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Lower Amygdala Volume in Men is Associated With Childhood Aggression, Early Psychopathic Traits, and Future Violence

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Abstract

Background

Reduced amygdala volume has been implicated in the development of severe and persistent aggression and the development of psychopathic personality. With longitudinal data, the current study examined whether male subjects with lower amygdala volume have a history of aggression and psychopathic features dating back to childhood and are at increased risk for engaging in future aggression/violence.

Methods

Participants were selected from a longitudinal study of 503 male subjects initially recruited when they were in the first grade in 1986–1987. At age 26, a subsample of 56 men with varying histories of violence was recruited for a neuroimaging substudy. Automated segmentation was used to index individual differences in amygdala volume. Analyses examined the association between amygdala volume and levels of aggression and psychopathic features of participants measured in childhood and adolescence. Analyses also examined whether amygdala volume was associated with violence and psychopathic traits assessed at a 3-year follow-up.

Results

Men with lower amygdala volume exhibited higher levels of aggression and psychopathic features from childhood to adulthood. Lower amygdala volume was also associated with aggression, violence, and psychopathic traits at a 3-year follow-up, even after controlling for earlier levels of these features. All effects remained after accounting for several potential confounds.

Conclusions

This represents the first prospective study to demonstrate that men with lower amygdala volume have a longstanding history of aggression and psychopathic features and are at increased risk for committing future violence. Studies should further examine whether specific amygdala abnormalities might be a useful biomarker for severe and persistent aggression.

Keywords

aggression, amygdala, longitudinal, psychopathy, violence, volume

Disciplines

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Abstract

Background—Reduced amygdala volume has been implicated in the development of severe and persistent aggression and the development of psychopathic personality. Using longitudinal data, the current study examined whether males with lower amygdala volume have a history of aggression and psychopathic features dating back to childhood, and are at increased risk for engaging in future aggression/violence.

Methods—Participants were selected from a longitudinal study of 503 males initially recruited when they were in the 1st grade in 1986–1987. At age 26, a subsample of 56 men with varying histories of violence was recruited for a neuroimaging substudy. Automated segmentation was used to index individual differences in amygdala volume. Analyses examined the association between amygdala volume and the participants' levels of aggression and psychopathic features measured in childhood and adolescence. Analyses also examined whether amygdala volume was associated with violence and psychopathic traits assessed at a 3-year follow-up.

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Conclusions—This represents the first prospective study to demonstrate that men with lower amygdala volume have a longstanding history of aggression and psychopathic features, and are at increased risk for committing future violence. Studies should further examine whether specific amygdala abnormalities may be a useful biomarker for severe and persistent aggression.

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Keywords

amygdala; volume; psychopathy; violence; aggression; longitudinal

Introduction

Severe antisocial and violent behavior has been linked to dysfunctional amygdala reactivity during a wide variety of emotional processing tasks (1, 2). Additionally, lower amygdala volume has been associated with aggression and psychopathic personality traits in children and adults (3–6). As such, amygdala volume may be a useful biomarker for delineating individuals at risk for exhibiting early emerging and persistent aggression and psychopathic personality features. However, no published longitudinal studies have examined whether amygdala volume is associated with psychopathic features and aggressive behavior measured from childhood into adulthood, or determined whether amygdala volume is associated with future violence. This study will leverage longitudinal data spanning an average of 22-years to comprehensively examine whether adult males with low amygdala volume have a longstanding developmental history of aggression and psychopathic features that persists into the future.

Amygdala Volume and Types of Aggression

The amygdala plays an important role in several aspects of emotion processing that have important implications for understanding the development of severe aggression (7). Individuals with damage to the amygdala often have problems recognizing distress cues in others and have difficulties establishing conditioned fear responses (7), and similar impairments have been observed in individuals with a high propensity for violence (1). Although structural studies have linked lower amygdala volume to aggressive behaviors (5, 6, 8), null findings have been reported (9–11). However, many prior studies did not identify males with an early emerging and persistent history of violence, a unique subgroup whose antisocial behavior may be driven in part by neurobiological abnormalities (12).

The inconsistent findings regarding amygdala volume may have also resulted from a failure to distinguish between aggression that is impulsive-affective-reactive (IAR) versus predatory-instrumental-proactive (PIP). IAR aggression is characterized by explosive anger outbursts in response to perceived threat or provocation, while PIP aggression involves goal-directed acts of violence typically committed with little emotional arousal (13). The amygdala is believed to play a role in both IAR and PIP aggression, albeit in different ways. Specifically, the amygdala is involved in the detection of emotionally salient information, particularly cues of potential threat/danger (7). Individuals with high IAR aggression over-interpret ambiguous social cues as hostile (14) and exhibit exaggerated amygdala responding when viewing emotionally ambiguous (6) and angry (15) facial expressions. Additionally, lower amygdala volume has been linked with higher IAR aggression (6) and trait anger (6, 16). In contrast, blunted amygdala reactivity to punishment and others' distress are believed to drive PIP aggression (13). Although a recent study found that PIP aggression was not associated with amygdala reactivity to fearful distress in others, it was associated with lower amygdala gray matter concentration (6).

Amygdala Volume and Psychopathic Traits

Amygdala abnormalities may play an important role in understanding violent behavior among men with psychopathic traits (1). Psychopathy includes a set of interpersonal (e.g., deceitful, manipulative), affective (e.g., callous, unemotional), and impulsive (e.g., thrill-seeking, irresponsible) features that are associated with chronic antisocial behavior (17, 18).

Psychopathic features have been associated with reduced amygdala reactivity to numerous emotional stimuli (e.g., punishment cues, others' distress), and these deficits putatively underlie the interpersonal/affective features of psychopathy (1, 2, 19, 20). However, structural studies linking amygdala volume with psychopathic traits have been mixed, with some reporting reduced gray matter volume (3, 4, 21), and others reporting non-significant associations (6, 11, 22).

Current Study

There are several limitations in the literature regarding the association between amygdala volume and features of aggression and psychopathy. First, it is not clear if men with a longstanding history of violence and psychopathic features spanning from childhood to early adulthood have lower amygdala volume. Second, no studies have examined whether lower amygdala volume is associated with IAP and/or PIP types of aggression in both adolescence and adulthood. Third, no published studies have examined whether men with reduced amygdala volume are at risk for *future* violence and exhibiting persistent psychopathic features. The current study will be the first to link adult amygdala volume with aggression, violence, and psychopathic traits repeatedly assessed across a 22-year period from childhood to adulthood.

Methods and Materials

Participants

Participants were 56 men recruited from the youngest cohort of the Pittsburgh Youth Study (PYS). The youngest cohort of the PYS consists of 503 boys selected from 1st graders attending the Pittsburgh public schools in 1986–87. PYS participants were recruited following an initial screening assessment that measured the boys' antisocial behaviors using a combination of parent, teacher, and self-report instruments. Boys who scored within the upper 30% on the screening (*n*=256), as well as a roughly equal number of boys randomly selected from the remaining 70% of the distribution (*n*=247) were selected for longitudinal follow-up. The racial composition of the follow-up sample is predominately Caucasian (40.6%) and African-American (55.7%). The first assessment took place when boys averaged 7.46 years of age (SD=.55). Assessments occurred every six months for four years, with annual assessments occurring for the next nine years. Two additional assessments were conducted when the men averaged 25.78 (SD=.96) and 29.25 (SD=1.11) years of age. All procedures were approved by the University of Pittsburgh IRB, and informed consent was obtained from all adult participants (23).

Neuroimaging Substudy

At age 26, a subsample of 56 men from the PYS with a history of chronic serious violence (CSV; *n*=20), transient serious violence (TSV; *n*=16), and no serious violence (NSV; *n*=20) were recruited for a neuroimaging substudy. The groups were delineated based on self-report assessments and official criminal records. Items from the Self-Report of Delinquency (SRD)(24) were used to assess past-year serious violence (i.e., rape, robbery, gang fighting, attacking with a weapon or to seriously hurt/kill) across assessments spanning ages 10–19 and again at age 26, just prior to the imaging assessment. At age 26, a 15-item Violence History Questionnaire (VHQ) (25) collected more detailed information about serious violence in the past year (e.g., kidnapping). Criminal charges for violence (e.g., homicide, robbery) were collected using juvenile, Pennsylvania state, and federal records. Groups were delineated as follows: 1) CSV men self-reported or were charged with violence across 4+ years; 2) TSV men self-reported or were charged with violence between 1–3 years; and 3) NSV men had no history of serious violence. Exclusion criteria included: 1) a prior history of a psychotic disorder according to the Diagnostic Interview Schedule for DSM-IV (26); 2)

use of psychotropic medications; 3) history of neurological disease, structural brain injury, post-concussive syndrome, and/or cardiovascular disease; 4) a full scale IQ below 70 on the Weschler Abbreviated Scale of Intelligence (27); and 5) current incarceration. Attempts were made to equate the groups on age, handedness, intelligence, and race.

Structural Data Acquisition

Participants completed a series of functional and structural neuroimaging scans using a 3.0 Tesla Siemens Allegra MRI scanner. The current study is based upon structural images obtained using high-resolution T1-weighted 3D gradient echo imaging with an SPGR sequence: axial plane, TR=1630ms, TE=2.48ms, flip angle=8°, number of excitations=1; bandwidth=210 Hz/pixel; echo spacing=6.8ms; matrix=256x256, FOV=204mm, 224 slices, .8mm isotropic thickness, 0mm gap.

Segmentation of Amygdala Volume

Segmentation and volumetric analysis of the amygdala was performed using FMRIB's Integrated Registration and Segmentation Tool (FIRST) in FMRIB's Software Library (FSL) version 4.1 (28). FIRST is a semi-automated subcortical segmentation tool that uses active shape and appearance models within a Bayesian framework based on information obtained from 336 manually-labeled T1 images (28). The 336 manually segmented and labeled T1-weighted brains have been parameterized as surface meshes and modeled as a point distribution model. FIRST searches through linear combinations of shape modes of variation for the most probable shape instance given the observed intensities in an individual's T1 image. Deformable surfaces are used to automatically parameterize the volumetric labels in terms of meshes. These surfaces are constrained to preserve point correspondence across the training data. Volumetric labels are parameterized by a 3D deformation of a surface model based on multivariate Gaussian assumptions. FIRST segmentation of subcortical structures has demonstrated median Dice overlaps with manual tracings from .70–.90, which is comparable or better than other automated methods (28).

FIRST processing was conducted using standardized procedures (28). Initially, the subcortical regions are separated from the rest of the cortex and white matter using a two-stage affine registration process that aligns the whole-head from native space to a standard space template (MNI152). Next a subcortical mask within the MNI space is used to achieve a more refined and robust alignment with the subcortical structures. An inverse transformation then brings the image back into native space, allowing for subsequent segmentation to be conducted with the original voxel intensities. Subcortical structures are segmented based on a Bayesian Appearance Model derived from the manually-traced training images using 50 modes of variation. The modes of variation are optimized based on leave-one-out cross-validation on the training set. Boundary correction takes place for each structure, and voxels are classified as belonging to a structure based on a statistical probability (z-score > 3.00; $p<.001$).

All segmentations were visually checked by a study investigator (K.E.) blind to participant characteristics with approximately 10 years of experience in neuroanatomy and segmentation techniques of MRI data. These checks confirmed that each segmentation was adjacent to the lateral ventricle and temporal horn, located anterior and slightly dorsal to the hippocampus, and demarcated from the hippocampus by the alveus and subiculum (see Figure S1). Average left and right amygdala volumes were then extracted for each subject and were z-scored prior to analyses to place them on a standard metric (i.e., standard deviation units). To control for overall intracranial volume (ICV), the sum of gray, white, and cerebrospinal fluid volumes was calculated using FIRST.

Measures

Childhood Measures (Mean Age 7.5 to 11)—Childhood levels of aggression and psychopathic features were measured using the Teacher Report Form (TRF) (29). The first 8 assessments (which occurred every 6 months) were used to cover early to late childhood. The aggressive behavior syndrome scale from the TRF was used to measure early physical fighting, threatening, and argumentativeness (29). Items from the TRF, and supplemental items added by the study originators, were used to assess the interpersonal/affective features of psychopathy in children. This interpersonal callousness (IC) scale has demonstrated evidence of reliability and construct validity in previous studies (30, 31). The TRF anxious/depressed and attention problems subscales were used to statistically control for problems that often co-occur with antisocial behavior.

Adolescent Measures (Mean Age 16)—Self-reported psychopathic traits and reactive/proactive aggression were collected at a single assessment in adolescence. The self-reported Child Psychopathy Scale - Revised (CPS-R) (32) is a validated measure assessing the affective, interpersonal, and unstable lifestyle components of psychopathy in adolescents. The self-reported Reactive and Proactive Aggression Questionnaire (33) contains two validated subscales assessing predatory/planned aggression and affective/impulsive aggression. The Youth Self-Report (YSR) (34) aggression subscale was used to measure combative behaviors, such as physical fighting, threating, and argumentativeness. The anxious/depressed and attention problems subscales from the YSR were used to control for problems that often co-occur with antisocial behavior.

Assessment Concurrent with Structural Scan (Mean Age 26)—The short form of the Self-Report of Psychopathy-III (SRP-III-SF) (35) was administered to assess the interpersonal, affective, and erratic lifestyle dimensions of psychopathy. The SRP-III-SF subscale assessing prior criminal behaviors was not administered. This measure has shown evidence of reliability and construct validity with adult males (36, 37). The aggression subscale from the Adult Self-Report (ASR) (38) and the verbal/physical aggression subscales from the Aggression Questionnaire-Short Form (AQ-SF) (39) assessed behaviors associated with aggression, hostility, and anger toward others. Additionally, the Impulsive-Premeditated Aggression Scale (40) measured the extent to which acts of aggression committed by participants involved uncontrolled anger outbursts (i.e., IAR aggression) or were part of a planned strategy to achieve a desired outcome (i.e., PIP aggression). The anxious/depressed subscale of the ASR and the total score from the Adult ADHD Self-Report Scale (ASRS) (41) were used to control for problems that often co-occur with antisocial behavior.

Post-Scan Follow-Up (Mean Age 29)—At the post-scan assessment, participants completed the physical/verbal aggression subscales from the AQ-SF and subscales from the SRP-III-SF. They were also re-administered the SRD which asked whether they had engaged in several violent acts (i.e., rape, robbery, attacking with a weapon or to seriously hurt, physical fighting) since their last interview. This self-report information was supplemented by official criminal record data collected from PA state and federal sources. Participants were considered violent since the structural scan if they self-reported violence and/or were charged with a violent crime during the follow-up period.

Potential Confounds—At the structural scan, information was collected on several potential confounds. The retrospective Childhood Trauma Scale (CTS) (42) assessed the amount of abuse and neglect the men experienced in childhood. A Health History Questionnaire assessed for a prior history of psychotropic medication use and mild traumatic brain injury (i.e., concussion). The DIS assessed for a lifetime history of affective, anxiety,

and substance use disorders. The Edinburgh Handedness Inventory (43) classifies participants as being either right or mixed/left handed. Any prior history of prison incarceration was collected from the PA Department of Corrections.

Data Analysis Plan

First, an ANOVA was used to compare men with a history of CSV, TSV, or NSV in terms of left and right amygdala volume. Linear regression was then used to examine the association between amygdala volume and individual differences in aggressive/psychopathic features at the time of the scan using the entire sample.

Next, analyses examined the association between amygdala volume and early aggression/psychopathic features across all participants. Population-average generalized estimating equations (GEE) were used for the repeated measurements of aggression/psychopathic features in childhood. An exchangeable correlation structure among the repeated assessments was specified. Ordinary linear regression was used to examine the association between amygdala volume and aggression/psychopathic traits at the single assessment point in adolescence.

A final set of analyses using all participants examined amygdala volume as a predictor of post-scan outcomes. Linear regression models were used for the outcomes of aggression and psychopathic traits at follow-up. Levels of these features at the time of the scan were included as covariates. A logistic regression using a penalized likelihood estimator appropriate for small samples (44) was used to examine whether amygdala volume was associated with any post-scan violence. The number of years men had engaged in serious violence prior to the scan was included as a covariate in this model.

Several covariates of no interest were considered as potential confounds, including total intracranial volume, race, age, handedness, and IQ, as well as a prior history of childhood maltreatment, concussion, prior incarceration, psychotropic medication use, internalizing disorders, substance abuse, and substance dependence. Within each developmental period, scales assessing co-occurring depression/anxiety and inattention/hyperactivity were also considered as potential confounds. For analyses focusing on post-scan violence, the number of days that elapsed between the neuroimaging scan and the follow-up data collection was included as a covariate. Potential confounds were entered into each model prior to the inclusion of amygdala volume using a backward stepwise procedure, with a liberal threshold of retaining predictors with a p-value $\leq .15$.

Results

Descriptive statistics for the study groups are presented in Table 1. Correlations between all measures assessing aggression and psychopathic traits are presented in Table S1.

Behaviors Assessed Concurrent with Structural Scan

There were no significant differences in left amygdala volume between NSV (M=1597, SD=295), TSV (M=1489, SD= 302), and CSV (M=1587, SD=312) men (F[2,53]=.66, p=.52). Right amygdala volume also did not significantly differ between NSV (M=1806, SD=429), TSV (M=1710, SD= 362), and CSV (M=1668, SD=286) men (F[2,53]=.75, p=.48). However, dimensional analyses using all participants indicated that lower left and right amygdala volume was associated with higher ASR aggression and higher levels of premeditated aggression (see Table 2). Lower left amygdala volume was also associated with higher levels of IAR aggression. Amygdala volume was not significantly related to verbal/physical aggression measured using the AQ-SF and overall levels of psychopathic

traits. Moreover, none of the facets of psychopathy were significantly associated with amygdala volume (*p*s > .20).

Behaviors Assessed in Childhood and Adolescence

Lower amygdala volume was significantly associated with measures of aggression and psychopathic features collected in childhood and adolescence (see Table 3). Lower left amygdala volume was associated with higher teacher-reported aggressive behaviors and interpersonal callousness across childhood. Lower right amygdala volume was associated with higher proactive aggression and overall psychopathic features in adolescence. In terms of the latter, right amygdala volume was significantly associated with the affective dimension (β=−.29, *p*<.05) of psychopathy, but not the interpersonal (β=−.16, *p*=.28) and lifestyle (β=−.20, *p*=.10) facets.

Post-Scan Outcomes

There were 21 men (37.5%) who engaged in violence across the post-scan follow-up, which included 5% of men in the NSV group (*N*=1), 37.5% of men in the TSV (*N*=6), and 70% of men in the CSV group (*N*=14). Lower left and right amygdala volumes were associated with an increased risk of committing violence, higher verbal/physical aggression, and increased psychopathic features at the follow-up, even after accounting for prior levels of these behaviors and potential confounds (see Table 4, *p*Figures 1–2). In terms of psychopathy facets, left amygdala volume was significantly associated with the lifestyle (β=−.24, <.05) dimension, but this effect only approached significance for the interpersonal (β=−.21, *p*=.05) and affective (β= −.25, *p*=.06) dimensions. In contrast, right amygdala volume was associated with the interpersonal dimension (β= −.22, *p*<.05), but not the affective (β= −.20, *p*=.11) and lifestyle (β= −.16, *p*=.14) facets.

Supplemental Analyses

When analyses were re-run excluding non-right handed men (*N*=5), the primary results were largely unchanged (see Table S2). To examine whether the findings exhibited evidence of anatomical specificity relative to nearby limbic regions, all analyses were re-run using right and left hippocampal volumes extracted using FIRST as predictors (see Table S3). Lower right hippocampal volume was associated with higher aggression on the ASR at the time of the scan. However, when right amygdala and hippocampal volumes were simultaneously entered as predictors of this outcome, amygdala volume remained a significant predictor (β= −.31, *p*<.05) and hippocampal volume became non-significant (β= −.08, *p*=.43).

Discussion

Although amygdala volume did not distinguish between men grouped according to whether or not they engaged in prior serious violence, men with lower amygdala volume exhibited higher levels of aggressive behavior and psychopathic features from childhood to early adulthood. Moreover, lower amygdala volume was associated with PIP aggression in adolescence and young adulthood. More importantly, this is the first study to demonstrate that adult men with lower amygdala volume were at increased risk for exhibiting *future* aggression, violence, and psychopathic traits, even after controlling for earlier levels of these features and several potential confounds. These results suggest that men with lower amygdala volumes have a longstanding developmental history of heightened aggression and psychopathic features dating back to early childhood.

Lower amygdala volume was associated with higher psychopathic features measured using multiple informants from childhood to adulthood. A growing number of studies have reported associations between psychopathic traits and lower amygdala volume (3, 4, 6). This

is the first longitudinal study to link lower amygdala volume to the interpersonal and/or affective features of psychopathy in childhood, adolescence, and adulthood. However, reduced amygdala volume was also associated with the impulsive lifestyle dimension of psychopathy at the adult follow-up. While some prior studies have found that lower amygdala volume is associated with all dimensions of psychopathy (3, 4), others have reported significant associations with just the unstable/antisocial lifestyle components (6). Together, these findings suggest that lower amygdala volume may be most robustly associated with the higher-order construct of psychopathy, rather than specific facets of the disorder.

Amygdala volume was not significantly associated with psychopathic features measured at the time of the neuroimaging scan. This lack of hypothesized association may have occurred because psychopathic traits were measured using self-report rather than interviewer ratings on the Psychopathy Checklist-Revised (45). However, the SRP-III-SF has shown evidence of construct validity in previous studies (36, 37), including being linked to reduced amygdala reactivity to fearful faces (36). This inconsistency could also be due to a lack of high temporal stability in psychopathic traits over periods of several years (46–48), with the current study finding only a moderate correlation (r=.50) between psychopathic features measured at age 26 and 29 (see Table S1). This instability is likely due to a combination of measurement error and “true” change in psychopathic features over time, and the former may have led to the inconsistent findings (49). In light of these issues, the fact that lower amygdala volume was related to psychopathic traits assessed using different informants across disparate developmental periods is particularly striking.

Lower amygdala volume was associated with increased aggression from childhood to adolescence, and an increased risk for engaging in future aggression and violence in adulthood. It was also associated with both PIP and IAR aggression in adulthood, but only with PIP aggression in adolescence. As with psychopathy, some inconsistencies were observed across measures assessing aggression/violence at different developmental periods. For example, amygdala volume did not differentiate men who varied in terms of the number of years in which they engaged in serious violence. This subgrouping method did not seem to accurately delineate the continuum of aggressive personality traits in men. Specifically, men in the CSV and TSV groups exhibited similar levels of aggression on several rating scales at the time of the scan. Additionally, placing all men without a history of serious violence in a single group overlooked individual differences in minor aggression. In general, the findings indicate that amygdala volume is most robustly associated with the larger continuum of aggressive behaviors, which is consistent with findings from studies using healthy adult populations (16, 50).

Limitations

The results from this study must be interpreted cautiously due to some methodological limitations. The current sample consisted solely of men, making it unclear whether the results will generalize to women. Gray matter volume was also measured at a single assessment in early adulthood. As such, it is unclear whether low amygdala volume preceded the development of childhood and adolescent aggression and psychopathic features. The current study also focused exclusively on amygdala volume since this region has been consistently implicated in development of severe antisocial behavior (1, 4). Although the findings did not translate to a nearby limbic region in supplemental analyses (i.e., hippocampus), structural differences in other brain regions may also be related to the phenotypes examined here. Similarly, future studies should examine whether manual tracings and surface-based methods for delineating more fine-grained differences in

amygdala nuclei morphology (e.g., basolateral complex) may help to better identify individuals at risk for developing aggression and psychopathic features (4).

While the current study involved theoretically focused analyses and controlled for numerous potential confounds, several outcomes were examined due to the longitudinal nature of the data. The use of multiple comparisons corrections is often debated, as these corrections increase the chance of making type II errors that minimize truly important findings and require the use of large samples (which are often prohibitively expensive in neuroimaging research) to detect modest effect sizes (51–54). Although the current results indicated a consistent negative association between amygdala volume and measures of aggression/psychopathic features, a strict Bonferroni correction would make the critical alpha level = .002 (.05/28). At this threshold, only the association between amygdala volume and aggressive behavior at the time of the scan would reach significance (see Table 2). As such, future studies with larger samples are needed to further validate these results.

Conclusions

This is the first study to demonstrate that lower amygdala volume is associated with features of aggression and psychopathy spanning from childhood to young adulthood. It is also the first investigation to demonstrate that lower amygdala volume is a significant risk factor for future violent behavior. Other investigators have found that children with deficient fear conditioning are at an increased risk for exhibiting adult criminal behavior, with abnormalities in the amygdala speculated to drive this association (55, 56). Although studies replicating these types of findings are needed, amygdala dysfunction may turn out to be an important biomarker for the development of severe and persistent aggression (56). However, multiple socio-contextual factors influence the development of antisocial behavior, and the relative influence that amygdala abnormalities play in the emergence and persistence of criminal behavior is in need of further study.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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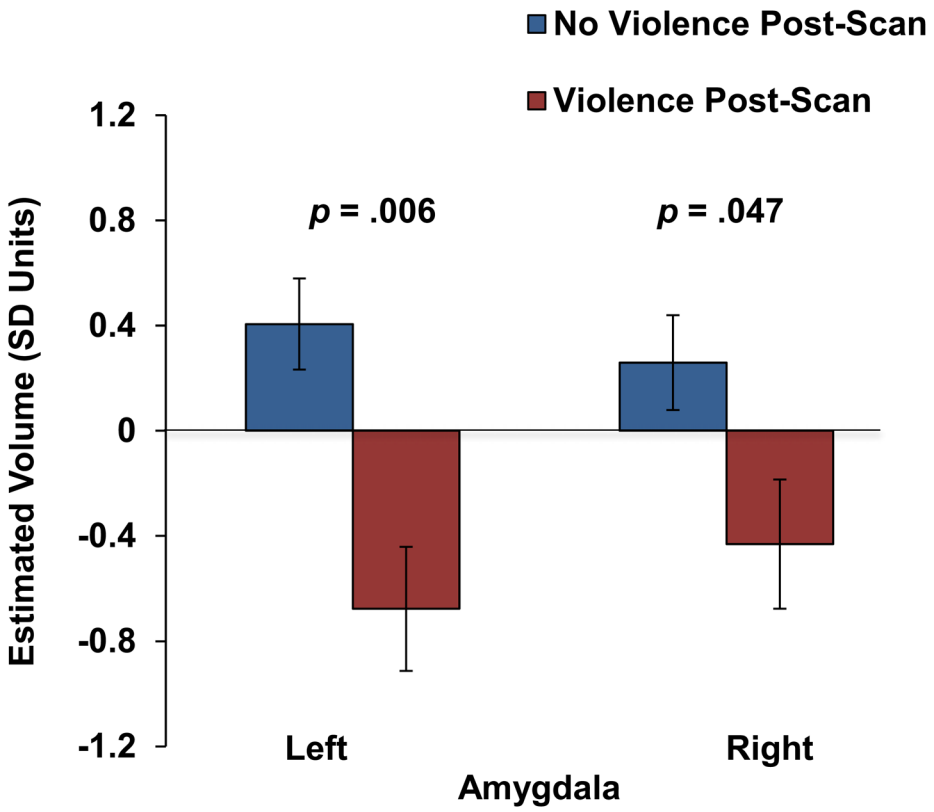

Figure 1.
Estimated mean amygdala volumes in men who committed violence during the post-scan follow-up and those who refrained from violence. Amygdala volumes are estimated marginal means after controlling for the number of years of prior violence. The *p*-values presented are based on the logistic regression model (see Table 4).

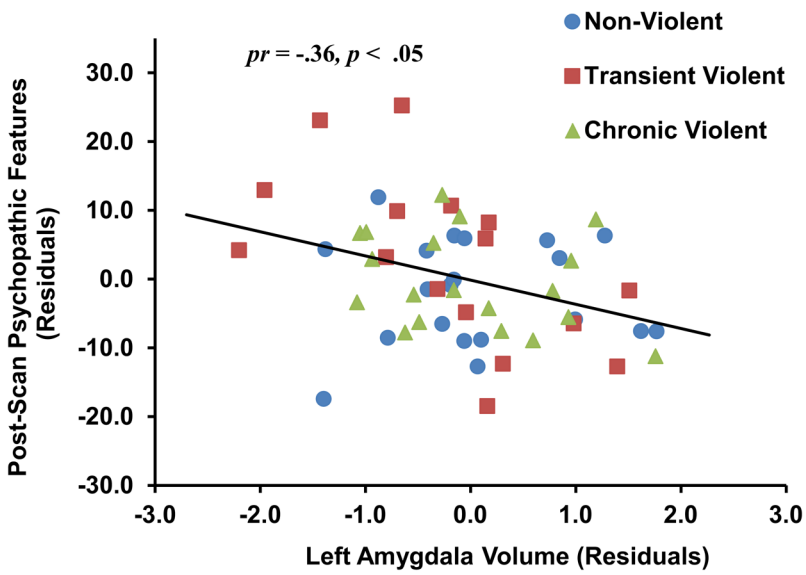

Figure 2.
Partial regression plot depicting the association between left amygdala volume and psychopathic traits at follow-up after controlling for psychopathic traits at the time of the scan and other model covariates. Amygdala volumes were transformed to z-scores prior to the analysis. Values on the x-axis and y-axis are residual scores after regressing each variable onto all other model covariates (i.e., $X-\hat{X}$ and $Y-\hat{Y}$, respectively). Residuals are shown with different shapes/colors based on violence groupings at the time of the scan for descriptive purposes. *pr* = partial correlation.

Table 1

Characteristics of Violence Groups at the Time of the Structural Neuroimaging Assessment

	No Serious Violence (*N*= 20)		Transient Violence (*N* = 16)		Chronic Violence (*N* = 20)			
	M*/*N	***SD*/%**	***M*/*N***	***SD*/%**	***M*/*N***	***SD*/%**	**χ^2/*F***	***p***
Age	26.76	0.95	26.53	0.86	26.55	1.20	0.29	0.750
Estimated intelligence	101.40	10.75	100.37	9.42	96.25	13.04	1.15	0.325
Race							FET	0.766
Caucasian	15.0%	3	6.3%	1	20.0%	4		
African-American	80.0%	16	87.5%	14	70.0%	14		
Other	5.0%	1	6.3%	1	10.0%	2		
Right handed	95.0%	19	100%	16	80.0%	16	FET	0.120
Aggression/Psychopathic Features								
Aggressive behavior (ASR)	1.9[a]	1.83	4.13[a]	3.46	7.65[b]	6.64	8.22	<0.001
Verbal/physical aggression (AQ-SF)	9.30[a]	3.10	14.00[b]	4.54	16.25[b]	5.12	13.28	<0.001
Premeditated aggression	18.00[a]	6.61	22.38[b]	5.29	25.00[b]	4.12	8.41	<0.001
Impulsive aggression	25.15[a]	6.33	30.75[b]	6.69	32.15[b]	7.31	5.85	0.005
Psychopathic features	118.31[a]	17.74	137.50[b]	26.64	143.85[b]	23.11	6.92	0.002
Potential Confounds								
Anxious/depressed	3.30[a]	4.54	2.50[a]	1.51	7.65[b]	7.26	5.39	0.007
ADHD symptom severity	7.55[ab]	3.33	6.81[a]	2.48	9.75[b]	4.66	3.22	0.048
Hx of substance abuse	15.0%[a]	3	50.0%[b]	8	60.0%[b]	12	9.11	0.009
Hx of substance dependence	0.0%[a]	0	18.8%[ab]	3	35.0%[b]	7	FET	0.010
Hx of internalizing disorders	0.0%	0	0.00%	0	15.0%	3	FET	0.102
Hx of psychotropic medication	10.0%	2	6.3%	1	35.0%	7	FET	0.070
Any prior concussion	25.0%	5	43.8%	7	55.0%	11	3.79	0.151
Prior incarceration	0.0%[a]	0	25.0%[b]	4	40.0%[b]	8	FET	0.003
Childhood maltreatment	41.30[a]	6.80	39.56[a]	5.77	50.71[b]	15.28	6.20	0.004

Note. Hx= History; ASR = Adult Self-Report; BPAG = Buss-Perry Aggression Questionnaire; FET = Fisher's Exact Test. For comparisons involving categorical variables fisher exact test were performed when expected cell counts were below five, otherwise chi-square tests were performed. ANOVA was used to test for group differences on continuous variables. Mean/percentages with different subscripts are significantly different in post hoc comparisons at $p < .05$.

Table 2

Associations Between Amygdala Volume and Concurrent Violence, Aggression and Psychopathic Features in Adulthood

	Amygdala Volume							
	Left				Right			
Dependent Variables	***B***	***SE***	***p***	**ΔR^2**	***B***	***SE***	***p***	**ΔR^2**
Verbal/physical aggression (AQ-SF)	−0.78	0.61	0.204	0.02	−0.75	0.61	0.229	0.02
Aggressive behavior (ASR)[a]	−0.34	0.07	<0.001	0.17	−0.29	0.08	0.001	0.11
Impulsive aggression	−2.30	0.80	0.006	0.10	−1.42	0.89	0.117	0.03
Premeditated aggression	−1.61	0.76	0.038	0.07	−1.76	0.76	0.024	0.08
Psychopathic features	0.43	1.75	0.806	0.00	1.11	1.76	0.532	0.00

Note. All estimates are after controlling for the potential confounds listed in the methods section using a backward stepwise inclusion procedure. Amygdala volumes were transformed to z-scores prior to the analysis. AQ-SF = Aggression Questionnaire-Short Form. ASR = Adult Self-Report.

[a] log transformed due to positive skew.

Table 3

Associations Between Adult Amygdala Volume and Earlier Aggressive Behavior and Psychopathic Features

	Amygdala Volume							
	Left				Right			
Dependent Variables	***B***	***SE***	***p***	**ΔR^2**	***B***	***SE***	***p***	**ΔR^2**
Childhood (Ages 7.5–11)								
Aggressive behavior[a]	−0.14	0.06	0.023	-	−0.04	0.06	0.491	-
Interpersonal callousness[a]	−0.15	0.06	0.015	-	−0.08	0.06	0.192	-
Adolescence (Age 16)								
Reactive aggression[a]	−0.09	0.07	0.200	0.03	−0.08	0.07	0.236	0.03
Proactive aggression[a]	−0.14	0.10	0.176	0.03	−0.21	0.10	0.038	0.06
Aggressive behavior (YSR)	−0.03	0.30	0.350	0.01	−0.06	0.03	0.064	0.04
Psychopathic features	−0.02	0.02	0.298	0.02	−0.42	0.02	0.043	0.06

Note. YSR= Youth Self-Report. All estimates are after controlling for potential confounds using a backward stepwise inclusion procedure. Amygdala volumes were transformed to z-scores prior to the analysis. Generalized estimating equations were used to analyze childhood variables, which were assessed every six months over the first eight waves of data collection. Due to missing data, there were 391 (interpersonal callousness) and 393 (aggressive behavior) observations out of a possible 448 for childhood outcomes. Complete data was available for 46 adolescent participants.

[a] log transformed due to positive skew.

Table 4

Associations Between Amygdala Volume and Measures of Future Violence, Aggression and Psychopathic Features at Post-Scan Follow-up

	Amygdala Volume							
	Left				Right			
Dependent Variables	***B***	***SE***	***p***	ΔR^2	***B***	***SE***	***p***	ΔR^2
Controlling for Prior Behavior								
Any post-scan violence	−1.17	0.42	0.006	-	−0.79	0.40	0.046	-
Verbal/physical aggression	−1.32	0.58	0.027	0.04	−1.27	0.63	0.049	0.03
Psychopathic features	−3.54	1.34	0.011	0.07	−2.89	1.29	0.029	0.05

Note. Estimates are after controlling for prior levels of each behavior at the time of the scan and the confounds listed in measures section using a backward stepwise procedure. Amygdala volumes were transformed to z-scores prior to the analysis. $N = 55$ for analyses involving self-report measures, as one participant did not complete the follow-up assessment.