ORIGINAL ARTICLE

Brain Pathology in Pedophilic Offenders

Evidence of Volume Reduction in the Right Amygdala and Related Diencephalic Structures

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Context: Pedophilic crime causes considerable public concern, but no causative factor of pedophilia has yet been pinpointed. In the past, etiological theories postulated a major impact of the environment, but recent studies increasingly emphasize the role of neurobiological factors, as well. However, the role of alterations in brain structures that are crucial in the development of sexual behavior has not yet been systematically studied in pedophilic subjects.

Objective: To examine whether pedophilic perpetrators show structural neuronal deficits in brain regions that are critical for sexual behavior and how these deficits relate to criminological characteristics.

Design: Amygdalar volume and gray matter of related structures that are critical for sexual development were compared in 15 nonviolent male pedophilic perpetrators (forensic inpatients) and 15 controls using complementary morphometric analyses (voxel-based morphometry and volumetry). Psychosocial adjustment and sexual offenses were also assessed.

Results: Pedophilic perpetrators showed a significant decrease of right amygdalar volume, compared with healthy controls ($P = .001$). We observed reduced gray matter in the right amygdala, hypothalamus (bilaterally), septal regions, substantia innominata, and bed nucleus of the striae terminalis. In 8 of the 15 perpetrators, enlargement of the anterior temporal horn of the right lateral ventricle that adjoins the amygdala could be recognized by routine qualitative clinical assessment. Smaller right amygdalar volumes were correlated with the propensity to commit uniform pedophilic sexual offenses exclusively ($P = .006$) but not with age ($P = .89$).

Conclusions: Pedophilic perpetrators show structural impairments of brain regions critical for sexual development. These impairments are not related to age, and their extent predicts how focused the scope of sexual offenses is on uniform pedophilic activity. Subtle defects of the right amygdala and closely related structures might be implicated in the pathogenesis of pedophilia and might possibly reflect developmental disturbances or environmental insults at critical periods.

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THE SEXUAL ABUSE OF CHILDREN is a major public health and criminological issue. Although, at present, no reliable data are available on the prevalence of pedophilia, it was recently reported that about 1 in 12 children in the United States has been sexually approached by an adult.[1] In contrast to tolerance of such behavior in ancient Greece, these days pedophilia is not socially acceptable. Instead, it is considered a paraphilia and has been operationally defined as a psychiatric disease.[2] The diagnostic criteria require that an adult experiences a sustained sexual attraction to prepubescent children and has acted on it or feels distressed by this sexual urge. Many attempts have been made to identify a pattern of neurocognitive and neurobiological markers reliably related to pedophilia. A recent meta-analysis by Cantor et al[3] revealed overall impaired intelligence in sexual offenders of children. However, no pattern of neurobiological characteristics has been documented consistently in a large sample of such offenders.[1] A variety of risk factors have been linked to increased incidence of pedophilic behavior: environmental risk factors (eg, childhood sexual abuse[4] and an inadequate attachment style resulting from a dysfunctional family[5]), neurobiological factors (eg, hormonal alterations[1,6]), and neurodevelopmental disturbances,[7] as well as acquired organic conditions, mainly involving frontal and temporal regions.[8,9]

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Previous imaging studies comparing groups of pedophilic patients with control groups are scarce. Functional neuroimaging studies using positron emission tomography have indicated a role for frontal and temporal abnormalities in pedophilia.[9,10] Structural studies based on computed tomography scans and their qualitative assessment have provided inconsistent results. Some have suggested abnormalities of temporal[11,12] as well as frontal[12] regions. Others have failed to find a significant association with structural brain anomaly.[13]

Whereas little is known about brain function in pedophilia, the structures involved in sexual behavior in other populations have been extensively studied. Frequently, patients with lesions of the anterior temporal lobes and the frontal lobes show changes in their sexual behavior.[8,14] These can vary from slight changes in sexual drive to full-blown symptoms of the Klüver-Bucy syndrome, which consist of hyperorality, so-called psychic blindness, hypersexuality, and changes in sexual preference.[15] Furthermore, it has been established in animals that a densely interconnected neural network involving the amygdala, hypothalamus, septal area, and cell groups in the adjacent substantia innominata plays a key role in determining sexual and mating behavior.[16,17] Functional imaging studies in healthy humans show that the homologous human structures are indeed involved in the processing of sexually arousing stimuli.[18] It has also been shown that men and women differentially recruit hypothalamic and amygdalar regions,[19] reflecting the dependence of sex-specific sexual behavior on these neural structures. The critical role of the amygdala in the framing of sexual behavior is confirmed by studies in animals, demonstrating that sexual behavior can be altered by stimulation of as well as lesions made to the medial amygdala, in a manner depending on previous sexual experience.[20-22] It must be noted, however, that in humans, as compared with animals, these emotional processes are subject to much stronger top-down control by higher cortical functions.[23]

Taken together, existing findings raise the possibility that deviant sexual behavior leading to pedophilic offenses might be related to structural anomalies in the network of brain regions regulating sexual function. However, no systematic study has analyzed this possibility with current high-resolution imaging methods yet. In the present study, we explored whether there are systematic structural differences between pedophilic perpetrators and healthy controls in relevant structures—specifically, the amygdala, hypothalamus, and related regions—and how these relate to the clinical characteristics of the perpetrators.

METHODS

SUBJECTS

Fifteen male patients meeting the diagnostic criteria for pedophilia according to the *DSM-IV-R*[2] were recruited from the State Forensic Hospital in Uchtspringe, Germany. None of the patients had neurological or other psychiatric diseases. Exclusion criteria were having claustrophobia, implants or other metallic parts inside the body, or a history of alcoholism or drug abuse. The study was approved by the local ethics committee (Ethikkommission) of the medical school at Otto-von-Guericke-University, Magdeburg. Written informed consent was obtained from all participants.

Verbal intelligence of the patients, as assessed with the Wortschatztest (vocabulary test),[24] was in the normal range (mean score ± SD, 97 ± 14.5), as was general intelligence (mean score ± SD, 110 ± 12), measured with the well-established German intelligence test Leistungsprüfsystem (performance testing system).[25] Fifteen healthy male volunteers were selected from the community as a control group, matched to the patient group for age (mean ± SD, patients, 40 ± 8.9 years [range, 27-57 years]; controls, 37.3 ± 6.5 years [range, 27-48 years]; $F_{1,28}$ = 1.23; P = .28). The patients showed a trend toward having fewer years of education than the controls (mean ± SD, patients, 12.4 ± 1.5 years; controls, 14.3 ± 3.5 years; $F_{1,28}$ = 3.87; P = .06). Age and years of education were entered as covariates in the analyses when appropriate. One pedophilic patient was left-handed; all other participants were right-handed.

CLINICAL ASSESSMENT

The patients had all committed sexual offenses involving children younger than 10 years of age. According to criminal records, the number of children abused ranged from 1 to about 10 (mean ± SD, 4.4 ± 2.7 children). In one patient, the total number was not available. Six patients had committed exclusively heterosexual offenses, 3 had committed exclusively homosexual offenses, and the remaining 6 had committed offenses involving both male and female children.

All patients were scored by experienced forensic psychiatrists (J.W. and U.G.) in a routine procedure applied to every inmate admitted to the hosting forensic institution for reasons of sexual misconduct. This examination included a structured professional judgement[26] according to the Sexual Violence Risk–20 (SVR-20) structured clinical checklist,[27] which has shown high predictive validity[26] (**Table 1**). It includes ratings according to the Psychopathy Checklist–Revised.[28] Scores of the SVR-20 scale are known to reliably reflect features relevant for criminological characterization and risk assessment and are routinely used for these purposes at the participating forensic institution to assess sexual offenders. Additionally, the Multiphasic Sex Inventory was administered to the perpetrators to obtain a more comprehensive characterization of their sexuality.[29]

MAGNETIC RESONANCE IMAGING

T1-Weighted magnetic resonance scans were obtained on a 1.5-T GE Signa Horizon LX scanner with the standard quadrature head coil (General Electric, Milwaukee, Wis). According to protocol previously reported,[30-32] we obtained a sagittal T1-weighted 3-dimensional data set (voxel size, 0.976 × 0.976 × 1.5 mm). The image sets were aligned to the transversal plane through the anterior and posterior commissure and then rotated 5° backward to allow for a uniform visualization of mediotemporal structures in the transversal plane.

ASSESSMENT OF BRAIN TISSUE REDUCTION BY QUALITATIVE GRADING OF CEREBROSPINAL FLUID SPACE ENLARGEMENT

In an initial analysis, reduction of brain tissue was estimated by qualitative clinical routine rating of the width of cerebrospinal fluid (CSF) spaces at the frontal lobes (frontal), sylvian fissures (sylvian), anterior mediotemporal lobe (anterior temporal horn of the lateral ventricles), and the posterior part of the temporal horn with the occipital horn of the lateral ven-

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tricle in both hemispheres. Cerebrospinal fluid space enlargement was assessed by visual inspection of T1-weighted brain scans. Enlargement of CSF spaces was graded according to the following scoring scheme: 0, normal; 1, questionably normal; 2, questionably enlarged; and 3, definitely enlarged. The CSF space grading was performed once by an experienced rater who was blind to the identity of the subjects (B.B.); intrarater reliability was assessed by rerating 10 randomly chosen images 5 weeks after the original rating. Cronbach α was greater than 0.83 for all locations.

AMYGDALAR VOLUME ASSESSMENT

Amygdalar volume was assessed for every subject individually by K.Z. (blind to subject identity), who applied manual volumetry according to an established protocol.[33] Additionally, special care was taken not to include anterior-superior hippocampal voxels by delineating the amygdala and hippocampus on sagittal slices. Deviating from the method of Pruessner et al,[33] we used the program MRIcro to draw the regions of interest (ROIs).[34] Amygdalar volume was calculated as the number of voxels in each ROI multiplied by their voxel volume ($0.975 \times 0.975 \times 1.5$ mm). Amygdalar volumes were normalized to intracranial volumes as derived from voxel-based morphometry (total intracranial volume: sum of gray matter, white matter, and cerebrospinal fluid segments) to obtain results unbiased by head size. Reliability was assessed by rerating 10 random subjects (Cronbach α: left, 0.96; right, 0.91).

VOXEL-BASED MORPHOMETRY

Voxel-based morphometry (VBM) was performed using the SPM2 package (Wellcome Department of Imaging Neuroscience, London, England; available at http://www.fil.ion.ucl.ac.uk/spm) according to the optimized VBM protocol described in detail elsewhere.[30,32,35] This yielded gray matter partitions in stereotactic Montreal Neurological Institute space. Voxel values were rescaled using the Jacobian determinants derived from the applied deformation fields to enable testing for the amount of gray matter in a region (local gray matter).[36] Gray matter images were smoothed using an isotropic Gaussian kernel of 8 mm full width at half maximum. Additionally, total intracranial volume was entered as a covariate in the statistical tests to control for effects due to head size.

To extend the analysis from amygdalar volume to alterations of other structures relevant in shaping sexual behavior, voxelwise group comparisons were calculated for the gray matter segments. Voxel intensity differences were then statistically assessed in predefined ROIs. Four ROIs were created manually in Montreal Neurological Institute space: (1) the left amygdala, (2) the right amygdala, (3) bilateral structures (septal region and bed nucleus striae terminalis [BNST]),[16] and (4) bilateral structures (hypothalamus and substantia innominata).[37,38] We report voxel clusters of significant size according to tests that were implemented relying on random field theory after voxelwise thresholding, with $P<.001$ (uncorrected).[39,40] Special care was taken not to violate the smoothness assumption, because VBM data can be highly nonstationary.[41] To account for this possible problem, smoothness was separately assessed for every ROI and entered in the analysis.

VBM VOLUME ASSESSMENT OF THE TEMPORAL HORN

Volumes of the temporal horns of the lateral ventricles were assessed in 4 quarters along the longitudinal axis using a completely data-driven approach relying on VBM. Native space CSF

Table 1. Group Results From the MSI and the SVR-20 Checklist

Item	Pedophilic Patients (n = 15)		Medical Students (n = 111)
	Z Score	Mean (SD)	Mean (SD)
MSI			
Social sexual desirability	–0.2	25.9 (7.4)	26.9 (4.9)
Sexual obsessions	1.1	5.1 (5.0)	2.5 (2.5)
Cognitive distortion/immaturity	4.6	9.1 (4.5)	1.8 (1.6)
Child molesting	9.9	21.1 (6.6)	2.3 (1.9)
Fantasy	4.6	5.7 (2.8)	0.6 (1.1)
Search/cruising	3.4	5.3 (2.3)	1.3 (1.2)
Assault	12.7	6.5 (1.6)	0.2 (0.5)
Aggravated assault	13.8	2.8 (1.6)	0.1 (0.2)
Incest	1.6	0.7 (1.0)	0.1 (0.4)
Girls	2.6	1.9 (1.2)	0.4 (0.6)
Boys	3.0	1.4 (1.1)	0.2 (0.4)
Rape	1.6	3.7 (6.2)	1.1 (1.6)
Exhibitionism	2.1	2.0 (1.5)	0.5 (0.7)
Atypical sexual behavior/ paraphilia	0.7	3.3 (3.7)	1.9 (2.0)
Fetishism	0.1	0.9 (0.9)	0.8 (0.9)
Voyeurism	1.4	1.5 (1.7)	0.5 (0.7)
Obscene calls	0.1	0.1 (0.4)	0.1 (0.4)
Bonding and penalization	–0.1	0.3 (0.7)	0.4 (0.8)
Sexual dysfunction	2.5	4.8 (3.0)	1.5 (1.3)
Sexual insufficiency	1.2	1.8 (1.3)	0.7 (0.9)
Premature ejaculation	0.0	0.5 (0.7)	0.5 (0.8)
Physical handicap	1.0	0.4 (0.7)	0.1 (0.3)
Impotence	3.9	2.1 (2.0)	0.2 (0.5)
Sexual knowledge	–0.3	16.1 (3.6)	17.0 (3.1)
SVR-20*			
Psychosocial adjustment			
Sexual deviance	. . .	1.9 (0.3)	. . .
Victim of child abuse	. . .	0.7 (0.9)	. . .
Psychopathy	. . .	0.2 (0.4)	. . .
Major mental illness	. . .	0.2 (0.6)	. . .
Substance use problems	. . .	0.4 (0.6)	. . .
Suicidal/homicidal ideation	. . .	0.5 (0.8)	. . .
Relationship problems	. . .	1.3 (0.6)	. . .
Employment problems	. . .	0.6 (0.7)	. . .
Past nonsexual violent offenses	. . .	0.2 (0.6)	. . .
Past nonviolent offenses	. . .	0.6 (0.9)	. . .
Past supervision failure	. . .	0.3 (0.7)	. . .
Sexual offenses			
High-density sex offenses	. . .	1.3 (0.7)	. . .
Multiple sex offense types	. . .	0.5 (0.7)	. . .
Physical harm to victim(s)	. . .	0.1 (0.4)	. . .
Uses weapons or threats of death	. . .	0.0 (0.0)	. . .
Escalation in frequency or severity	. . .	1.2 (0.7)	. . .
Extreme minimization or denial	. . .	0.8 (0.8)	. . .
Attitudes that support or condone offenses	. . .	0.9 (0.8)	. . .
Future plans			
Lacks realistic plans	. . .	0.7 (0.8)	. . .
Negative attitude toward intervention	. . .	0.3 (0.5)	. . .

Abbreviations: MSI, Multiphasic Sex Inventory; SVR-20, Sexual Violence Risk–20; ellipses, test was not performed.

*Scores range from 0 to 2 (0 = not at all, 1 = partially applies, 2 = definitely applies).[27]

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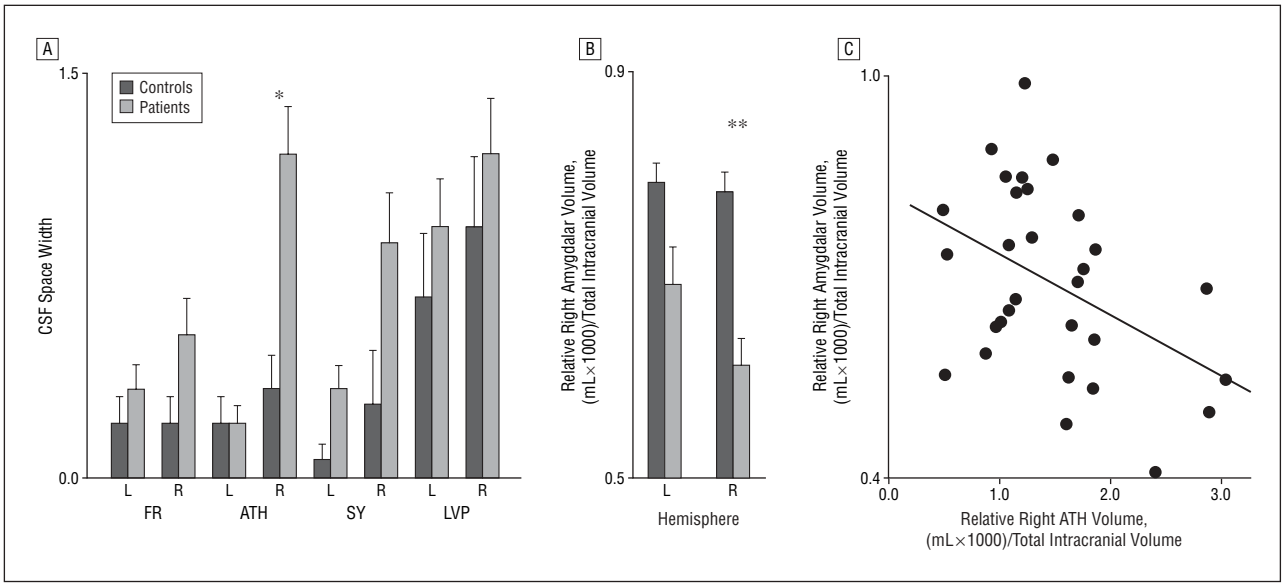

Figure 1. A, Estimated brain tissue reductions according to visual inspection of cerebrospinal fluid (CSF) space enlargement (0=normal width, 1=questionably normal, 2=questionably enlarged, and 3=definitely enlarged) for controls and patients differ only for the right anterior temporal horn. Asterisk indicates $P<.05$. B, Relative right amygdalar volume is reduced in pedophilic patients. Double asterisk indicates $P<.01$. C, Right amygdalar volume is inversely correlated with right anterior temporal horn (ATH) volume ($r=-0.43$; $P=.02$). Error bars denote standard error of the mean. FR indicates frontal region; L, left; LVP, lateral ventricle, posterior; R, right; and SY, sylvian fissure.

segments of the individual subjects were transformed to normal Montreal Neurological Institute space. This was done by using SPM2 and a site template created from the smoothed (full width at half maximum, 8 mm), normalized individual CSF segments of the subjects. Transformed segments were masked, with ROIs bilaterally covering the temporal horn. Masked segments were compared with unmasked segments to assure that (1) CSF of the temporal horn was included exclusively and (2) no parts of the temporal horn were excluded in any of the individuals. Temporal horns were then subdivided longitudinally into 4 segments of equal length that were retransformed to native space. The volume of these segments in native space was assessed bilaterally and related to total intracranial volume prior to statistical assessment.

RELATIONSHIP BETWEEN AMYGDALAR VOLUME REDUCTION AND CLINICAL PARAMETERS

To test for a relationship between reduced amygdalar volume and clinical parameters, a subset of 4 standardized clinical scores were selected from the SVR-20, which specifically describes the characteristics of the sexual crimes of the patients (eg, frequency of sexual offenses, multiple sexual offense types, physical harm to victims, and serious threat to victims). Because no perpetrator had seriously threatened his victims or used weapons, the last of these scores was dropped. Stepwise regression analysis was performed entering the clinical scores as predictor variables for amygdalar volume of the right and left side separately. Robustness of the resulting relationship was assessed by comparing amygdalar size in perpetrators with high vs low scores on the predictor variable.

We also examined the hypothesis that any of the subset of Multiphasic Sex Inventory scores describing pedophilic sexual preferences might be related to amygdalar volume. Thus, the 8 scores of this subset were entered as predictor variables in 2 stepwise linear regression analyses, with right and left amygdalar volume as dependent variables. Robustness was assessed as previously described.

RESULTS

QUALITATIVE CSF WIDTH ASSESSMENT

A 3-way omnibus analysis of covariance (ANCOVA; region × hemisphere × group; covariates, age and years of education) revealed that there was no significant difference in overall CSF width between patients and controls ($F_{1,26}=6.73$; $P=.07$; $\eta^2=0.12$; power=0.45) but that CSF enlargement differed between regions ($F_{3,78}=3.1$; $P=.04$; $\eta^2=0.11$; power=0.63). Also, patients showed a stronger accentuation of CSF enlargement on the right side than the controls did (group × hemisphere; $F_{1,26}=14.09$; $P=.001$; $\eta^2=0.35$; power=0.95).

Post hoc group comparisons at all locations (1-way ANCOVAs) exclusively revealed a pronounced enlargement of the anterior right temporal horn in the patients ($F_{1,26}=9.14$; $P=.045$ [Bonferroni corrected]; $\eta^2=0.26$; power=0.83; all other locations $P>.05$). This is the part of the temporal horn situated immediately medial of the amygdala. The scores for all locations and both groups are shown in **Figure 1**A. **Figure 2**A illustrates right temporal horn enlargement in more than half of the patients, recognizable by mere qualitative routine assessments of the scans.

AMYGDALAR VOLUME

Analyses of amygdalar volumes reflected the right-sided ventricular enlargement observed in the patients. A 2-way ANCOVA (group × hemisphere; covariates, age and years of education) revealed that, overall, amygdalar volume was significantly smaller in the pedophilic patients than in the controls by about 17% (Figure 1B; $F_{1,26}=8.03$; $P=.009$; $\eta^2=0.24$; power=0.78). The difference was more pronounced on the right side (patients, –22%; SD, 15%), com-

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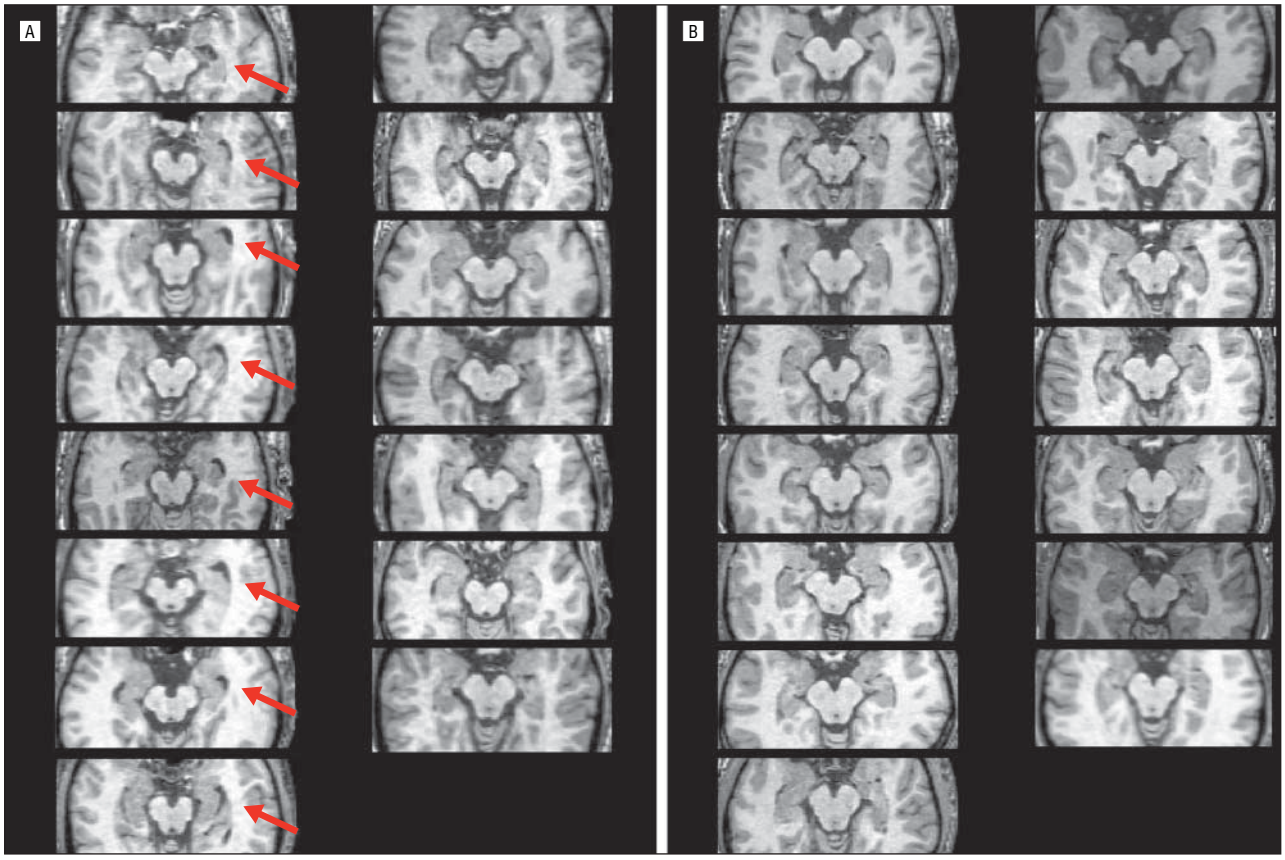

Figure 2. Right anterior temporal horn widening in pedophilic perpetrators. Transversal sections through the individual brains of patients (A) and controls (B). Arrows point to widened temporal horns. The widening is evident from visual inspection in about half of the patients (8 of 15).

pared with the left side (patients, –13%; SD, 19%; group × hemisphere; $F_{1,26}=5.83$; $P=.02$; $\eta^2=0.18$; power=0.64). Separate post hoc 1-way ANCOVA for each side revealed a significant group difference for the right side exclusively (right, $F_{1,26}=12.83$; $P=.002$ [Bonferroni corrected]; $\eta^2=0.33$; power=0.93; left, $F_{1,26}=3.65$; $P=.14$ [Bonferroni corrected]; $\eta^2=0.12$; power=0.45). Right amygdalar volume was not correlated with age (pedophilic group, $r=-0.04$; $P=.89$; control group, $r=-0.16$; $P=.56$; whole group, $r=-0.19$; $P=.31$).

VOXEL-BASED MORPHOMETRY

Assessment of local gray matter in the amygdalar ROIs yielded significant gray matter deficits in the patients on the right side only (detailed results of the group comparisons are given in **Table 2** for all ROIs; see also **Figure 3**). The ROI comprising the septal region and BNST bihemispherically as well as the one comprising the hypothalamus and substantia innominata bihemispherically yielded clusters where perpetrators had gray matter deficits. These were present bilaterally in the BNST, hypothalamus, and substantia innominata but were only unilaterally present on the right side in the septal region (Figure 3).

VBM VOLUME ASSESSMENT OF THE TEMPORAL HORN

Having macroscopically rated the brain atrophy at the previously mentioned landmark locations, we verified right anterior temporal horn enlargement in the patients by applying a purely data-driven, rater-independent approach relying on VBM.[36] Consistent with the above results, volume differences of the temporal horn were evident only for the right anterior segment. There was no overall volume difference of the temporal horn between groups (3-way ANCOVA, hemisphere × segment × group; covariates, age and education; group, $F_{1,26}=1.87$; $P=.18$; $\eta^2=0.07$; power=0.26), but the group × hemisphere interaction ($F_{1,26}=6.27$; $P=.02$; $\eta^2=0.19$; power=0.67) and the hemisphere × segment interaction ($F_{3,78}=3.57$; $P=.047$; $\eta^2=0.12$; power=0.57) were significant. Post hoc analyses (ANCOVA, group × hemisphere) showed a right-sided relative widening in the anterior quarter of the temporal horn bordering the amygdala ($F_{1,26}=8.49$; $P=.03$ [Bonferroni corrected]; $\eta^2=0.25$; power=0.80). It was significantly more pronounced in the patients than in the controls ($F_{1,26}=7.23$; $P=.049$ [Bonferroni corrected]; $\eta^2=0.22$; power=0.74). No such difference between sides or between groups was evident for the remaining parts of the temporal horn. Separate post hoc group comparisons of single temporal horn segments on each side disclosed enlargement in the patients only for the right anterior segment (1-way ANCOVA; $F_{1,26}=5.89$; $P=.02$ [not corrected, did not survive correction]; $\eta^2=0.19$; power=0.65). Furthermore, in the right hemisphere only, amygdalar volume was inversely correlated with the volume of the bordering anterior segment of the temporal horn (Figure 1C; $r=-0.43$; $P=.02$).

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Table 2. Local Gray Matter in the ROI Analyses Where Offenders Had Less Gray Matter Than Controls*

Anatomical Structure	Side	Cluster Size, Voxels	*P* Value: Cluster Corrected	*P* Value: Cluster Uncorrected	T Value Maxima	*Z* Score Maxima	MNI Coordinates, mm: x	y	z
ROI amygdala									
Amygdala	R	700	<.001	<.001	4.89	4.1	28	1	–14
Amygdala	R	. . .	. . .	. . .	4.5	3.85	30	–7	–12
Amygdala	R	. . .	. . .	. . .	4.49	3.85	21	1	–12
Amygdala	R	. . .	. . .	. . .	3.74	3.33	18	2	–15
Amygdala	R	69	<.001	<.001	4.29	3.71	23	7	–21
ROI hypothalamus and innominate substance									
Hypothalamus	L	1234	<.001	.001	4.69	3.97	–5	–3	–12
Hypothalamus	R	. . .	. . .	. . .	4.15	3.62	6	–1	–12
Innominate substance	L	. . .	. . .	. . .	5.18	4.28	–10	5	–9
Innominate substance	R	. . .	. . .	. . .	5.18	4.28	22	5	–6
Innominate substance	R	. . .	. . .	. . .	4.96	4.14	24	3	–10
Innominate substance	R	. . .	. . .	. . .	3.98	3.5	14	2	–12
Innominate substance	R	. . .	. . .	. . .	3.93	3.46	9	6	–10
Innominate substance	R	. . .	. . .	. . .	3.8	3.37	6	5	–7
ROI BNST and septal region									
BNST	L	432	.001	.02	4.74	4.01	–6	7	–5
BNST	L	. . .	. . .	. . .	4.63	3.94	–7	5	–1
BNST	R	. . .	. . .	. . .	4.06	3.56	4	5	–3
Septal region	R	. . .	. . .	. . .	3.88	3.43	6	7	–6
Septal region	R	. . .	. . .	. . .	3.78	3.36	5	3	6
Septal region	R	. . .	. . .	. . .	3.72	3.31	1	3	7

Abbreviations: BNST, bed nucleus striae terminalis; L, left; MNI, Montreal Neurological Institute; R, right; ROI, region of interest.

*Shown are the significant clusters (threshold $P<.05$, corrected for multiple comparisons, small volume correction for ROIs). Local *Z* score maxima more than 4 mm apart are displayed for every cluster. No significant cluster was detected in the left amygdala.

RELATIONSHIP OF AMYGDALAR VOLUME AND PSYCHOLOGICAL PARAMETERS

A stepwise regression analysis revealed that, of the subset of SVR-20 scores describing the characteristics of the sexual offenses of the patients, the score for multiple sexual offense types[27] was exclusively related to relative right amygdalar volume (model, $F_{1,13}=10.54$; $P=.006$; multiple offense types, $\beta=0.67$; $P=.006$; post hoc Spearman rank correlation $\rho=0.69$; $P=.005$). This result indicates that patients with lower right amygdalar volumes tended to commit solely stereotypical clandestine pedophilic offenses, while those with higher volume committed more diverse sexual offenses, also targeting underage children in varying age groups. To assess the robustness of this relationship, the patients were split into 2 groups. One group consisted of those with uniform stereotypical pedophilic offenses (SVR-20, multiple offense types rank=0; n=10), and a second consisted of those with multiple offense types (SVR-20, multiple offense types rank=1-2; n=5). A 1-way analysis of variance showed a significantly different amygdalar volume between groups (low mean, 0.55; SD, 0.07; high mean, 0.73; SD, 0.11; $F_{1,13}=16.81$; $P=.001$; $\eta^2=0.56$; power=0.97) (**Figure 4**). This result was also evident when covarying out age and years of education (ANCOVA, multiplicity × volume; covariates, age and education; $F_{1,11}=7.37$; $P=.02$; $\eta^2=0.40$; power=0.70).

Furthermore, lower right amygdalar volumes were related not only to a stronger focus of the sexual offenses on stereotypical pedophilic activity, as shown, but also to higher incestuous child abuse rates. Regression analyses with the subset of 7 scores from the Multiphasic Sex Inventory that characterized pedophilic crimes showed that only incest rate was related to reduced right amygdalar volume (model, $F_{1,13}=4.93$; $P=.045$; incest rate, $\beta=0.52$; $P=.045$; post hoc Spearman rank correlation $\rho=-0.58$; $P=.02$). Here, however, the comparison (non-incest- [n=9] vs incest-committing [n=6] perpetrators) did not reveal a significant group difference (1-way analysis of variance, $F_{1,13}=2.29$; $P=.15$; $\eta^2=0.15$; power=0.29). Amygdalar volume was related neither to high frequency of sexual fantasies, victim search, sexual assaults, nor Psychopathy Checklist–Revised scores.

COMMENT

In this study, we examined whether pedophilic perpetrators display structural neuronal changes in regions that are crucial in the development of human sexual behavior. We found that the pedophilic perpetrators had a significantly smaller amygdalar volume, with the difference predominating on the right side. Amygdalar volume reduction was not age dependent or progressive and thus does not appear to reflect classical atrophy or a degenerative process emerging over time. It might rather be explained by a developmental disorder or pre-existing hypoplasia. Lower right amygdalar volume correlated with the enlargement of the anterior temporal horn, which was recognizable in the majority of the perpetrators even by

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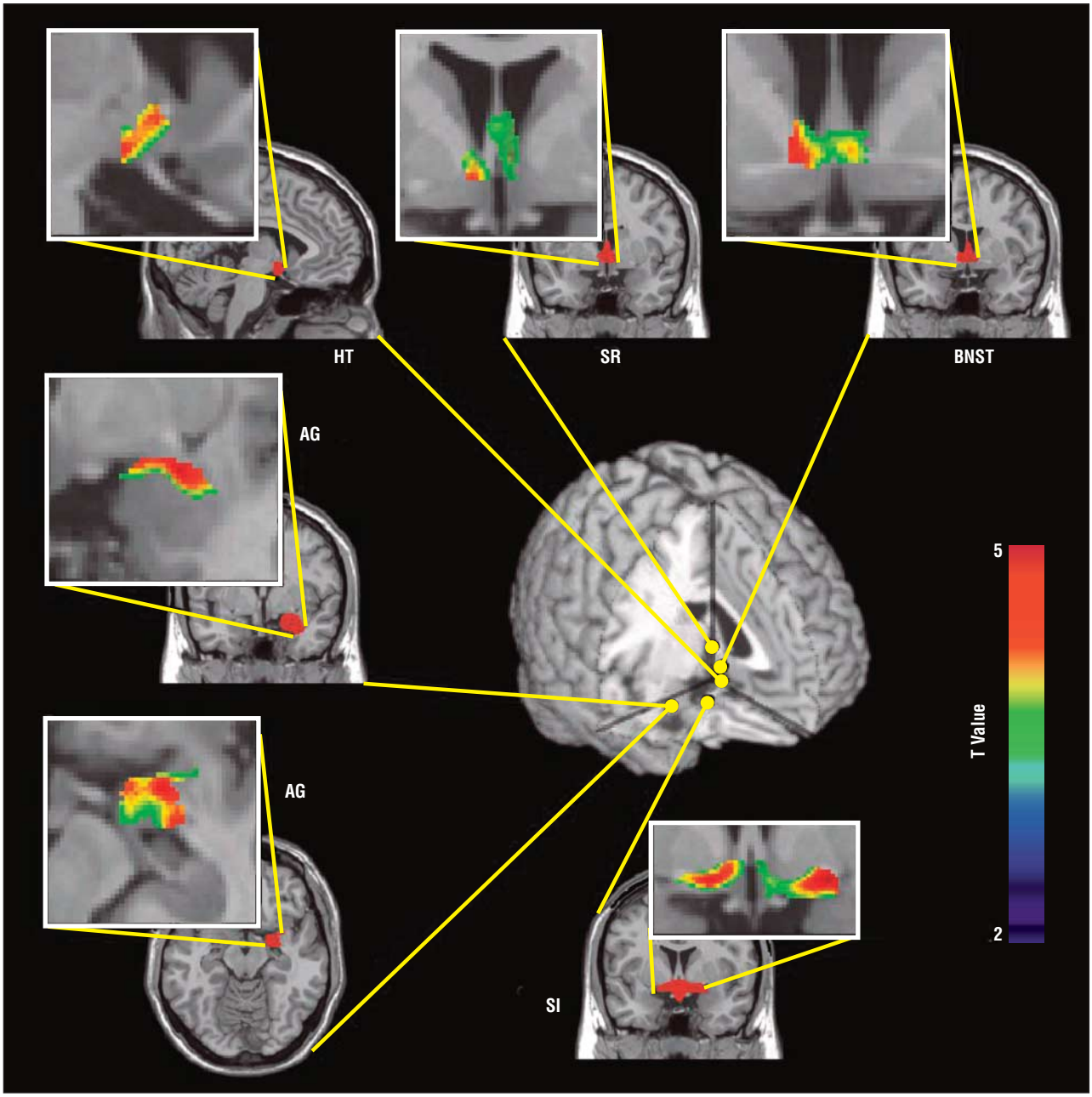

Figure 3. Local gray matter reduction in pedophilic perpetrators. Shown are the region of interest analyses for the amygdala (AG), hypothalamus (HT), and bed nucleus striae terminalis (BNST), as well as the septal region (SR) and substantia innominata (SI). Magnetic resonance imaging data are projected onto a canonical Montreal Neurological Institute brain. Whole-head sections (in the background) display the regions of interest (in red) on the appropriate slice; the inserts display enlarged views, showing the areas within the regions of interest where patients had a significantly reduced amount of local gray matter. Insert colors code T values of the voxelwise group comparisons (with a threshold at $P<.05$, corrected for multiple comparisons).

mere routine inspection of the magnetic resonance imaging scans (Figure 2).

This lateralization of amygdalar changes is consistent with the findings of Mendez et al,[9] who described a frontotemporal hypoactivity that was predominantly right sided in 2 pedophilic patients. It is also consistent with the notion of a differential role of the left and the right amygdala in the regulation of sexual behavior. Earlier studies in humans indicate that temporal lobe lesions affect sexual function more frequently with right-sided than with left-sided damage.[14] Also, they suggest that right-sided lesions tend to enhance libido, while left-sided ones tend to impair it.[42] Taken in this context, our results suggest that pedophilia might be accompanied by hypersexuality, a possibility that should be addressed by future studies.

The rater-independent VBM analysis corroborated the finding of a right-sided amygdalar alteration, with the patients showing a decreased amount of gray matter in the right amygdala and no such difference in the left (Figure 3). Furthermore, the VBM analysis also showed structural changes in other regions implicated in the development and regulation of sexual behavior. Gray matter reduction was present in the septal region and the

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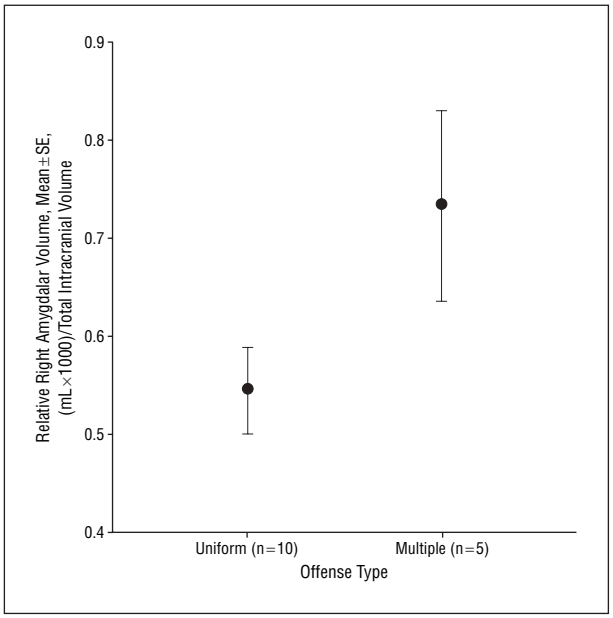

Figure 4. Relative right amygdalar volume in offenders and diversity of sexual crimes. Patients whose offenses involved uniform pedophilic activity only (uniform offense type) showed a significantly lower right amygdalar volume than those with more diverse offenses (multiple offense types).

BNST; it was also present bilaterally in hypothalamic areas, extending to adjacent parts of the substantia innominata (Figure 3). The hypothalamus, substantia innominata, septal region, and BNST encompass neuron clusters that are relevant to sexual behavior. They are densely neurally connected with the central and medial amygdalar nuclei and therefore have been regarded as the extended amygdala.[17] Because abnormal volumes of the BNST have been reported in transsexuals,[43] these alterations may not be specific to pedophilia but may rather be a feature of sexual abnormalities in general.

Gray matter reduction in the right amygdala was widespread and apparently also affected regions encompassing parts of the medial nucleus (Figure 3). Different amygdalar nuclei are constituents of quite distinct functional brain circuits,[44,45] and their function and connectivity are rather well conserved evolutionarily.[46,47] In male animals, the homologous medial amygdalar nucleus, as well as the BNST and hypothalamus, are implicated in the species-typical behavioral response to receptive estrous females by modulating the influence of olfactory, pheromonal, and other sensory cues.[17] Importantly, the influence of this nucleus on sexual behavior varies as a function of previous sexual experience. Medial amygdala lesions in male animals with antecedent sexual experience reduce their postlesional sexual motivation,[20,48] whereas in sexually inexperienced males, such lesions completely extinguish any sexual response to females.[21] Recent studies support the conclusion that the medial amygdala influences appetitive, rather than consumatory, aspects of sexual behavior.[49] Also, they have demonstrated that stimulation of the medial amygdala differentially modulates appetitive behavior depending on prior sexual experience.[22] This effect results from long-term changes of neuronal response properties in the medial amygdala and the medial preoptic area of the hypothalamus, induced by first-time exposure to females. Apparently, it reflects an indispensable nonrecurring facilitation process in normal sexual maturation.[22,50] Deficits in these structures that exist through childhood and especially adolescence might thus interfere with the development of normal appetitive behavior elicited by exposure to females and promote responses to rather inappropriate stimuli.

Given defective sexual maturation resulting from amygdalar impairment, we expected a relationship between amygdalar impairment and the criminological characteristics of the sexual offenses. Assessment of the SVR-20 scores describing the criminological characteristics of the pedophilic offenses revealed that low right amygdalar volume was correlated with an offense pattern more focused on uniform pedophilic activity. Moreover, low right amygdalar volume was also associated with prevalence of incestuous pedophilic activity. By contrast, no relation to psychopathy scores was evident, reflecting psychological characteristics independent of sexuality.

Because small right amygdalar volume was not dependent on age, the present results suggest a major contribution of a neurodevelopmental deficit to the formation of pedophilic sexual preference. During adolescence, 2 conceptually separable but temporally coordinated processes lead to the development of a reproductively mature individual: gonadal and behavioral maturation. Behavioral sexual maturation is influenced by gonadal maturation via the organizational effects of gonadal steroid hormones on neuron populations in the amygdala, hypothalamus, BNST, and septal regions, which are richly endowed with gonadal steroid receptors.[16,51] Sexual maturation encompasses the acquisition of sensory associations as well as sexual salience attribution.[22,50,51] As a consequence of this neural reorganization induced by gonadal steroids and modulated by experience, neuroendocrine and neurochemical reactions to pheromonal and other sensory cues begin to convey sexual salience and elicit mating behavior,[51] though the impact of pheromones is diminished in humans.[37,52] At this point, a dysfunction of the medial amygdala and related structures might interfere with sexual maturation, leaving the affected individual without the normally emerging sexual salience of sensory associations that are crucial for mature sexual behavior. Furthermore, a devaluation of pre-existing infantile sexual interest in other children, postulated by Freund and Kuban[53] to occur in the course of puberty, might thereby fail to appear. This might lead to a combination of an infantile sexual preference with an adult sexual drive that is mainly governed by gonadal steroids.[53,54] This explanation is consistent also with the observation that head injuries before puberty are associated with pedophilia, whereas head injuries during adulthood are not.[7] Biologically disturbed maturation of sexual behavior is also well in line with a previously proposed pathogenetic model of pedophilia that posits that a pedophilic orientation may develop on the basis of predominantly temporal brain anomalies.[10] Whether this orientation is manifested in behavior depends on accompanying factors, such as sociopathy, empathy deficits, and cognitive distortions.[55]

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Notwithstanding the essential importance of the amygdala in the development of sexual behavior, observations in patients with Urbach-Wiethe syndrome, a rare disease leading to bilateral amygdalar destruction, have not revealed an overt propensity to pedophilia in affected individuals.[56] However, considerable clinicopathologic diversity is present in this syndrome, with intracranial lesions developing inconstantly and variably throughout life[57-59]; therefore, they do not necessarily interfere with sexual maturation during puberty.

As has been pointed out previously, certain subpopulations can be distinguished among child molesters by means of criminological, socioeconomic, and other psychological characteristics, including intelligence,[60-62] which also differ with respect to their prognosis.[63,64] These characteristics are likely to interact with the influence of neurobiological factors, as well. Here, we examined a sample of true pedophiles with unimpaired intelligence, while child molesters in general show a wide range of intelligence, with an average below that of healthy controls.[3] Thus, on the basis of our data, we cannot assess whether child molesters with impaired intelligence display similar neurobiological features or whether they should even be considered as a distinct clinical entity.[65,66] Such an assessment is an important topic for future studies.

On the basis of the present data, it is not possible to infer the etiology of the structural impairment and its exact pathogenetic role in pedophilia. The structural changes might result from prenatal or early life disturbances, such as neurodevelopmental problems,[7] defective organizational effects of gonadal steroids, or other intrauterine neurohormonal events.[54] By contrast, chronic stress seems unlikely as a cause of amygdalar atrophy, because the amygdala (unlike the hippocampus) displays stress-induced hypertrophy rather than atrophy.[67] Nevertheless, the consequences of early sexual abuse (frequently reported by the perpetrators) on amygdalar structure might differ and therefore must be specifically addressed.

Our results provide evidence that structural deficits of the right amygdala and closely connected structures, presumably of neurodevelopmental origin, are related to the sexual deviance of pedophilic perpetrators. Further studies should address the impact of environmental insults and how structural alterations interact with other environmental influences (such as the psychosocial setting during childhood and adolescence) that are allegedly causative in the development of pedophilia.

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