cortical [47] regions using the Desikan-Killiany atlas [41] for cortical regions and the FreeSurfer default subcortical automated segmentation [47] for subcortical regions. The ROIs used in the analyses included bilateral MFC, OFC, ACC, pericalcarine, insula, amygdala, and striatum (caudate, nucleus accumbens, putamen). Region-specific volumetric parameters were compared between AG and NG using multivariate analysis of covariance (MANCOVA). Age and ICV were used as covariates in all analyses [48]. A threshold of $p \leq 0.05$ was used to interpret region-specific differences in GMV. Multiple comparison correction was not included in the current study. With respect to our exploratory analyses of the individual regions (Table 2), it is advised that they are taken with caution, as they would not survive Bonferroni multiple comparison testing.

2.5 Follow-up analysis

2.5.1 Potential confounds

Several participants were on various categories of psychiatric medications including antipsychotics ($N = 17$), stimulants ($N = 40$), and Selective Serotonin Reuptake Inhibitors (SSRIs) ($N = 31$). See Table 1 for all details regarding medications including prevalence rates and significant levels between groups. Although there were no differences between groups on medications, to account for any potential confounds, a follow-up MANCOVA was performed, including the psychiatric medications mentioned above as covariates, maintaining age and ICV as covariates. As described in Sect. 2.4.3, multiple comparison correction was not applied for our exploratory analyses of the contributory role of individual regions to the MANCOVA group effect and therefore it is advised that significant regions reported in Table 3 are to be taken with caution.

Table 2 Differences in Grey Matter Volume (GMV): Aggressive Adolescents vs. Non-Aggressive Adolescents

MANCOVA for GMV (covariates: age & ICV)						
Regions	**p-value**		**F-value**		**Effect Size: pη²**	
	LH	***RH***	***LH***	***RH***	***LH***	***RH***
Lateral Orbitofrontal Cortex	0.03**	0.06*	4.54	3.67	0.02	0.02
Medial Orbitofrontal Cortex	0.85	0.84	0.04	0.04	0.00	0.00
Rostral Middle Frontal Cortex	0.10	0.44	2.75	0.59	0.02	0.00
Caudal Middle Frontal Cortex	0.67	0.09	0.19	2.91	0.00	0.02
Rostral Anterior Cingulate	0.05**	0.02**	3.80	5.54	0.02	0.03
Caudal Anterior Cingulate	0.02**	0.01**	5.21	6.37	0.03	0.03
Pericalcarine	0.44	0.49	0.59	0.48	0.00	0.00
Insula	0.77	0.53	0.09	0.40	0.00	0.00
Amygdala	0.54	0.34	0.38	0.93	0.00	0.01
Caudate	0.02**	0.03**	5.61	4.60	0.03	0.03
Nucleus Accumbens	0.89	0.95	0.02	0.00	0.00	0.00
Putamen	0.66	0.74	0.20	0.11	0.00	0.00

MANCOVA = Multivariate Analysis of Covariance; ICV = intracranial volume; LH/RH = Left/Right Hemisphere

**$p \leq 0.05$ (aggressive adolescents < non-aggressive adolescents)

*Regions approaching significance

Table 3 Medication Effects Follow-up Analysis

MANCOVA for GMV (covariates: age, ICV, antipsychotics, stimulants, SSRIs)						
Regions	***p*-values**		**F-value**		**Effect Size: pη²**	
	LH	**RH**	**LH**	**RH**	**LH**	**RH**
Lateral Orbitofrontal Cortex	0.03**	0.06*	4.80	3.69	0.03	0.02
Medial Orbitofrontal Cortex	0.75	0.70	0.11	0.15	0.00	0.00
Rostral Middle Frontal Cortex	0.09	0.42	2.89	0.66	0.02	0.00
Caudal Middle Frontal Cortex	0.63	0.13	0.23	2.37	0.00	0.01
Rostral Anterior Cingulate	0.06*	0.02**	3.52	5.25	0.02	0.03
Caudal Anterior Cingulate	0.02**	0.01**	5.48	6.70	0.03	0.04
Pericalcarine	0.35	0.54	0.88	0.38	0.01	0.00
Insula	0.76	0.52	0.10	0.42	0.00	0.00
Amygdala	0.45	0.25	0.58	1.34	0.00	0.01
Caudate	0.02**	0.03**	5.37	4.56	0.03	0.03
Nucleus Accumbens	0.92	0.92	0.01	0.01	0.00	0.00
Putamen	0.52	0.63	0.41	0.23	0.00	0.00

MANCOVA = Multivariate Analysis of Covariance; ICV = intracranial volume; SSRIs = Selective Serotonin Reuptake Inhibitors; LH/RH, Left/Right Hemisphere

**$p \leq 0.05$ (aggressive adolescents < non-aggressive adolescents)

*Regions approaching significance

3 Results

3.1 Demographic characteristics and covariates

There were no significant differences in sex ($X^2 = 1.25$, $p = 0.27$), age [$t(170) = -0.40$, $p = 0.69$], IQ [$t(183) = -1.13$, $p = 0.26$] or ICV [$t(183) = 0.41$, $p = 0.69$] (Table 1).

3.2 Aggression scores

Mean and standard deviation of each aggression incident category are as follows, verbal aggression [Mean = 2.73 (SD = 3.42)], physical aggression [Mean = 0.92 (SD = 1.29)], property damage [Mean = 0.15 (SD = 0.36)], physical assault on adult [Mean = 0.02 (SD = 0.14)], physical assault on youth [Mean = 0.44 (SD = 0.79)]. Out of the 97 participants in AG,

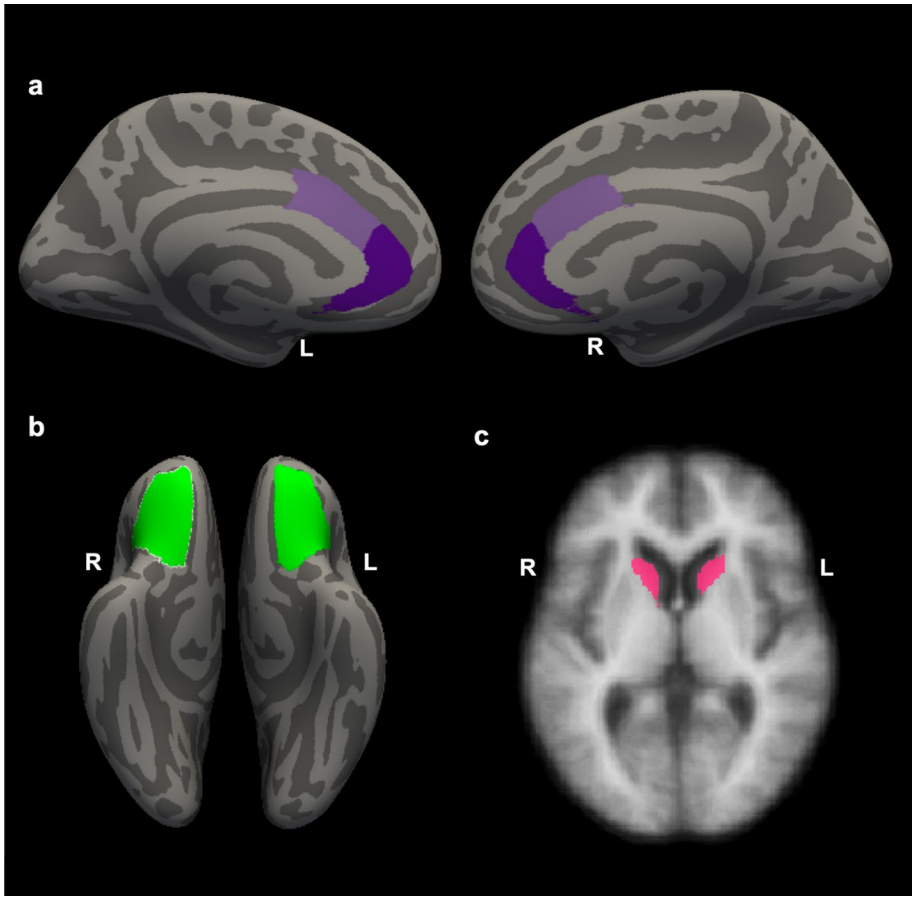

Fig. 1 Region-Specific Differences in Grey Matter Volume (GMV) Grey matter volume (GMV) of the bilateral rostral (dark purple; **a**) and caudal (light purple; **a**) anterior cingulate cortex (ACC), left lateral orbitofrontal cortex (OFC) (green; **b**), and bilateral caudate (pink; **c**) was significantly different between adolescents who were aggressive and adolescents who were not aggressive (aggressive adolescents < non-aggressive adolescents). GMV of the right lateral OFC (green; **b**) was approaching significance where lower GMV was observed in adolescents who were aggressive (aggressive adolescents < non-aggressive adolescents), *figure created using FreeSurfer (RRID:SCR_001847)*

62 of them exhibited more than one aggressive incident (63.92%). Our Pearson correlation revealed a significant positive association between RPQ total scores, and real-time aggression mean scores ($r = 0.25$, $p = 0.003$).

3.3 Region-specific group differences in GMV

Our MANCOVA showed significant volumetric group differences [$F(24,158) = 1.61$, $p = 0.05$]. Specifically, at $p \leq 0.05$, there were significant volumetric differences in the left lateral OFC [$F(1,183) = 4.54$, $p = 0.03$], left caudal ACC [$F(1,183) = 5.21$, $p = 0.02$], right caudal ACC [$F(1,183) = 6.37$, $p = 0.01$], left rostral ACC [$F(1,183) = 3.80$, $p = 0.05$], right rostral ACC [$F(1,183) = 5.54$, $p = 0.02$], left caudate [$F(1,183) = 5.61$, $p = 0.02$], and right caudate [$F(1,183) = 4.60$, $p = 0.03$] where lower GMV was observed in adolescents in AG (see Fig. 1). For full details including effect sizes and results approaching significance, see Table 2.

3.4 Follow-up findings

Our follow-up MANCOVA using the three psychiatric medications as covariates (antipsychotics, stimulants, and SSRIs) sustained the significant results found in the main analysis [$F(24,155) = 1.60$, $p = 0.05$]. For full details see Table 3.

4 Discussion

The aim of this study was to assess morphometric alterations in GMV of pre-defined ROIs (MFC, OFC, ACC, pericalcarine, insula, amygdala, and striatum) in adolescents exhibiting aggression compared with non-aggressive adolescents. We found that GMV of the left lateral OFC, bilateral caudal ACC, bilateral rostral ACC, and bilateral caudate was significantly lower in adolescents exhibiting aggression as compared to non-aggressive adolescents. Additionally, GMV of the right lateral OFC approached significance, where adolescents exhibiting aggression had lower GMV compared with non-aggressive adolescents. We did not see any significant GMV differences in the MFC, pericalcarine, insula, amygdala, nucleus accumbens, or putamen.

Our current findings of lower GMV in orbitofrontal, cingulate, and striatal regions regarding aggression are highly supported in the literature [6, 7, 11, 17, 18, 24]. As these regions are commonly reported to be interconnected both structurally [49–51] and functionally [52–54], we believe that lower GMV in these areas may contribute to shared developmental issues. Evidence suggests that behavioral manifestations are likely the result of interactions across multiple white matter tracts, rather than a single brain region [55]. Furthermore, although white matter integrity was not assessed in the current study, it is important to note that individual differences within white matter tracts provide insight into factors that may play a role in a variety of cognitive processes, such as decision making [56–58].

Cortico-striatal connections are commonly reported throughout the literature, including structural connections projecting from the OFC and ACC terminating in the caudate nucleus [49, 50]. Functional connectivity has also been detected within cortico-striatal regions, often associated with decision-making [59, 60]. In the current study we saw lower GMV in cortical regions (i.e., ACC, OFC) as well as striatal regions (i.e., caudate). In addition, the OFC, ACC, and caudate have all been implicated in decision-making processes [61–63]. Therefore, we believe GMV deficits in the current regions could be representative of decision-making abnormalities in the population studied.

Four caveats should be considered within the current study. The first being that we did not have data regarding potential prenatal substance exposures, or whether youth were raised by their biological families, which may impact the specificity and generalizability of the results, as this heterogeneity could potentially have led to neurodevelopmental or behavioral outcomes [64, 65]. In addition, several of our participants were prescribed psychiatric medications including SSRIs, antipsychotics, and stimulants. However, the rate of psychiatric medication usage was not significantly different between groups (see Table 1). Furthermore, our follow-up MANCOVA included SSRIs, antipsychotics, and stimulants as covariates, and our results strongly resembled those of our main analysis. Therefore, our results were not driven by medication use.

The second caveat is that the adolescents included in this study received residential treatment in the Boys Town Residential Treatment Center. However, all data were collected shortly after their arrival to the Boys Town campus (within 3 months) and all

participants across the two groups received treatment. Therefore, it is unlikely that treatment played a significant role in structural variance or the suppression of aggressive behaviors. We did not have access to detailed historical or antecedent data on aggressive incidents prior to residential admission, therefore we cannot say for sure if adolescents in NG were temporarily suppressing aggressive behaviors during the three months that aggressive incidents were measured. However, we do feel confident that aggressive behavior was not temporarily suppressed for the following three reasons: (1) We observed a significant positive association between real time aggression and self-reported pre-admission aggression levels. (2) The standard of care at Boys Town's Residential Treatment Center typically includes extensive referral paperwork including medical records detailing prior visits to psychiatrists, pediatricians, psychotherapists, etc., which is reviewed prior to admission to ensure that the patient will benefit from residential care. Although we do not have access to these data in our current study, we do believe this extensive review of antecedent medical record data provides justification that the behaviors that our participants were presenting with, including aggressive behaviors, were likely present prior to admission to residential treatment. (3) Admission into residential treatment, where there are high rates of disruptive behavior disorders, would assume that the youth are exhibiting one or more conditions severely enough that no lower level of care was appropriate and all outpatient interventions had failed, therefore suppression of aggressive behavior is unlikely.

Another notable caveat is the limitation to FreeSurfer's precision in automated segmentation. Inaccuracies have particularly been noted in small subregions [66, 67], including the amygdala and cingulate gyrus [67–71], both regions included within the ROIs of the current study. Specifically, prior work has noted that the Desikan-Killiany atlas [41] often mistakenly labels the anterior mid-cingulate cortex (aMCC) as the caudal ACC [67]. Therefore, caution is warranted in the over-interpretation of findings localized to regions such as the pACC, aMCC, and medial temporal lobe, as the Desikan-Killiany atlas [41] may not align seamlessly with cytoarchitectonic definitions [67]. Therefore, we recommend that future studies utilize multi-modal imaging or atlas refinement techniques (e.g., ex vivo-informed atlases or ultra-high-resolution MRI) when higher anatomical precision is required, especially in smaller subregions.

Lastly, the current MANCOVA results indicate that there were group differences across the regions studied. However, we did not correct for multiple comparisons on our follow-up analyses examining the contributory role of our hypothesized individual regions. The results indicated that individual regions showed group differences but not to a strength that would survive multiple comparison correction. As such, the individual region results should be treated with caution.

In conclusion, this study is one of very few analyzing region-specific structural differences reflective of real-time aggressive episodes rather than data acquired through a questionnaire format. In line with previous work, we found negative relationships between aggression and GMV of the left lateral OFC, bilateral caudal ACC, bilateral rostral ACC, and bilateral caudate. In addition, we found marginal negative relationships between aggression and GMV in the right lateral OFC. Our results provide insight regarding the structural brain biomarkers of real-time aggression. Based on our finding of lower GMV in regions supporting decision making including the ACC, OFC, and caudate, we believe our results may reflect discrepancies in higher decision-making

processes. This is important because it may aid clinicians in identifying a target behavior when developing treatment plans designed to reduce aggressive behaviors.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1007/s44192-025-00273-8.

Supplementary Material 1

Acknowledgements
This project was in part supported by the National Institute of Mental Health award number K22-MH109558 (RJRB). We would specifically like thank Ron Copsey, Kim VanHorn, Michael Wright, Mark Timm, Michelle Kelly, and Sarah Johnson for their assistance in data collection. In addition, we would like to thank all subjects for participation in our study.

Author contributions
A. D., M. H., J. B. L., M. D., and P. T. collected behavioral and imaging data. M. H. and S. B. pre-processed the T1w acquisitions and analyzed the data. M. H. drafted the manuscript. M. D. provided psychiatric expertise throughout the study. R. J. B., K. B., and P. T. contributed to the conceptual design of the work and writing of the manuscript. All authors revised and approved the final version. S. B. supervised all aspects of the study and contributed to the writing of the manuscript.

Funding
This project was in part supported by the National Institute of Mental Health award number K22-MH109558 (RJRB). The funders did not contribute in any way to the design and conduct of this research; data collection, management, analysis, or interpretation; the preparation, review, or final approval of the manuscript; or the process of submitting the manuscript for publication.

Data availability
Due to IRB restrictions, the data used in this project are not publicly available. However, upon reasonable request, the data may be made available by the corresponding author.

Code availability
To estimate volumetric parameters and process anatomical brain images, the "recon-all" pipeline from the FreeSurfer (RRID:SCR_001847) toolbox (Version 6.0; https://surfer.nmr.mgh.harvard.edu) was used. Quality control measures adhered to the ENIGMA (RRID:SCR_005515) cortical surface segmentations protocol (for full details and scripts, http://enigma.usc.edu/).

Declarations

Conflict of interest
Sahil Bajaj is on the editorial board of *Discover Mental Health* and receives no compensation as member of the editorial board. There are no other conflicts of interest for the authors to disclose.

Ethics approval
All authors declare that the study procedures comply with the ethical standards and guidelines of the national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, revised in 2008. The study was approved by the Boys Town National Research Hospital IRB.

Consent to participate
Informed consent was obtained from all participant's parents/legal guardians prior to any study procedures. In addition, assent was obtained from all participants prior to any study procedures.

Consent to publish
Informed consent for publication of aggregate data was obtained from all participant's parents/legal guardians prior to any study procedures. In addition, assent was obtained from all participants prior to any study procedure. This manuscript does not contain any individual or identifiable participant data.

Author details
[1]Multimodal Clinical Neuroimaging Laboratory (MCNL), Center for Neurobehavioral Research, Boys Town National Research Hospital, Boys Town, NE, USA
[2]Present address: Department of Neurological Sciences, College of Medicine, University of Nebraska Medical Center (UNMC), Omaha, NE, USA
[3]Present address: Clinical Health, Emotion, and Neuroscience (CHEN) Laboratory, Department of Neurological Sciences, College of Medicine, University of Nebraska Medical Center (UNMC), Omaha, NE, USA
[4]Present address: Child and Family Translational Research Center, Boys Town National Research Hospital, Boys Town, NE, USA
[5]Center for Brain, Biology, and Behavior, University of Nebraska-Lincoln, Lincoln, NE, USA
[6]Child and Adolescent Mental Health Centre, Mental Health Services, Capital Region of Denmark, Copenhagen, Denmark
[7]Center for Neurobehavioral Research, Boys Town National Research Hospital, Boys Town, NE, USA
[8]Child and Adolescent Psychiatric Inpatient Center, Boys Town National Research Hospital, Boys Town, NE, USA
[9]Present address: Department of Cancer Systems Imaging, Division of Diagnostic Imaging, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Received: 7 March 2025 / Accepted: 5 August 2025
Published online: 18 August 2025

References

1. Bambauer KZ, Connor DF. Characteristics of aggression in clinically referred children. CNS Spectr. 2005;10(9):709–18. https://doi.org/10.1017/S1092852900019702.
2. Magalotti SR, Neudecker M, Zaraa SG, McVoy MK. Understanding chronic aggression and its treatment in children and adolescents. Curr Psychiatry Rep. 2019;21(12):1–12. https://doi.org/10.1007/S11920-019-1105-1/METRICS.
3. Buchmann A, Hohmann S, Brandeis D, Banaschewski T, Poustka L. Aggression in children and adolescents. Curr Top Behav Neurosci. 2014;17:421–42. https://doi.org/10.1007/7854_2013_261.
4. Raaijmakers MA, Posthumus JA, van Hout BA, van Engeland H, Matthys W. Cross-sectional study into the costs and impact on family functioning of 4-year-old children with aggressive behavior. Prev Sci. 2011;12(2):192. https://doi.org/10.1007/S11121-011-0204-Y.
5. Boes AD, Tranel D, Anderson SW, Nopoulos P. Right anterior cingulate: a neuroanatomical correlate of aggression and defiance in boys. Behav Neurosci. 2008;122(3):677–84. https://doi.org/10.1037/0735-7044.122.3.677.
6. Fairchild G, Passamonti L, Hurford G, et al. Brain structure abnormalities in early-onset and adolescent-onset conduct disorder. Am J Psychiatry. 2011;168(6):624–33. https://doi.org/10.1176/APPI.AJP.2010.10081184.
7. Gorka AX, Norman RE, Radtke SR, Carré JM, Hariri AR. Anterior cingulate cortex gray matter volume mediates an association between 2D:4D ratio and trait aggression in women but not men. Psychoneuroendocrinology. 2015;56:148–56. https://doi.org/10.1016/J.PSYNEUEN.2015.03.004.
8. Long H, Fan M, Li Q, et al. Structural and functional biomarkers of the insula subregions predict sex differences in aggression subscales. Hum Brain Mapp. 2022;43(9):2923–35. https://doi.org/10.1002/HBM.25826.
9. Naaijen J, Mulder LM, Ilbegi S, et al. Specific cortical and subcortical alterations for reactive and proactive aggression in children and adolescents with disruptive behavior. NeuroImage: Clinical. 2020;27: 102344. https://doi.org/10.1016/J.NICL.2020.102344.
10. Sihag S, Naze S, Taghdiri F, et al. Functional brain activity constrained by structural connectivity reveals cohort-specific features for serum neurofilament light chain. Commun Med. 2022. https://doi.org/10.1038/S43856-021-00065-5.
11. Wang H, Zhu WF, Xia LX. Brain structural correlates of aggression types from the perspective of disinhibition–control: a voxel-based morphometric study. Curr Psychol. 2022. https://doi.org/10.1007/S12144-022-02712-Z.
12. Coccaro EF, Fitzgerald DA, Lee R, McCloskey M, Phan KL. Frontolimbic morphometric abnormalities in intermittent explosive disorder and aggression. Biol Psychiatry Cogn Neurosci Neuroimaging. 2016;1(1):32–8. https://doi.org/10.1016/J.BPSC.2015.09.006.
13. Yang Y, Joshi SH, Jahanshad N, Thompson PM, Baker LA. Neural correlates of proactive and reactive aggression in adolescent twins. Aggress Behav. 2017;43(3):230–40. https://doi.org/10.1002/AB.21683.
14. Gregory S, Ffytche D, Simmons A, et al. The antisocial brain: psychopathy matters: a structural MRI investigation of antisocial male violent offenders. Arch Gen Psychiatry. 2012;69(9):962–72. https://doi.org/10.1001/ARCHGENPSYCHIATRY.2012.222.
15. Raine A, Lencz T, Bihrle S, LaCasse L, Colletti P. Reduced prefrontal gray matter volume and reduced autonomic activity in antisocial personality disorder. Arch Gen Psychiatry. 2000;57(2):119–27. https://doi.org/10.1001/ARCHPSYC.57.2.119.
16. Yang Y, Raine A, Lencz T, Bihrle S, LaCasse L, Colletti P. Volume reduction in prefrontal gray matter in unsuccessful criminal psychopaths. Biol Psychiatry. 2005;57(10):1103–8. https://doi.org/10.1016/J.BIOPSYCH.2005.01.021.
17. Ducharme S, Hudziak JJ, Botteron KN, et al. Right anterior cingulate cortical thickness and bilateral striatal volume correlate with child behavior checklist aggressive behavior scores in healthy children. Biol Psychiatry. 2011;70(3):283–90. https://doi.org/10.1016/J.BIOPSYCH.2011.03.015.
18. Bounoua N, Miglin R, Spielberg JM, Sadeh N. Childhood assaultive trauma and physical aggression: links with cortical thickness in prefrontal and occipital cortices. NeuroImage: Clinical. 2020;27: 102321. https://doi.org/10.1016/J.NICL.2020.102321.
19. Raschle NM, Menks WM, Fehlbaum LV, Tshomba E, Stadler C. Structural and functional alterations in right dorsomedial prefrontal and left insular cortex co-localize in adolescents with aggressive behaviour: an ALE meta-analysis. PLoS ONE. 2015;10(9): e0136553. https://doi.org/10.1371/JOURNAL.PONE.0136553.
20. Pardini DA, Raine A, Erickson K, Loeber R. Lower amygdala volume in men is associated with childhood aggression, early psychopathic traits, and future violence. Biol Psychiatry. 2014;75(1):73–80. https://doi.org/10.1016/J.BIOPSYCH.2013.04.003.
21. Widmayer S, Sowislo JF, Jungfer HA, et al. Structural magnetic resonance imaging correlates of aggression in psychosis: a systematic review and effect size analysis. Front Psychiatry. 2018. https://doi.org/10.3389/FPSYT.2018.00217.
22. Bannon SM, Salis KL, Daniel OK. Structural brain abnormalities in aggression and violent behavior. Aggress Violent Behav. 2015;25:323–31. https://doi.org/10.1016/J.AVB.2015.09.016.
23. Göttlich M, Buades-Rotger M, Wiechert J, Beyer F, Krämer UM. Structural covariance of amygdala subregions is associated with trait aggression and endogenous testosterone in healthy individuals. Neuropsychologia. 2022;165: 108113. https://doi.org/10.1016/J.NEUROPSYCHOLOGIA.2021.108113.
24. Miglin R, Rodriguez S, Bounoua N, Sadeh N. A multidimensional examination of psychopathy traits and gray matter volume in adults. Soc Cogn Affect Neurosci. 2022;17(7):662–72. https://doi.org/10.1093/scan/nsab131.
25. Xavier Castellanos F, Lee PP, Sharp W, et al. Developmental trajectories of brain volume abnormalities in children and adolescents with attention-deficit/hyperactivity disorder. JAMA. 2002;288(14):1740–8. https://doi.org/10.1001/JAMA.288.14.1740.
26. Hoptman MJ, Volavka J, Weiss EM, et al. Quantitative MRI measures of orbitofrontal cortex in patients with chronic schizophrenia or schizoaffective disorder. Psychiatry Res Neuroimaging. 2005;140(2):133–45. https://doi.org/10.1016/J.PSCYCHRESNS.2005.07.004.
27. Zhu X, Wang K, Cao A, Zhang Y, Qiu J. Personality traits and negative affect mediate the relationship between cortical thickness of superior frontal cortex and aggressive behavior. Neurosci Lett. 2020;718: 134728. https://doi.org/10.1016/J.NEULET.2019.134728.

28. Richard R, RChris F, FRobert K. Handbook of research methods in personality psychology. (Robins Richard, Fraley C, Krueger R, eds.). Guilford Publications; 2009. Accessed January 23, 2023. https://books.google.com/books/about/Handbook_of_Research_Methods_in_Personal.html?id=-VTvN3aPw8sC
29. Pryor JB, Gibbons FX, Wicklund RA, Fazio RH, Hood R. Self-focused attention and self-report validity. J Pers. 1977;45(4):513–27. https://doi.org/10.1111/J.1467-6494.1977.TB00168.X.
30. Morsbach SK, Prinz RJ. Understanding and improving the validity of self-report of parenting. Clin Child Fam Psychol Rev. 2006;9(1):1–21. https://doi.org/10.1007/S10567-006-0001-5.
31. Wojciszke B. Morality and competence in person- and self-perception. Eur Rev Soc Psychol. 2005;16(1):155–88. https://doi.org/10.1080/10463280500229619.
32. Wilkins D, Khan M, Stabler L, Newlands F, Mcdonnell J. Evaluating the quality of social work supervision in UK children's services: comparing self-report and independent observations. Clin Soc Work J. 2018;46(4):350–60. https://doi.org/10.1007/S10615-018-0680-7/TABLES/5.
33. Blair RJ, Zhang RU, Bashford-Largo J, et al. Reduced neural responsiveness to looming stimuli is associated with increased aggression. Soc Cogn Affect Neurosci. 2021;16(10):1091–9. https://doi.org/10.1093/SCAN/NSAB058.
34. Bashford-Largo J, Blair RJR, Blair KS, et al. Cortical volume alterations in the limbic network in adolescents with high reactive aggression. Dev Psychopathol. 2025. https://doi.org/10.1017/S0954579424000750.
35. Wechsler D. Wechsler abbreviated scale of intelligence-second edition (WASI-II). NCS Pearson; 2011. Accessed January 24, 2023. https://www.pearsonassessments.com/store/usassessments/en/Store/Professional-Assessments/Cognition-%26-Neuro/Wechsler-Abbreviated-Scale-of-Intelligence-%7C-Second-Edition/p/100000593.html
36. Wechsler D. Wechsler adult intelligence scale®, Third Edition (WAIS®-III). Pearson Assessment Inc.; 1997. Accessed January 24, 2023. https://www.pearsonassessments.com/store/usassessments/en/Store/Professional-Assessments/Cognition-%26-Neuro/Wechsler-Adult-Intelligence-Scale-%7C-Third-Edition/p/100000243.html
37. Wechsler D. Manual for the Wechsler abbreviated scale of intelligence. Published online 1999.
38. Boys Town. Boys Town national database manual: Youth care data systems (Version 4.5.80.0). Boys Town; 2018.
39. Dale AM, Fischl B, Sereno MI. Cortical surface-based analysis: I segmentation and surface reconstruction. Neuroimage. 1999;9(2):179–94. https://doi.org/10.1006/NIMG.1998.0395.
40. Fischl B, Sereno MI, Dale AM. Cortical surface-based analysis: II: inflation, flattening, and a surface-based coordinate system. Neuroimage. 1999;9(2):195–207. https://doi.org/10.1006/NIMG.1998.0396.
41. Desikan RS, Ségonne F, Fischl B, et al. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. Neuroimage. 2006;31(3):968–80. https://doi.org/10.1016/J.NEUROIMAGE.2006.01.021.
42. Fischl B, Van Der Kouwe A, Destrieux C, et al. Automatically parcellating the human cerebral cortex. Cereb Cortex. 2004;14(1):11–22. https://doi.org/10.1093/CERCOR/BHG087.
43. Ségonne F, Grimson E, Fischl B. A genetic algorithm for the topology correction of cortical surfaces. Inf Process Med Imaging. 2005;19:393–405. https://doi.org/10.1007/11505730_33.
44. Reuter M, Rosas HD, Fischl B. Highly accurate inverse consistent registration: a robust approach. Neuroimage. 2010;53(4):1181–96. https://doi.org/10.1016/J.NEUROIMAGE.2010.07.020.
45. Backhausen LL, Herting MM, Buse J, Roessner V, Smolka MN, Vetter NC. Quality control of structural MRI images applied using FreeSurfer-a hands-on workflow to rate motion artifacts. Front Neurosci. 2016;10:220586. https://doi.org/10.3389/FNINS.2016.00558/BIBTEX.
46. Stein JL, Medland SE, Vasquez AA, et al. Identification of common variants associated with human hippocampal and intracranial volumes. Nat Genet. 2012;44(5):552–61. https://doi.org/10.1038/NG.2250.
47. Fischl B, Salat DH, Busa E, et al. Whole brain segmentation: automated labeling of neuroanatomical structures in the human brain. Neuron. 2002;33(3):341–55. https://doi.org/10.1016/S0896-6273(02)00569-X.
48. Barnes J, Ridgway GR, Bartlett J, et al. Head size, age and gender adjustment in MRI studies: a necessary nuisance? Neuroimage. 2010;53(4):1244–55. https://doi.org/10.1016/J.NEUROIMAGE.2010.06.025.
49. Jarbo K, Verstynen TD. Converging structural and functional connectivity of orbitofrontal, dorsolateral prefrontal, and posterior parietal cortex in the human striatum. J Neurosci. 2015;35(9):3865–78. https://doi.org/10.1523/JNEUROSCI.2636-14.2015.
50. Averbeck BB, Lehman J, Jacobson M, Haber SN. Estimates of projection overlap and zones of convergence within frontal-striatal circuits. J Neurosci. 2014;34(29):9497–505. https://doi.org/10.1523/JNEUROSCI.5806-12.2014.
51. Verstynen TD, Badre D, Jarbo K, Schneider W. Microstructural organizational patterns in the human corticostriatal system. J Neurophysiol. 2012;107(11):2984–95. https://doi.org/10.1152/JN.00995.2011.
52. Shipp S. The functional logic of corticostriatal connections. Brain Struct Funct. 2017;222(2):669–706. https://doi.org/10.1007/S00429-016-1250-9.
53. Jung WH, Jang JH, Park JW, et al. Unravelling the intrinsic functional organization of the human striatum: a parcellation and connectivity study based on resting-state FMRI. PLoS ONE. 2014. https://doi.org/10.1371/JOURNAL.PONE.0106768.
54. Choi EY, Thomas Yeo BT, Buckner RL. The organization of the human striatum estimated by intrinsic functional connectivity. J Neurophysiol. 2012;108(8):2242–63. https://doi.org/10.1152/JN.00270.2012.
55. Otchy TM, Wolff SBE, Rhee JY, et al. Acute off-target effects of neural circuit manipulations. Nature. 2015;528(7582):358–63. https://doi.org/10.1038/nature16442.
56. Forstmann BU, Anwander A, Schäfer A, et al. Cortico-striatal connections predict control over speed and accuracy in perceptual decision making. Proc Natl Acad Sci U S A. 2010;107(36):15916–20. https://doi.org/10.1073/PNAS.1004932107/SUPPL_FILE/SAPP.PDF.
57. Ystad M, Hodneland E, Adolfsdottir S, et al. Cortico-striatal connectivity and cognition in normal aging: a combined DTI and resting state fMRI study. Neuroimage. 2011;55(1):24–31. https://doi.org/10.1016/J.NEUROIMAGE.2010.11.016.
58. Klauser P, Cropley VL, Baumann PS, et al. White matter alterations between brain network hubs underlie processing speed impairment in patients with schizophrenia. Schizophr Bull Open. 2021;2(1): sgab033. https://doi.org/10.1093/SCHIZBULLOPEN/SGAB033.
59. Gelskov SV, Madsen KH, Ramsøy TZ, Siebner HR. Aberrant neural signatures of decision-making: pathological gamblers display cortico-striatal hypersensitivity to extreme gambles. Neuroimage. 2016;128:342–52. https://doi.org/10.1016/J.NEUROIMAGE.2016.01.002.

60. Hosking JG, Kastman EK, Dorfman HM, et al. Disrupted prefrontal regulation of striatal subjective value signals in psychopathy. Neuron. 2017;95(1):221-231.e4. https://doi.org/10.1016/J.NEURON.2017.06.030.
61. Yau Y, Dadar M, Taylor M, et al. Neural correlates of evidence and urgency during human perceptual decision-making in dynamically changing conditions. Cereb Cortex. 2020;30(10):5471–83. https://doi.org/10.1093/CERCOR/BHAA129.
62. Rolls ET. Emotion, motivation, decision-making, the orbitofrontal cortex, anterior cingulate cortex, and the amygdala. Brain Struct Funct. 2023;228(5):1201–57. https://doi.org/10.1007/S00429-023-02644-9.
63. Kennerley SW, Walton ME, Behrens TEJ, Buckley MJ, Rushworth MFS. Optimal decision making and the anterior cingulate cortex. Nat Neurosci. 2006;9(7):940–7. https://doi.org/10.1038/nn1724.
64. Julian MM. Age at adoption from institutional care as a window into the lasting effects of early experiences. Clin Child Fam Psychol Rev. 2013;16(2):101–45. https://doi.org/10.1007/S10567-013-0130-6.
65. Merhar SL, Kline JE, Braimah A, et al. Prenatal opioid exposure is associated with smaller brain volumes in multiple regions. Pediatr Res. 2021;90(2):397–402. https://doi.org/10.1038/S41390-020-01265-W.
66. Wisse LEM, Chételat G, Daugherty AM, et al. Hippocampal subfield volumetry from structural isotropic 1 mm3 MRI scans: a note of caution. Hum Brain Mapp. 2021;42(2):539–50. https://doi.org/10.1002/HBM.25234.
67. Aghamohammadi-Sereshki A, Pietrasik W, Malykhin NV. Aging, cingulate cortex, and cognition: insights from structural MRI, emotional recognition, and theory of mind. Brain Struct Funct. 2024;229(3):657–80. https://doi.org/10.1007/S00429-023-02753-5.
68. Alexander B, Georgiou-Karistianis N, Beare R, et al. Accuracy of automated amygdala MRI segmentation approaches in Huntington's disease in the IMAGE-HD cohort. Hum Brain Mapp. 2020;41(7):1875–88. https://doi.org/10.1002/HBM.24918.
69. Guenette JP, Stern RA, Tripodis Y, et al. Automated versus manual segmentation of brain region volumes in former football players. NeuroImage: Clin. 2018;18:888–96. https://doi.org/10.1016/j.nicl.2018.03.026.
70. Jayakar R, Tone EB, Crosson B, et al. Amygdala volume and social anxiety symptom severity: does segmentation technique matter? Psychiatry Res Neuroimaging. 2020. https://doi.org/10.1016/j.pscychresns.2019.111006.
71. Kahhale I, Buser NJ, Madan CR, Hanson JL. Quantifying numerical and spatial reliability of hippocampal and amygdala subdivisions in freesurfer. Brain Inform. 2023;10(1): 9. https://doi.org/10.1186/S40708-023-00189-5.

Publisher's Note