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

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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.

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 might 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 male subjects with low amygdala volume have a longstanding developmental history of aggression and psychopathic features that persists into the future.

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 male subjects with an early emerging and persistent history of violence, a unique subgroup whose antisocial behavior might be driven in part by neurobiological abnormalities (12).

The inconsistent findings with regard to amygdala volume might have also resulted from a failure to distinguish between aggression that is impulsive-affective-reactive (IAR) versus predatory-instrumental-proactive (PIP). The IAR aggression is characterized by explosive anger outbursts in response to perceived threat or provocation, whereas 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 to the distress of others 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 abnormalities might play an important role in understanding violent behavior among men with psychopathic traits (1). Psychopathy includes a set of interpersonal (e.g., deceitful,

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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, the distress of others), 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 nonsignificant associations (6,11,22).

There are several limitations in the literature with regard to the association between amygdala volume and features of aggression and psychopathy. First, it is not clear whether 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 IAR 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 first-graders attending the Pittsburgh public schools in 1986–1987. The PYS participants were recruited after an initial screening assessment that measured the antisocial behaviors of the boys with 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 6 months for 4 years, with annual assessments occurring for the next 9 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 Institutional Review Board, 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 on the basis of self-report assessments and official criminal records. Items from the Self-Report of Delinquency (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 before the imaging assessment. At age 26, a 15-item Violence History Questionnaire (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 with 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 and 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, postconcussive 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 with a 3.0 Tesla Siemens Allegra magnetic resonance imaging (MRI) scanner (Siemens, Munich, Germany). The current study is based upon structural images obtained with high-resolution T1-weighted 3-dimensional gradient echo imaging with an spoiled gradient recoil sequence: axial plane, repetition time = 1630 msec, echo time = 2.48 msec, flip angle = 8°, number of excitations = 1; bandwidth = 210 Hz/pixel; echo spacing = 6.8 msec; matrix = 256 × 256, field of view = 204 mm, 224 slices, .8-mm isotropic thickness, 0-mm gap.

Segmentation of Amygdala Volume

Segmentation and volumetric analysis of the amygdala was performed with the FMRIB's Integrated Registration and Segmentation Tool (FIRST) in the FMRIB 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 the T1 image of an individual. 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 3-dimensional 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 to .90, which is comparable or better than other automated methods (28).

FIRST processing was conducted with standardized procedures (28). Initially, the subcortical regions are separated from the rest of the cortex and white matter with a two-stage affine registration process that aligns the whole-head from native space to a standard space template (Montreal Neurological Institute-152). Next a subcortical mask within the Montreal Neurological Institute 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 on the basis of a Bayesian Appearance Model derived from the manually traced training images with 50 modes of variation. The modes of variation are optimized on the basis of 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 on the basis of 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 (Figure S1 in Supplement 1). Average left and right amygdala volumes were then extracted for each subject and were Z-scored before analyses to place them on a standard metric (i.e., SD units). To control for overall intracranial volume, the sum of gray, white, and cerebrospinal fluid volumes was calculated with FIRST.

Measures

Childhood Measures: Mean Age 7.5–11 Years. Childhood levels of aggression and psychopathic features were measured with the Teacher Report Form (TRF) (29). The first eight 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 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 Years. Self-reported psychopathic traits and reactive/proactive aggression were collected at a single assessment in adolescence. The self-reported Child Psychopathy Scale—Revised (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 (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 Youth Self-Report were used to control for problems that often co-occur with antisocial behavior.

Assessment Concurrent with Structural Scan: Mean Age 26 Years. 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 male subjects (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 (41) were used to control for problems that often co-occur with antisocial behavior.

Postscan Follow-Up: Mean Age 29 Years. At the postscan 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 Self-Report of Delinquency, 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 Pennsylvania state and federal sources. Participants were considered violent since the time of 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 (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 Diagnostic Interview Schedule for the DSM-IV 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 Pennsylvania Department of Corrections.

Data Analysis Plan

First, an analysis of variance 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 with the entire sample.

Next, analyses examined the association between amygdala volume and early aggression/psychopathic features across all participants. Population-average generalized estimating equations 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 with all participants examined amygdala volume as a predictor of postscan 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 with a penalized likelihood estimator appropriate for small samples (44) was used to examine whether amygdala volume was associated with any postcan violence. The number of years men had engaged in serious violence before 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 before the inclusion of amygdala volume with a

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)		χ^2/F	p
	Mean/%	SD/n	Mean/%	SD/n	Mean/%	SD/n		
Age	26.76	.95	26.53	.86	26.55	1.20	.29	.750
Estimated Intelligence	101.40	10.75	100.37	9.42	96.25	13.04	1.15	.325
Race							FET	.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	.120
Aggression/Psychopathic Features								
Aggressive behavior (ASR)	1.9_a	1.83	4.13_a	3.46	7.65_b	6.64	8.22	<.001
Verbal/physical aggression (AQ-SF)	9.30_a	3.10	14.00_b	4.54	16.25_b	5.12	13.28	<.001
Premeditated aggression	18.00_a	6.61	22.38_b	5.29	25.00_b	4.12	8.41	<.001
Impulsive aggression	25.15_a	6.33	30.75_b	6.69	32.15_b	7.31	5.85	.005
Psychopathic features	118.31_a	17.74	137.50_b	26.64	143.85_b	23.11	6.92	.002
Potential Confounds								
Anxious/depressed	3.30_a	4.54	2.50_a	1.51	7.65_b	7.26	5.39	.007
ADHD symptom severity	7.55_{ab}	3.33	6.81_a	2.48	9.75_b	4.66	3.22	.048
Hx of substance abuse	$15.0\%_a$	3	$50.0\%_b$	8	$60.0\%_b$	12	9.11	.009
Hx of substance dependence	$.0\%_a$	0	$18.8\%_{ab}$	3	$35.0\%_b$	7	FET	.010
Hx of internalizing disorders	.0%	0	.00%	0	15.0%	3	FET	.102
Hx of psychotropic medication	10.0%	2	6.3%	1	35.0%	7	FET	.070
Any prior concussion	25.0%	5	43.8%	7	55.0%	11	3.79	.151
Prior incarceration	$.0\%_a$	0	$25.0\%_b$	4	$40.0\%_b$	8	FET	.003
Childhood maltreatment	41.30_a	6.80	39.56_a	5.77	50.71_b	15.28	6.20	.004

For comparisons involving categorical variables, Fisher exact test (FET) was performed when expected cell counts were below five; otherwise χ^2 tests were performed. Analysis of variance was used to test for group differences on continuous variables. Mean/percentages with different subscripts are significantly different in post hoc comparisons at $p < .05$.

ADHD, attention-deficit/hyperactivity disorder; AQ-SF, Aggression Questionnaire—Short Form; ASR, Adult Self-Report; BPAG, Buss-Perry Aggression Questionnaire; Hx, history.

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)	−.78	.61	.204	.02	−.75	.61	.229	.02
Aggressive Behavior (ASR)[a]	−.34	.07	<.001	.17	−.29	.08	.001	.11
Impulsive Aggression	−2.30	.80	.006	.10	−1.42	.89	.117	.03
Premeditated Aggression	−1.61	.76	.038	.07	−1.76	.76	.024	.08
Psychopathic Features	.43	1.75	.806	.00	1.11	1.76	.532	.00

All estimates are after controlling for the potential confounds listed in the methods section with a backward stepwise inclusion procedure. Amygdala volumes were transformed to Z-scores before the analysis.

AQ-SF, Aggression Questionnaire-Short Form; ASR, Adult Self-Report; B, unstandardized regression coefficient.

[a]Log transformed due to positive skew.

backward stepwise procedure, with a liberal threshold of retaining predictors with a *p* value ≤ .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 in Supplement 1.

Behaviors Assessed Concurrent with Structural Scan

There were no significant differences in left amygdala volume between NSV (mean = 1597, SD = 295), TSV (mean = 1489, SD = 302), and CSV (mean = 1587, SD = 312) men ($F_{2,53}$ = .66, p = .52). Right amygdala volume also did not significantly differ between NSV (mean = 1806, SD = 429), TSV (mean = 1710, SD = 362), and CSV (mean = 1668, SD = 286) men ($F_{2,53}$ = .75, p = .48). However, dimensional analyses with all participants indicated that lower left and right amygdala volume was associated with higher ASR aggression and higher levels of premeditated aggression (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 with the AQ-SF and overall levels of psychopathic traits. Moreover, none of the facets of psychopathy were significantly associated with amygdala volume (p values > .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 (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 (Figures 1 and 2; Table 4; and Figure S2 in Supplement 1). In terms of psychopathy facets, left amygdala volume was significantly associated with the lifestyle (β = −.24, p < .05) dimension, but this effect only approached significance for the interpersonal (β = −.21, p = .05)

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]	−.14	.06	.023	—	−.04	.06	.491	—
Interpersonal callousness[a]	−.15	.06	.015	—	−.08	.06	.192	—
Adolescence (age 16)								
Reactive aggression[a]	−.09	.07	.200	.03	−.08	.07	.236	.03
Proactive aggression[a]	−.14	.10	.176	.03	−.21	.10	.038	.06
Aggressive behavior (YSR)	−.03	.30	.350	.01	−.06	.03	.064	.04
Psychopathic features	−.02	.02	.298	.02	−.42	.02	.043	.06

All estimates are after controlling for potential confounds with a backward stepwise inclusion procedure. Amygdala volumes were transformed to Z-scores before the analysis. Generalized estimating equations were used to analyze childhood variables, which were assessed every 6 months over the first eight waves of data collection. Due to missing data, there were 391 (interpersonal callousness) and 393 (aggressive behavior) observations of a possible 448 for childhood outcomes. Complete data were available for 46 adolescent participants.

B, unstandardized regression coefficient; YSR, Youth Self-Report.
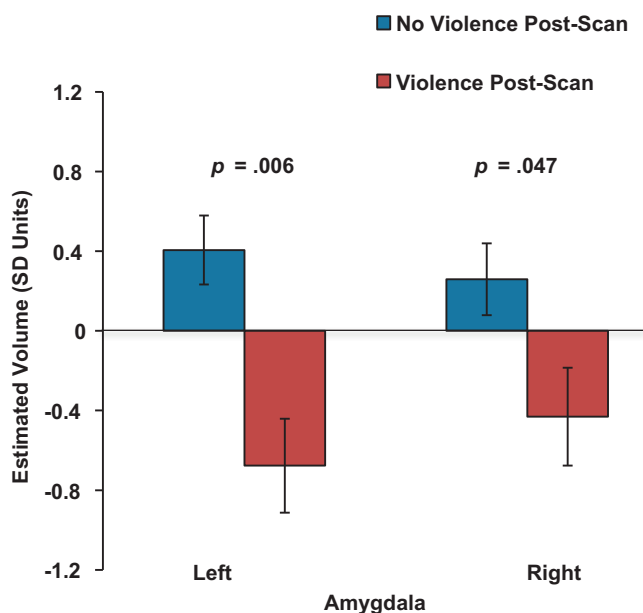
[a]Log transformed due to positive skew.

Figure 1. Estimated mean amygdala volumes in men who committed violence during the postscan 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 (Table 4).

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 (Table S2 in Supplement 1). All analyses were re-run with right and left hippocampal volumes extracted with FIRST as predictors (Table S2 in Supplement 1), to examine whether the findings exhibited evidence of anatomical specificity relative to nearby limbic regions. 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 nonsignificant (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 long-standing developmental history of heightened aggression and psychopathic features dating back to early childhood.

Lower amygdala volume was associated with higher psychopathic features measured with 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. Although 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 might 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 might have occurred because psychopathic traits were measured with 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 years (Table S1 in Supplement 1). This instability is likely due to a combination of measurement error and "true" change in psychopathic features over time, and the former might have led to the inconsistent findings (49). In light of these issues, the fact that lower amygdala volume was related to psychopathic traits assessed with different informants across disparate developmental periods is particularly striking.
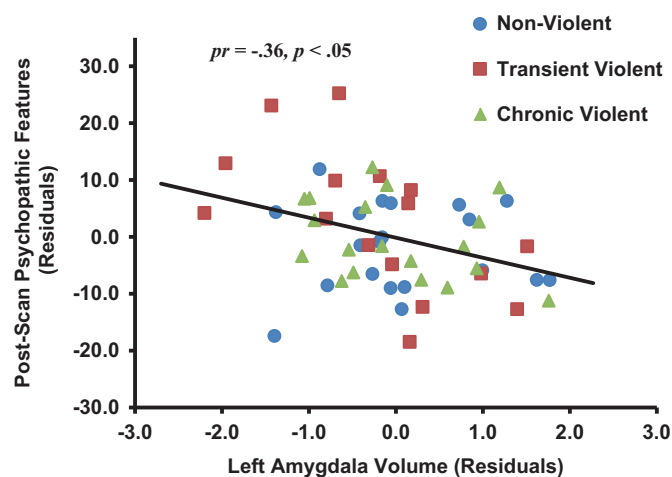

Figure 2. Partial regression plot depicting the association between left amygdala volume and psychopathic traits at follow-up after controlling for psychopathic traits at the time of the scan and other model covariates. Amygdala volumes were transformed to *Z*-scores before the analysis. Values on the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

Table 4. Associations Between Amygdala Volume and Measures of Future Violence, Aggression, and Psychopathic Features at Postscan Follow-Up

	Amygdala Volume							
	Left				Right			
Dependent Variables	B	SE	p	ΔR^2	B	SE	p	ΔR^2
Controlling for Prior Behavior								
Any postscan violence	−1.17	.42	.006	—	−.79	.40	.046	—
Verbal/physical aggression	−1.32	.58	.027	.04	−1.27	.63	.049	.03
Psychopathic features	−3.54	1.34	.011	.07	−2.89	1.29	.029	.05

Estimates are after controlling for prior levels of each behavior at the time of the scan and the confounds listed in the Measures section with a backward stepwise procedure. Amygdala volumes were transformed to *Z*-scores before the analysis. *N* = 55 for analyses involving self-report measures, because 1 participant did not complete the follow-up assessment. B, unstandardized regression coefficient.

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. Some inconsistencies were observed across measures assessing aggression/violence at different developmental periods, as with psychopathy. 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).

Study 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, because 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 might 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) might help to better identify individuals at risk for developing aggression and psychopathic features (4).

Although 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, because 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 α 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 (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 might 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.

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