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Structural brain abnormalities in the frontostriatal system and cerebellum in pedophilia

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Abstract

Even though previous neuropsychological studies and clinical case reports have suggested an association between pedophilia and frontocortical dysfunction, our knowledge about the neurobiological mechanisms underlying pedophilia is still fragmentary. Specifically, the brain morphology of such disorders has not yet been investigated using MR imaging techniques.

Whole brain structural T1-weighted MR images from 18 pedophile patients (9 attracted to males, 9 attracted to females) and 24 healthy age-matched control subjects (12 hetero- and 12 homosexual) from a comparable socioeconomic stratum were processed by using optimized automated voxel-based morphometry within multiple linear regression analyses.

Compared to the homosexual and heterosexual control subjects, pedophiles showed decreased gray matter volume in the ventral striatum (also extending into the nucl. accumbens), the orbitofrontal cortex and the cerebellum.

These observations further indicate an association between frontostriatal morphometric abnormalities and pedophilia. In this respect these findings may support the hypothesis that there is a shared etiopathological mechanism in all obsessive–compulsive spectrum disorders.

Keywords: Mri; Voxel-based morphometry; Sexual deviance; Sexual orientation; Pedophilia

1. Introduction

Pedophilia is a psychiatric disorder of great public concern, characterized by intense sexually arousing urges and behaviors focused on sexual activity with a prepubescent child. According to estimates of the German authorities (Bundeskriminalamt), the incidence of child sexual abuse in Germany is as high as 550 cases per day (200,000 per year), though only every 20th case is recorded. For the U.S., the estimates are as high as 500,000 per year (Fuller, 1989).

Variations in sexual preferences in men may have multiple causes; genetically initiated events, experience-induced learning, brain structure, and certainly features of an ancestral environment (Quinsey, 2003). Despite multiple investigations, evidence of a causal relationship between abnormal brain functioning and pedophilia has remained elusive. Numerous studies have discussed associations between behavioral disinhibition, frontal abnormalities, and impaired cognitive executive functioning. Although recent data from neuropsychological, personality, sexual history, plethysmography, and neuroimaging research suggest that pedophilia is linked to early

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neurodevelopment perturbations (Cantor et al., 2004; Cohen et al., 2002), the neurobiological basis of the disorder is still largely unknown.

It has been suggested that sexual compulsive disorders such as pedophilia may be related to the obsessive–compulsive spectrum disorders (OCD spectrum), including impulse-control disorders such as pathological gambling, kleptomania and trichotillomania, disorders associated with bodily preoccupation, and neurological disorders such as Tourette's syndrome (Stein, 2000; Castle and Phillips, 2006; Hollander, 1998). Although the etiology of all these disorders is not well understood, substantial phenomenological and genetical overlap exists (e.g. repetitive and poorly inhibited behaviors, dopamine receptor alleles, etc., Chamberlain et al., 2005), and pharmacological treatments that modulate levels of 5-HT have been shown to be effective in all of them (Chamberlain et al., 2005; Stein, 2000; Bradford, 2001). Studies on structural brain alterations in obsessive–compulsive (OC) and spectrum disorders showed abnormalities in frontostriatal circuits, the basal ganglia, and insulo-opercular regions as well as the cerebellum (see Jenike et al., 1996; Pujol et al., 2004; Valente et al., 2005; Szeszko et al., 2004; Szeszko et al., 2005) that were comparable to those discussed for aggressive and violent behavior (Raine et al., 2000; Bufkin and Luttrell, 2005).

It has been argued that structural alterations might be responsible for the development of functional deficiencies in the context of social or antisocial behavior. This leads to the hypothesis that pedophilic subjects may show structural deficiencies in brain regions that are part of the frontostriatal system. The striato-thalamo-cortical network initially reported by Alexander et al. (Alexander and Crutcher, 1990; Alexander et al., 1986, 1990) is closely associated with both the dopaminergic innervations of the frontal lobes and the pathophysiology of impulsive, addictive and compulsive behavioral propensities. In particular, the lateral orbitofrontal loop (Mega and Cummings, 2001) seemed to be associated with disinhibition and stimulus-controlled behavior, such as sexual compulsive behaviors. However, apart from two anecdotal case studies (Burns and Swerdlow, 2003; Mendez et al., 2000) no data regarding the characteristics of brain structure in paraphilia using modern MR imaging techniques have so far been reported.

Here, we report on the first study using voxel-based-morphometry (VBM) to investigate abnormalities in brain morphology in pedophiles. VBM is a fully automated, whole-brain image analysis technique that involves the voxel-wise comparison volumes of segmented gray and white matter of two groups of subjects (Ashburner and Friston, 2000; Good et al., 2001). It has the advantage that macroscopic differences are discounted using normalization, and differences in local tissue composition can be explored without resorting to the use of manually placed regions of interest. Furthermore, no a priori hypothesis regarding the localization of group differences is required. We hypothesized that subtle abnormalities in the frontostriatal and limbic system are apparent in pedophiles, in contrast to age-, sex- and socio-demographic-matched healthy controls. According to our hypothesis, alterations in these systems may underscore that pedophiles share similar neurobiological features with the wide OCD spectrum, including impulsive or antisocial behavior.

2. Methods

2.1. Subjects

Out of a population of 200 sex offenders from two high-security forensic treatment facilities, we screened 60 male child molesters for participation in this study. Those included in the study met the DSM-IV criteria for pedophilia were exclusively attracted to male or female children, not limited to incest, and were not on medication. Typologically, only child molesters from the interpersonal type with a high deviant fixation level were included (Knight and Prentky, 1990). Out of the 22 pedophile patients who met these criteria, 18 (9 exclusively attracted to girls and 9 to boys) with a mean age of 37.7 years (±7.9 SD, range 22–54) were prepared to take part in the examination. Three subjects refused participation; one because of neurological impairments.

Twenty-four healthy male volunteers (12 homosexually oriented and 12 hetero-sexually) with a mean age of 33.6 years (±7.2 SD, range 22–46) were recruited to match the patient group for age, sexual orientation, handedness, and education level, though the latter criterion could not be full achieved (see Table 1). Sexual orientation was assessed by the volunteers themselves using the Kinsey Scale (Kinsey et al., 1948). Only those subjects were included who scored 0 or 1 (exclusively or predominantly heterosexual), or 5 or 6 (exclusively or predominantly homosexual). Controls with a history of neurological or systemic illness, head injury or substance abuse, and a personal or family history of psychiatric illness were excluded. Permission to conduct the study was obtained from the ethics committee of the Faculty of Medicine, University of Duisburg-Essen, Germany. Written informed consent was obtained from all participants.

2.2. Diagnostic assessment

All diagnoses shown in Table 2 are based on the DSM-IV criteria and were confirmed using the Structural Clinical Interview for Axis I DSM-IV Disorders (SCID I) and the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID II) (Wittchen et al., 1997; American Psychiatric Association, 1994).

For crime assessment, we analyzed the court reports. Only those patients with a history of repeated sexual abuse of children were included in the study.

The WIP (a reduced version of the German Wechsler Adult Intelligence Scale) was employed to assess global intelligence (Dahl, 1986). Further, the Wisconsin Card Sorting Test (WCST-64) (Kongs et al., 2000) was used to

Table 1
Characteristics of study groups[a]

Characteristic	Group		
	Control ($N = 24$)	Pedophilia ($N = 18$)	Statistic
Demographic			
Age	33.63 ± 7.07	37.67 ± 7.99	$F_{1,40} = 3.01$, $p = 0.091$
Years of education	13.38 ± 2.88	10.89 ± 1.96	$F_{1,40} = 27.20$, $p = 0.000$
(Last) Employment[b]	3.18 ± 1.54	2.51 ± 1.12	$U = 184.00$, $p = 0.402$
Cognitive and physical			
Full scale intelligence, IQ	110.17 ± 8.51	101.83 ± 8.21	$F_{1,40} = 7.87$, $p = 0.008$
Visual-spatial memory	5.75 ± 1.03	4.89 ± 0.83	$F_{1,40} = 8.41$, $p = 0.006$
Alertness	106.63 ± 12.47	100.47 ± 10.57	$F_{1,39} = 2.74$, $p = 0.106$
Executive functioning, *T*-score	50.25 ± 5.37	46.72 ± 6.91	$F_{1,40} = 3.47$, $p = 0.070$
Handedness, $N =$ (right/left)	$N = (21/3)$	$N = (16/2)$	$U = 213.00$, $p = 0.892$
Weight (kg)	78.25 ± 11.33	89.23 ± 21.20	$F_{1,40} = 4.72$, $p = 0.036$
Criminal			
Number of abuses (court report)	–	7.47 ± 3.22	
Length of stay in a forensic hospital (in years)	–	5.94 ± 2.86	
Personality (MMPI-2)			
Psychopathy, *T*-score	57.50 ± 9.82	72.00 ± 10.60	$F_{1,40} = 20.97$, $p = 0.000$
Schizophrenia, *T*-score	53.58 ± 11.03	66.61 ± 9.94	$F_{1,40} = 15.60$, $p = 0.000$
Depression, *T*-score	53.33 ± 10.90	64.33 ± 9.36	$F_{1,40} = 11.80$, $p = 0.001$
Obsessiveness, *T*-score	48.17 ± 10.84	61.06 ± 11.35	$F_{1,40} = 13.97$, $p = 0.001$
Alcoholism (MAC-R), *T*-score	48.63 ± 9.94	55.78 ± 10.07	$F_{1,40} = 5.27$, $p = 0.027$
Psychosexual aspects (MSI)			
Sexual obsessiveness	3.13 ± 3.2	8.39 ± 4.9	$F_{1,40} = 17.68$, $p = 0.000$
Child sexual abuse	2.33 ± 2.2	22.5 ± 6.2	$F_{1,40} = 223.2$, $p = 0.000$

[a] All data are given as means ±SD unless otherwise indicated, MAC-R indicates MacAndrew Alcoholism Scale-Revised.
[b] (Last) Employment was classified as follows: 1 = out of work; 2 = vocational training; 3 = help/ unskilled worker; 4 = employee/clerks; 5 = officer.

estimate executive functioning (e.g. cognitive flexibility [set shifting] and abstract reasoning), the D2 Attention-Deficit Test (Brickenkamp, 1994), and the Corsi Block-Tapping Test (Schellig, 1997) for estimating alertness, and the visuospatial or working memory capacity.

All subjects underwent testing for basic measures of personality and psycho-sexual aspects using the Minnesota Multiphasic Personality Inventory, Version 2 (MMPI-2) (Hathaway et al., 2001), and the Multiphasic Sexuality Inventory (MSI) (Deegener, 1995). Demographic and psychosocial measures, also shown in Table 1, were derived from our own psychosocial questionnaire, including age, height, weight, family status, education level, life events, daily hassles, and contentedness in different life areas.

2.3. MRI procedure and statistical analysis

Structural MR imaging was conducted on a scanner (Siemens Sonata, Erlangen, Germany) with a magnet of 1.5-T field strength using a standard volume head coil. After an initial alignment sequence of 10 s, a three-dimensional (3D) Tl-weighted fast low angle shot (FLASH) echo sequence (TR 10 ms, TE 4.5 ms, flip angle 30°, FOV 240 mm, 256 × 256 matrix, slice-thickness 1.5 mm) was acquired for each subject. During the scanning procedure, all participants were comfortably placed, and their heads were fixated within the head coil with special cushions.

Data were processed on a standard IBM-compatible PC using SPM2 statistical parametric mapping software (Welcome Department of Cognitive Neurology, London) and working in an analysis environment (MATLAB; the Math Works Inc, Natick, Mass). The images were reoriented into oblique axial slices aligned parallel to the anterior–posterior commissural axis with the origin set to the anterior commissure.

Next, the images were processed according to a method that optimizes segmentation for VBM (Good et al., 2001), as recently reported (Grosskreutz et al., 2006). In brief, this involves first the creation of a customized template, followed by an iterative procedure for segmentation and normalization of images.

The whole-brain images were spatially normalized to the standard Montreal Neurological Institute (MNI) Tl template in SPM2 and resliced to 1 × 1 × 1 isotropic voxels. Normalization involved two steps: estimation of the optimum 12 parameter af-fine transformation, followed by 16 non-linear iterations (Ashburner and Friston, 2000). Normalized structural images were then averaged and the resulting image was smoothed with an 8 mm Gaussian kernel to create a customized template with scanner-specific contrast which was also appropriate for the study sample. The images were secondary normalized to the customized Tl template. The resultant images were segmented into white matter, gray matter and CSF, using image intensity non-uniformity corrections (Ashburner

Table 2
Rates of axis I and axis II comorbid disorders in 18 male pedophilic sex offenders

Disorder	Current		Lifetime	
	N	%	*N*	%
Any axis I disorder	8	44.4	12	66.6
Any mood disorder	3	16.6	8	44.4
Major depression	1	5.5	7	38.8
Dysthymia	2	11.1	2	11.1
Any anxiety disorder	6	33.3	8	44.4
Panic disorder	1	5.5	1	5.5
Social phobia	4	22.2	5	27.7
Simple phobia	2	11.1	3	16.6
Obsessive–compulsive disorder	0	0.0	1	5.5
Posttraumatic stress disorder	3	16.6	5	27.7
Any psychoactive substance use disorder	0	0.0	7	38.8
Alcohol	0	0.0	7	38.8
Cannabis	0	0.0	1	5.5
Cocaine	0	0.0	1	5.5
Polydrug use	0	0.0	1	5.5
Any psychotic disorder	0	0.0	0	0.0
Any eating disorder	1	5.5	1	5.5
Binge eating	1	5.5	1	5.5
Any axis II disorder	11	61.1		
Cluster A	3	16.6		
Paranoid	2	11.1		
Schizoid	1	5.5		
Schizotypical	0	0.0		
Cluster B	6	33.3		
Histrionic	0	0.0		
Narcissistic	3	16.6		
Borderline	4	22.2		
Antisocial	3	16.6		
Cluster C	7	38.8		
Avoidant	6	33.3		
Dependent	1	5.5		
Obsessive–compulsive	3	16.6		

and Friston, 2000). Gray matter, white matter and CSF segments were averaged and smoothed with an 8 mm Gaussian kernel to create template images for the three classes of tissues.

The original axial structural images underwent automatic segmentation and brain extraction, producing extracted gray and white matter partitions in native space. Extracted images for each tissue type were normalized to their tissue-specific templates. The optimized normalization parameters obtained for each tissue compartment in this step were applied to the original whole-brain images. The resulting three models were resliced to a final voxel size of 1 mm^3. Each optimally normalized tissue-specific whole-brain model was then segmented to isolate the corresponding tissue compartment producing gray matter, white matter, and CSF maps in MNI space. Voxel values in segmented images were multiplied by the Jacobian determinants derived from spatial normalization to provide intensity correction for induced regional volumetric changes, thus preserving within-voxel volumes that may have been altered during non-linear normalization. The analysis of these 'modulated' data tests for regional differences in absolute tissue volume. The images were smoothed to 8 mm using a FWHM (full width half-maximum) Gaussian filter to minimize individual gyral variations and to increase the statistical validity of the analysis. As a consequence of smoothing, each voxel in these 'modulated' images contains an absolute measure of tissue volume from around that voxel.

One-way ANOVA and *F*-test, or the Mann/Whitney *U*-test, were used to compare continuous and categorical demographic variables for pedophiles and healthy controls.

Processed images of each tissue class were analyzed in the framework of the general linear model and the theory of Gaussian random fields (Poline et al., 1997). This framework allows the testing, on a voxel-by-voxel basis, of the null hypothesis that the tissue volumes in the two populations (patients and controls) are the same. The resulting statistical parameters constitute a SPM of the t statistic (SPM (t)). Group comparison of pedophile patients and healthy controls was performed in SPM2 using the model 'compare-populations: one scan/subject (ANCOVA)'. During modulation we incorporated the correction for volume change induced by spatial normalization. Therefore, it was appropriate to include the global mean voxel value of each tissue class as a covariate, to determine the region-specific pattern of loss or gain within each compartment, as well as to remove any variance due to differences in head size. Potentially confounding variables, such as age, global intelligence, and consumption of alcohol, were also entered as covariates into the main SPM group analysis. Additionally, regression analyses with personality measures were explored using the SPM2 model 'single subject: covariates only'. As for the group comparisons, ANCOVA with the mean voxel value was used to normalize image intensity in the different tissue maps to allow identification of the regional pattern of these correlations.

Resulting statistical parametric maps were derived at a significance level of $p < 0.001$, uncorrected with an extent threshold of 100 voxels. Only voxels which survived correction for multiple comparisons in the entire volume using the false discovery rate (FDR) method ($p < 0.05$) were considered as significant (Genovese et al., 2002).

Since this was the first VBM study in pedophiles, we focused on the more exploratory approach of a whole brain analysis, although this kind of analysis bears the disadvantage that there is substantial loss of statistical power due to the large number of comparisons. Therefore, for regions where an effect was hypothesized, namely the frontostriatal and limbic system, insulo-opercular segments and the cerebellum (see Section 1), a small volume correction (SVC) limited to the volume of these particular regions was performed. Here, we controlled for multiple comparisons by using the family wise error (FWE) method ($p < 0.05$).

3. Results

Mean (±SD) intracranial volume did not significantly differ between patients with pedophilia and control subjects (1291 ± 0.2 and 1341 ± 0.1; $p = 0.371$).

Compared with healthy controls, patients with pedophilia showed a significantly lower amount of gray matter volume in the bilateral orbitofrontal cortex, the bilateral insula, the bilateral ventral striatum (putamen), and some limbic gyri (cingulate and parahippocampal). Additionally, bilateral alterations in part VIIB caudal aspect of tuber; cerebellum nomenclature of Schmahmann et al. (1999) of the posterior lobe and right part IX (Uvula) of the anterior vermis were observed. In contrast, no regions showed absolute increases in gray matter volume for pedophiles. Fig. 1 shows the gray matter volume decreases in pedophilia in eight axial views. These images summarize and expand the description of our primary results by mapping the distribution of the observed brain changes in pedophilia more comprehensively. Significant peak differences in voxel volumes observed between patients and control subjects are reported in Table 3 as well as the remaining significant voxels, if, in addition to brain volume, age and consumption of alcohol, the global intelligence level was also entered as a potentially confounding covariate in the group analysis.

No region displayed statistically significant decreases or increases in white matter or CSF volume in patients with pedophilia compared with controls. Additionally, no brain alterations were found in relation to sexual gender orientation in controls.

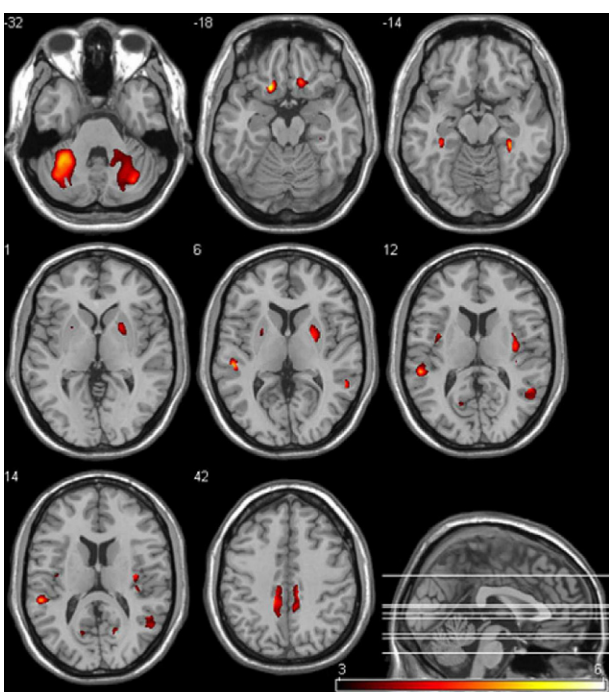

Fig. 1. A statistical parametric map showing significantly decreased gray matter volumes in pedophile patients compared with healthy controls. Height threshold: $t = 3.30$; $p = 0.001$ (uncorrected) extended threshold 100 voxels. The map is projected on a standard normalized Tl-weighted image in selected axial slices displayed in neurological convention. The color bar represents the t-score. The numbers in the top left corner of each section represent the z MNI coordinate. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Using the SPM2 model 'single subjects, covariates only', separate analyses were conducted for relevant clinical measures that seem to play a role in pedophilia (Quinsey, 2003; Cantor et al., 2004; Cohen et al., 2002; Raymond et al., 1999). This allowed examination of the specificity of the reported findings for pedophile behavior, since the observed differences in brain morphology could also be due to specific comorbid symptoms. Because clinical measures were part of the disorder we did not use them as confounding variables in the previous ANCOVA. As group differences between patients and control subjects were found only in the gray matter segments, no covariate analyses were performed for white matter and CSF volumes.

The obsessiveness T-score as assessed by the MMPI-2 was negatively correlated with frontostriatal structures, including the bilateral ventral striatum and the bilateral orbitofrontal cortices. Additionally, volume reductions in the left posterior lobe of the cerebellum were found (Fig. 2a and Table 4). The regression analysis with the Depression Scale and the gray matter volume reductions in pedophilia is shown in Fig. 2b. The mediofrontal and orbitofrontal structural atrophies were negatively correlated to depression and to obsessiveness (Table 4).

There was no correlation between gray matter volumes and most of the neuro-psychological parameters shown in Table 1 like alertness, visuospatial memory, etc. (data not shown). In addition, separate analyses were also conducted for schizophrenic symptoms, social introversion, antisocial behavior, psychopathy, etc., and length of stay in a forensic hospital. However, none of these variables predicted any anatomical change in the pedophilic brain.

4. Discussion

The neurobiological mechanisms underlying paraphilic sexual behavior are largely unknown and a neuroanatomical correlate for pedophilia has not been identified thus far. In this first MRI study of pedophilia, an optimized version of the voxel-based morphometric method was employed to identify and characterize differences in the brain structure associated with pedophilia. We observed reductions in gray matter volume in the bilateral orbitofrontal cortex, the bilateral insula, the bilateral ventral striatum (also extending into the nucleus accumbens) and some limbic gyri (cingulate and parahippocampal) compared to healthy controls. Furthermore, bilateral alterations in part VIIB (caudal aspect of tuber) of the posterior cerebellum and right part IX (Uvula) of the anterior vermis were observed. In contrast, we found neither relative volume increases for pedophiles, nor any structural brain alterations in relation to sexual gender orientation in controls. Additionally, conducting regression analyses with several co-morbid symptoms and brain structure revealed a significant negative correlation between obsessiveness/depression and pedophilic brain morphology.

The specificity of the observed difference between pedophile patients and healthy controls was confirmed by

Table 3
Regional gray matter volume decreases in patients with pedophilia compared to those in control subjects

Brain region	Hemisphere	BA	MNI coordinates			Cluster size	T Value	$P_{\text{FDR-corr}}$	$P_{\text{FWE-corr}}$ (SVC)
			x	y	z				
Cerebellum									
VIIB+ (caudal aspect of tuber)	R		30	−71	−53	35,628	5.66	0.002	0.011[a]
	L		*−33*	*−45*	*−39*		*5.57*	*0.002*	*0.015*[a]
IX+ (uvula)	*L*		*−43*	*−50*	*−43*		*5.49*	*0.002*	*0.018*[a]
Frontal Lobe									
Inferior frontal gyrus	L	47	−15	22	−20	603	5.61	0.002	0.013[a]
	R	47	15	26	−19	396	4.64	0.002	0.010
Cingulate gyrus	R	31	11	−30	45	2428	4.91	0.002	0.005
	R	31	−11	−36	42		4.58	0.002	0.011
	L	31	11	−42	45		3.97	0.005	0.005
Posterior cingulate gyrus	L	30	−14	−65	12	649	3.55	0.009	0.015
Insula	*L*	*13*	*−35*	*0*	*12*	*121*	*3.80*	*0.006*	*0.035*
	R	*13*	*38*	*−10*	*13*	*1510*	*4.40*	*0.003*	*0.008*
Parietal Lobe									
Precuneus	L	31	−10	−74	20	649	4.46	0.003	–
	R	31	13	−73	20	287	3.81	0.006	–
Temporal Lobe									
Parahippocampal gyrus	R	37	33	−36	−12	345	5.33	0.002	0.028[a]
	L	36	−32	−32	−14	182	4.41	0.003	0.001
Superior temporal gyrus	*L*	*41*	*−50*	*−28*	*6*	*1121*	*4.86*	*0.002*	–
	R	*22*	*51*	*−51*	*11*	*608*	*4.46*	*0.003*	–
Middle temporal gyrus	R	38	40	9	−45	150	3.45	0.010	–
Subcortical regions									
Ventral striatum (Putamen)	R		26	0	7	1510	4.35	0.003	0.009
	L		−22	6	5	108	3.64	0.008	0.038

Coordinates (in mm) of significant local maxima more than 8 mm apart are given for information in MNI space (Montreal Neurological Institute, http://www.bic.mni.mcgill.ca). Volume reductions in the regions printed in italic letters lost significance, if the IQ was entered as a covariate into the SPM group analysis. P values are given after false discovery rate (FDR) correction for the entire volume. For regions where an effect was hypothesized (see introduction), a small volume correction (SVC) was performed. Here, P values are given after family wise error (FWE) correction for the particular volume.

[+] Cerebellum nomenclature of Schmahmann et al. (1999).

[a] Regions which survived FWE correction for the entire brain volume ($p < 0.05$). BA = Brodmann area, R = right, L = left.

conducting several ANCOVAs with potentially confounding variables, such as age, global intelligence, consumption of alcohol, etc., which – except for global intelligence – did not significantly contribute to the observed morphological alterations in pedophilia. The pedophile subjects in this study were on average less intelligent than normal controls. Consistent with other studies, global intelligence exemplified some structural abnormalities, including the temporal and cerebellar alterations but not those in the frontostriatal regions (Frangou et al., 2004; Haier et al., 2004). Possibly, the morphological abnormalities, that correspond to cognitive impairment, signify that pedophilia is linked to early neurodevelopmental perturbations as previously hypothesized (Cantor et al., 2004). The volume reductions observed in several interconnected parts of the frontostriatal brain, such as the orbitofrontal cortex and putamen, seem to form a neurophysiological circuit, which may contribute to the patho-physiology of pedophilia. This circuit is probably not specific for pedophilia, but may also be involved in other deviant behaviors like addictive, impulsive or compulsive behaviors. This is supported by the fact that most of the frontostriatal alterations correlated with obsessiveness and depression in the pedophiliacs.

Interestingly, these brain areas belong to the serotonergic system which has been shown to play a crucial role in the pathophysiology of such disturbances (Chamberlain et al., 2005; Stein, 2000). However, global involvement of 5-HT in the sense of the formerly postulated serotonin deficiency hypotheses is no longer likely. Instead, theories of 5-HT receptor-dysregulation, receptor imbalance and second-messenger disturbances in determining OC and spectrum disorders have been developed and warrant further investigation (Chamberlain et al., 2005; Baumgarten and Grozdanovic, 1995).

In addition to serotonergic mechanisms, the dopaminergic system – which has projections to the prefrontal cortex and the cerebellum – may also play an important modulatory role in the pathophysiology of pedophilia. In particular, this is indicated by the relation between obsessiveness and structural alterations in the ventral striatum including the nucleus accumbens, which contains a high density of dopaminergic neurons and plays a major role in reward

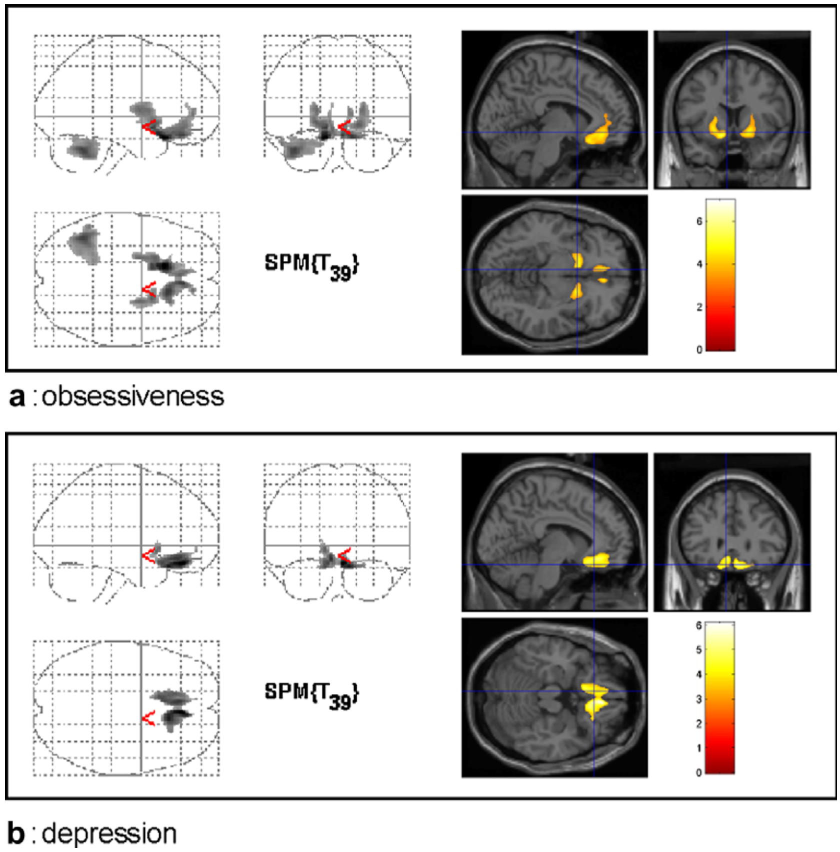

Fig. 2. Statistical parametric t map of gray matter volume reduction in pedophilia. Clusters of more than 1000 voxels showing uncorrected $p < 0.001$ are displayed in neurological convention. The three orthogonal planes on the left side represent a typical maximum intensity projection "glass brain", and the set of images on the right side illustrates results superimposed on normalized three planar structural images in selected planes. The color bar represents the t-score. (a) Covariate analysis with obsessiveness (MMPI-2); (b) depression (MMPI-2). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 4
Pattern of regional correlations in patients and control subjects for representative voxels

Brain region	Hemisphere	BA	MNI coordinates			Cluster size	T Value	$P_{\text{FDR-corr}}$	$P_{\text{FWE-corr}}$ (SVC)
			x	y	z				
Obsessiveness									
Inferior frontal gyrus	L	47	−13	20	−22	10,137	7.00	0.001	0.001[a]
Medial frontal gyrus	R	25	13	24	−19		5.44	0.005	0.002
Ventral striatum (Putamen)	L		−13	10	−12		5.37	0.005	0.003
	R		19	9	−8	2512	4.73	0.008	0.016
VIIAt^{+} (post lobe of the cerebellum – tuber)	L		−41	−55	−34	8940	5.30	0.006	0.003
Depression									
Medial frontal gyrus	R	11	5	38	−18	7218	6.10	0.038	0.020[a]
	L	11	−6	33	−13		5.06	0.039	0.007
Rectal gyrus (frontal lobe)	R	11	11	25	−21		5.39	0.039	0.003

[a] The same conventions apply as for Table 3.

processing (Comings and Blum, 2000; Schultz et al., 2000). A genetically predisposed reward deficiency syndrome, describing a disturbance in dopaminergic neurotransmission involved in the reward mechanism of impulsive (including antisocial), addictive and compulsive behaviors, may additionally contribute to the etiology of pedophilia (Blum et al., 2000). The structural changes reported here might underlie disturbances in reward processing in pedophilia, since the striatum and the orbitofrontal cortex are involved in reward detection and expectation (Schultz et al., 2000; Hollerman et al., 1998), whereas the nucleus accumbens is the central mediator of the system.

The frontostriatal system serves to modulate behavioral responses and interacts with other brain systems, such as the cerebellum (Middleton and Strick, 2000), where abnormalities have also been observed. The cerebellar hemispheres affect fine motor and cognitive responses, whereas the medial rostral cerebellum affects arousal, autonomic behavior, and emotional responsiveness. The anterior vermis and associated fastigial nucleus are considered to be the ''limbic cerebellum'', which is directly connected to the ventral tegmental area that provides dopaminergic input to the ventral striatum and facilitates neural activity in the septal region. Relative decreases in gray-matter volume in the ventral part of the striatum and in the functionally related rostral cerebellum (Part IX – uvula) were found in the current study. Thus, cerebellar involvement in the pathogenesis of pedophilia comparable to that in OCD may be a possibility, although the alterations observed in OCD were inconsistent. Both gray-matter volume decreases and increases were observed in OCD (Pujol et al., 2004; Chacko et al., 2000). However, there is every indication that disorders in the OCD spectrum, including pedophilia, show different alterations in various parts of the circuit mentioned above.

The neuropsychological deficits found in pedophilia are also observed in addictive behaviors (Lyvers and Yakimoff, 2003), OCD (Moritz et al., 2002), antisocial personality disorder, and psychopathy (Goyer et al., 1994; Raine et al., 2003; Raine et al., 2000). In particular, difficulties with regard to rule-adopting behavior, impulse control, and cognitive flexibility are exemplified by patients who find it difficult to act in conformity with social norms. Neurobiologically these functions have been associated with the anterior cingulate gyrus, as well as the dorsolateral-prefrontal cortex (MacDonald et al., 2000). Consistent with these structural results, the importance of the orbitofrontal cortex in controlling antisocial behavior, or for ''guiding behavioral responses'' has been emphasized before (Blair, 2004; Ernst et al., 2004). In this respect, our results may be restricted to pedophiles who are exclusively attracted to children and are not able to discourage themselves from the sexual abuse of children. The remaining reductions in the precuneus, involved in visual attention (Corbetta et al., 1995) and imagery (Lundstrom et al., 2003), and posterior cingulate gyrus, hypothetically involved in serotonergic-modulated impulsive aggression (New et al., 2002), may reflect the changed neurophysiologic circuit in pedophilia.

Independent of the question of structural brain abnormalities in paraphilia, the fact that there was no evidence for structural brain alterations in relation to sexual gender orientation in controls seems to conflict with current assumptions about homosexuality. Several studies have documented differences in brain morphology between men who prefer adult male partners and those preferring female partners (LeVay, 1991; Swaab and Hofman, 1988). We have to admit though that the intermingling of heterosexual and homosexual populations was suboptimal, as the small sample size does not allow for a reasonable statistical comparison of both subsamples in each group. However, as the essential morphological abnormalities pertain to small hypothalamic nuclei, the MRI technology employed here was probably not able to detect such small alterations.

5. Summary

In summary, this study confirms the association between frontostriatal morphometric abnormalities and pedophilia. In this respect, these findings may underscore the hypothesis that a neural substrate is shared by a wide range of psychiatric spectrum disorders characterized by inadequate urges and poorly inhibited repetitive behavior (Sheppard et al., 1999; Tost et al., 2004). To date the specificity of these findings remains residual, as does the question as to how the alterations influence the symptoms with respect to deviant behavior. This has to be examined further with a more specific design including pedophiles, community samples and another antisocial group. Additionally, specific alterations in information processing, especially the reward deficiency system in impulsive, addictive and (sexually) compulsive behaviors, have to be analyzed comparatively, using functional imaging techniques.

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