

# Brain response to visual sexual stimuli in homosexual pedophiles

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**Objective:** The neurobiological mechanisms of deviant sexual preferences such as pedophilia are largely unknown. The objective of this study was to analyze whether brain activation patterns of homosexual pedophiles differed from those of a nonpedophile homosexual control group during visual sexual stimulation. **Method:** A consecutive sample of 11 pedophile forensic inpatients exclusively attracted to boys and 12 age-matched homosexual control participants from a comparable socioeconomic stratum underwent functional magnetic resonance imaging during a visual sexual stimulation procedure that used sexually stimulating and emotionally neutral photographs. Sexual arousal was assessed according to a subjective rating scale. **Results:** In contrast to sexually neutral pictures, in both groups sexually arousing pictures having both homosexual and pedophile content activated brain areas known to be involved in processing visual stimuli containing emotional content, including the occipitotemporal and prefrontal cortices. However, during presentation of the respective sexual stimuli, the thalamus, globus pallidus and striatum, which correspond to the key areas of the brain involved in sexual arousal and behaviour, showed significant activation in pedophiles, but not in control subjects. **Conclusions:** Central processing of visual sexual stimuli in homosexual pedophiles seems to be comparable to that in nonpedophile control subjects. However, compared with homosexual control subjects, activation patterns in pedophiles refer more strongly to subcortical regions, which have previously been discussed in the context of processing reward signals and also play an important role in addictive and stimulus-controlled behaviour. Thus future studies should further elucidate the specificity of these brain regions for the processing of sexual stimuli in pedophilia and should address the generally weaker activation pattern in homosexual men.

**Objectif :** Les mécanismes neurobiologiques des préférences sexuelles déviantes comme la pédophilie sont en grande partie inconnus. Cette étude visait à déterminer si les habitudes d'activation du cerveau des pédophiles homosexuels différaient de celles d'un groupe de sujets témoins homosexuels non pédophiles au cours d'une stimulation sexuelle visuelle. **Méthode :** Un échantillon consécutif de 11 patients pédophiles hospitalisés en milieu judiciaire attirés exclusivement par les garçons et 12 participants témoins homosexuels jumelés selon l'âge provenant d'une strate socioéconomique comparable ont subi une imagerie par résonance magnétique fonctionnelle au cours d'une stimulation sexuelle visuelle produite au moyen de photographies excitantes sur le plan sexuel et neutres sur le plan affectif. On a évalué l'excitation sexuelle en fonction d'une échelle d'évaluation subjective. **Résultats :** Contrairement aux images neutres sur le plan sexuel, les images excitantes sur le plan sexuel comportant un contenu à la fois homosexuel et pédophile ont activé, chez les sujets des deux groupes, des régions du cerveau reconnues pour participer au traitement des stimuli visuels comportant du contenu émotionnel, y compris les cortex occipitotemporal et préfrontal. Au cours de la présentation des stimuli sexuels respectifs, le thalamus, le pallidum et le corps strié qui correspondent aux régions clés du cerveau impliquées dans l'excitation et le comportement sexuels ont toutefois montré une activation importante chez les pédophiles, mais non chez les sujets témoins. **Conclusions :** Le traitement central des stimuli sexuels visuels chez les pédophiles homosexuels semble être comparable à celui qui se produit chez des sujets témoins

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non pédophiles. Comparativement à des sujets témoins homosexuels, les habitudes d'activation chez les pédophiles sont toutefois reliées plus fortement aux régions sous-corticales dont on a déjà discuté dans le contexte du traitement des signaux de récompense et qui jouent aussi un rôle important dans les comportements d'asservissement et contrôlés par les stimuli. C'est pourquoi des études futures devraient préciser davantage la spécificité de ces régions du cerveau pour ce qui est du traitement des stimuli sexuels chez les pédophiles et devraient porter sur les tendances d'activation généralement plus faibles chez les hommes homosexuels.

## Introduction

Pedophilia is a psychiatric disorder of high public concern characterized by intense, sexually arousing urges and behaviours that focus on sexual activity with a prepubescent child.<sup>1</sup> According to the estimates of the German authorities, the incidence of child sexual abuse in Germany is as high as 550 cases daily (200 000 annually), though only every 20th case is recorded. For the United States, the estimates are as high as 500 000 annually.<sup>2</sup> With regard to pedophilia, numerous studies have discussed associations between behavioural disinhibition, frontal abnormalities and impaired cognitive executive functioning.<sup>3–6</sup> Although recent data from neuropsychological, sexual history, plethysmography and neuroimaging investigations suggest that pedophilia is linked to early neurodevelopmental perturbations,<sup>4,7</sup> the neurobiological basis of the disorder is still unidentified.

Human sexual arousal is a multidimensional experience comprising physiological and psychological processes. Modern imaging techniques allow the *in vivo* observation of brain activation correlated with sensory or cognitive processing and emotional states.<sup>8</sup> Previous studies<sup>9–19</sup> using functional magnetic resonance imaging (fMRI) or positron emission tomography (PET) and remote sexual stimuli such as visual erotica have shown increased neural activity in several areas, including the inferior right frontal cortex, the inferior temporal cortex, the left anterior cingulate cortex and the right insula, possibly representing a distributed network.

Moreover, imaging studies have revealed hypoactive frontal lobes in patients with impulsive personality disorders and in violent psychiatric inpatients.<sup>20–22</sup> Additionally, in the etiology of psychopathic, antisocial and violent behaviour in general, imaging data implicate brain differences in the prefrontal cortex, hippocampus, parahippocampal gyrus, angular gyrus, cingulate gyrus, basal ganglia and amygdala.<sup>23</sup> Although critically reviewed recently,<sup>24</sup> some studies suggest frontotemporal dysfunctions in pedophilia,<sup>4,7,25,26</sup> indicating that a wide range of psychiatric disorders (i.e., obsessive-compulsive [OC] spectrum disorders) may share a neural substrate characterized by inadequate urges and poorly inhibited repetitive thoughts or cognitions or behaviours.<sup>27,28</sup> However, some older studies on frontal lobe functioning in pedophilia failed to find such an association and instead suggested a more general neuropathology (for a detailed discussion see Blanchard et al<sup>24</sup>), although these results were mainly derived from computertomographic investigations, which do not provide sufficient spatial resolution. Additional research using modern imaging techniques such as PET or fMRI is therefore needed to examine these hypotheses further.

Although a difference of opinion exists concerning which illnesses should be included in the category of OC spectrum disorders, the symptom domain (i.e., the presence of obsessions or repetitive behaviours, or both) is the usual starting point for determining whether a given disorder is a spectrum candidate. Apart from obsessive-compulsive disorder, OC symptoms can be found in several disorders, including Tourette syndrome, body dysmorphic disorder, hypochondriasis and trichotillomania; it is often hypothesized that these disorders belong to the OC spectrum. However, the eating disorders, autism, pathological gambling, kleptomania, depersonalization disorder, sexual compulsions and paraphilias are sometimes also included in the OC spectrum.<sup>29</sup> Not only are all these disorders highly comorbid, they also share phenomenological similarities and biological correlates and may therefore resemble alternative phenotypic expressions of a related genetic background.<sup>30</sup> This hypothesis is in line with the concept that a genetically driven state of reward deficiency is a common denominator in the delineated spectrum.<sup>31,32</sup> From a neuronal point of view, the cortico-striato-thalamo-cortical network initially described by Alexander and colleagues<sup>33</sup> seems to be of specific importance. This network is closely associated with the dopaminergic innervations of the frontal lobes corresponding to the reward system and is related to the pathophysiology of OC spectrum disorders.<sup>5,34</sup>

However, empirical evidence of a causal relation between abnormal brain functioning and pedophilia has remained elusive. An imaging study using PET demonstrated that there is persistently decreased glucose metabolism in the right inferior temporal and superior ventral frontal gyrus.<sup>7</sup> An fMRI case study of 1 homosexual pedophile suggested abnormalities in the fusiform gyrus and the right orbitofrontal cortex during visual sexual stimulation.<sup>35</sup> Our own recent morphometric study using structural MRI found decreased grey matter volume in the ventral striatum, also affecting the nucleus accumbens, the orbitofrontal cortex and the cerebellum in pedophiles.<sup>36</sup> These findings may underline an association between frontostriatal morphometric abnormalities and pedophilia and may support the hypothesis that there is a shared etiopathological mechanism in OC spectrum disorders. However, apart from 2 anecdotal case reports<sup>25,26</sup> that also suggest temporal and orbitofrontal disturbances, no data obtained from fMRI techniques have been reported on characteristics of brain function in pedophilia. Moreover, it is completely unknown whether neuronal activation patterns during visual sexual stimulation depend on the normative deviance of the respective sexual interest.

Therefore, using the fMRI technique and photographs of nude boys and men as well as control stimuli (dressed boys and men), we compared the neuronal responses of

pedophiles who were exclusively attracted to male children with those of healthy homosexual control subjects. From the preliminary data described above, we hypothesized that, in pedophiles, there would be alterations in the activation pattern in the frontostriatal system and closely related structures such as the thalamus.

## Methods

### Subjects

We recruited a consecutive sample of 11 homosexual pedophile patients from 2 high-security forensic hospitals. All the patients recruited met the DSM-IV criteria for pedophilia, were exclusively attracted to male children, had molested at least 2 child victims and were not limited to incest. Owing to clinical reports and the results of our own examination, we only included child molesters of the interpersonal type with a high deviant fixation level, who admitted being pedophilic, and whose offenses in general were nonviolent.<sup>37</sup> We recruited 12 healthy homosexual volunteers to match the patient group for age, handedness, socioeconomic stratum and education level (Table 1). Of the participants, 7 pedophile patients and 9 control subjects had participated in a previous morphometric study.<sup>35</sup>

**Table 1: Characteristics of study groups**

Characteristic	Group; mean (and SD)*		Statistic
	Control (n = 12)	Pedophilia (n = 11)	
Demographic			
Age, y	32.0 (6.8)	37.0 (7.5)	$F_{1,21} = 2.52$ , $p = 0.13$
Education, y	12.81 (2.47)	11.15 (1.73)	$F_{1,21} = 9.31$ , $p = 0.03$
Last employment†	2.94 (1.01)	2.41 (0.71)	$F_{1,21} = 1.85$ , $p = 0.26$
Cognitive and physical			
Full-scale intelligence, T score	55.00 (7.92)	52.56 (8.59)	$F_{1,21} = 0.46$ , $p = 0.50$
Visuospatial memory	5.67 (1.15)	5.00 (0.87)	$F_{1,21} = 2.10$ , $p = 0.16$
Alertness	401.50 (95.51)	371.67 (90.05)	$F_{1,21} = 0.53$ , $p = 0.48$
Executive functioning, T score	49.92 (5.94)	49.00 (7.09)	$F_{1,21} = 0.10$ , $p = 0.75$
Handedness, n = (right/left)	(11/1)	(10/1)	NA
Weight, kg	78.67 (12.03)	93.00 (20.96)	$F_{1,21} = 3.93$ , $p = 0.06$
Criminal			
Number of abused victims (court report)	NA	7.02 (3.23)	NA
Length of stay in a forensic hospital, y	NA	6.12 (2.74)	NA

SD = standard deviation; NA = not applicable

\*Unless otherwise indicated.

†Last employment was classified as follows: 1 = out of work; 2 = vocational training; 3 = help or unskilled worker; 4 = employee or clerk; 5 = manager or officer.

Sexual orientation was self-assessed with the Kinsey Scale,<sup>38</sup> which attempts to measure sexual orientation on a 7-point scale from 0 (exclusively heterosexual) to 6 (exclusively homosexual). We included only subjects who scored 5 or 6 points (exclusively or predominantly homosexual). We excluded subjects with other disorders that could be related to neuropsychological impairment (significant physical or neurologic illness, a history of head injury, neurodegenerative disorder, substance abuse or dependence in the last year or mental retardation). Also excluded were control subjects with a personal or family history of psychiatric illness. Altogether, we excluded 4 pedophiles and 2 control subjects: 3 because of a medium score on the Kinsey Scale and 3 because of significant neuropsychological impairment. We used various tests to ascertain neuropsychological performance. A reduced version of the German Wechsler Adult Intelligence Scale was employed to assess global intelligence.<sup>39</sup> The Wisconsin Card Sorting Test<sup>40</sup> was used to estimate executive functioning (e.g., cognitive flexibility [set shifting] and abstract reasoning). The D2 Attention-Deficit Test<sup>41</sup> and the Corsi Block Tapping Test<sup>42</sup> were used to estimate information-processing rate, alertness and visuospatial working memory capacity. The psychiatric history of the pedophile sample consisted of a currently high rate of axis I comorbidity (45.5%, with a lifetime rate of 63.6%) with the foremost being mood and anxiety disorders such as social phobia. The axis II comorbidity consisted primarily of cluster B (36.4%) and C disorders (45.5%) such as avoidant and borderline personality disorders. All subjects gave informed consent to participate, and the study was approved by the ethics committee of the Faculty of Medicine, University of Duisburg-Essen, Germany. A neuroradiologist reviewed the brain MRIs. No gross abnormalities were reported.

### Experimental design

Functional imaging was performed as a block design. All subjects underwent 2 consecutive counterbalanced functional imaging sessions. Each session consisted of 14 epochs of 2 types of stimuli, 1 sexually arousing (7 epochs) and 1 neutral (7 epochs). In each session, slides of nude boys or men were employed as sexually arousing stimuli, whereas the neutral stimuli were slides of different dressed boys or men. Each epoch lasted 38.5 seconds and consisted of 1 slide with a photograph of 1 person only. In each session, sexually arousing stimuli were alternated with neutral stimuli. Session and epoch order were counterbalanced between subjects to prevent effects due to presentation order. All subjects were instructed to relax in the setting and to let the arousal occur.

Erotic and nonerotic stimuli for the nonparaphilic group were taken from the International Affective Picture System<sup>43</sup> and were validated for arousal and emotional valence. The sexually arousing and neutral stimuli for the paraphilic group were obtained from different sources such as Internet, mail-order house or art catalogues. These were evaluated for potential sexual arousal and general attractiveness by another sample of pedophilic forensic inpatients in a preliminary study that used a 10-cm visual analogue scale (VAS)

ranging from “not at all” to “extremely.” Only pictures that yielded the highest ratings (as sexual stimuli) or the lowest ratings (as neutral stimuli) for sexual arousal and attractiveness in the preliminary study were selected for the fMRI experiment.

Immediately after functional imaging, individual sexual arousal was assessed by subjective rating on a VAS based on the Acute Sexual Experience Scale (ASES).<sup>44</sup> To minimize false responses due to social desirability bias or awareness of the experimenter’s presence, we again assured subjects that all data were evaluated anonymously, and the VAS ratings were completed in a separate room.

### MRI data acquisition and processing

All images were acquired with the use of a conventional 1.5 T magnetic resonance scanner (Sonata, Siemens, Erlangen, Germany) with a phased-array head coil. Thirty-six transversal  $T_2$ -weighted slices were acquired with the use of an echo-planar imaging technique (repetition time 3500 ms, echo time 55 ms, flip angle 90°, field of view 220–240 mm, matrix 64) with 3-mm slice thickness and a 10% gap.

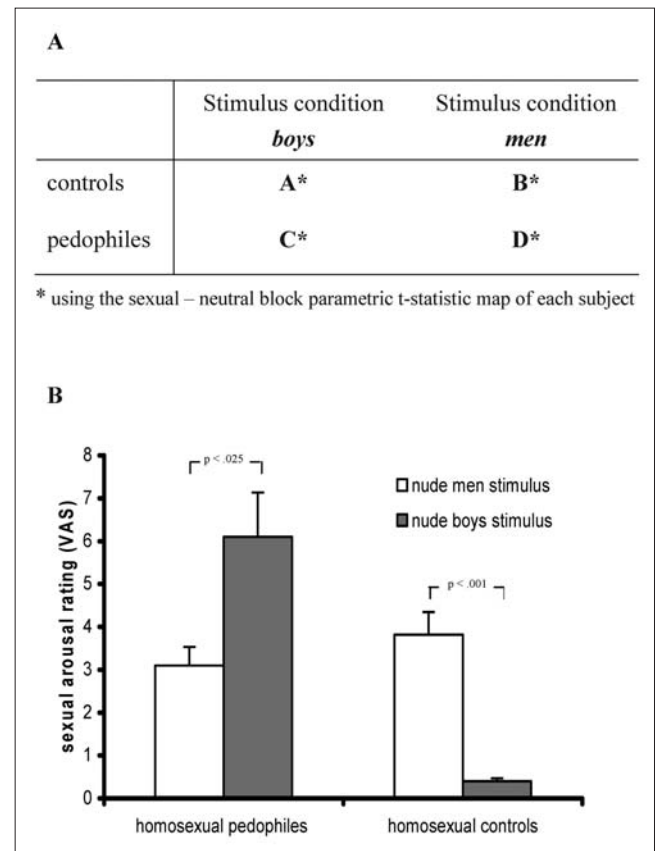
### Statistical data analysis

For data analysis, we used Statistic Parametric Mapping software (SPM02, Wellcome Department of Cognitive Neurology, London, UK). The first 3 scans in each session were eliminated from data analysis to account for  $T_1$  relaxation effects. Prior to statistical analysis, images were realigned by means of sinc interpolation and normalized to a standard space (Montreal Neurological Institute<sup>45</sup>) by means of trilinear interpolation. Images were smoothed with an isotropic Gaussian kernel with 9-mm full width at half maximum. A voxel-by-voxel comparison according to the general linear model was used to calculate differences in activation between the 2 alternating conditions. The model consisted of a boxcar function convolved with the hemodynamic response function and its corresponding temporal derivative. High-pass filtering with a cut-off of 128 seconds and low-pass filtering with the hemodynamic response function was applied. For the analysis of group-specific effects, single-subject contrast images were entered into a random effects model based on a 2-sample  $t$  test. Significant signal changes for each contrast were assessed on a voxel-by-voxel basis.<sup>46</sup> The resulting set of voxel values for each contrast represented a statistical parametric map of the statistic. For visualization of neural activity, superthreshold pixels were overlaid on the high-resolution  $T_1$ -weighted single subject images provided by SPM02.

Contrasts within each condition led to parametric  $t$  statistic maps for each subject. Areas of significant neural activation were identified for these contrasts by whole-brain analyses with a statistical threshold of  $p_{\text{uncorrected}} < 0.001$  and a spatial extent of at least 5 adjacent voxels. Intra- and intergroup differences in activation were then assessed by a second-level analysis with condition or group as a random effects factor and using the parametric  $t$  statistic maps for each subject. To examine differences in the neural response to sexually arous-

ing as opposed to neutral blocks, we first performed 1-sample  $t$  tests on the second level, using the individual statistical activation maps for each subject. In addition, we performed regression analyses to identify regions that correlated with the sexual arousal ratings of each subject. The correlation coefficients between signal changes in the significant activated clusters in each subject and the corresponding VAS ratings were calculated separately by means of bivariate Pearson correlations with an  $\alpha$  of  $p < 0.01$ .

For each group, we evaluated the processing specificity of the activation patterns induced by the specific sexual interest stimuli. We compared the 2 groups once during the men condition and once during the boys condition, using 2-sample  $t$  tests. Finally, to compare general activation patterns during visual sexual stimulation, the pedophile response to the nude as opposed to the dressed boys condition was subtracted from the activation maps of control subjects viewing nude as opposed to dressed men. For all second-level analyses, the statistical threshold was set to  $p < 0.05$  (false discovery rate-corrected), with a spatial extent of at least 10 adja-



**Fig. 1:** (A) The study design is illustrated to show the different intra- and intergroup contrasts in a  $2 \times 2$  matrix. The sexual versus neutral block parametric  $t$  statistic map of each subject was employed. (B) Subjective ratings of visual stimuli in homosexual control subjects ( $n = 12$ ) and homosexual pedophiles ( $n = 11$ ). Each subject rated 7 slides of nude boys and men on a 10-cm visual analogue scale. Data are presented as mean and standard error of the mean.

cent voxels. To simplify the different intra- and intergroup contrasts described below, we use the abbreviations A–D as indicated in the  $2 \times 2$  matrix illustrated in Figure 1A. Numerous analyses (such as neuropsychological tests, voxel-based morphometry [VBM] and fMRI) run the risk of inflating type I error rates in small samples and should therefore be performed only in larger samples or should be corrected for number of analyses. With regard to our previous VBM study<sup>36</sup> and the results in the current investigation, the latter were not corrected for the number of analyses because the VBM and fMRI analyses were not performed in exactly the same subject samples.

We analyzed VAS ratings according to a 2-factor analysis of variance with repeated-measures and with the stimulus condition as a within-subject factor. Student's *t* test was used to assess additional effects of the stimulus conditions (boys v. men) separately in pedophiles and control subjects.

## Results

Subjects with paraphilic and nonparaphilic homosexual preferences rated the sexual stimuli as equivalently sexually arousing (no main effect of group affiliation:  $F_{1,21} = 0.440$ ,  $p < 0.514$ ). However, a significant interaction effect ( $F_{1,21} = 17.662$ ,  $p < 0.001$ ) indicated that both groups reported the stimuli of their respective preference to be more arousing than the opposite stimuli. Further, the *t* statistics calculated separately in pedophiles and control subjects for the stimulus conditions (boys v. men) revealed significant differences between the VAS ratings of homosexual control subjects ( $t_{11} = 4.582$ ,  $p < 0.001$ ), and pedophiles ( $t_{10} = -2.695$ ,  $p < 0.025$ ) (Fig. 1B).

### Intragroup contrasts and regression analyses

The activation pattern of the 1-sample *t* test under each of the

**Table 2: Brain regions activated as demonstrated by a random effects group analysis of the sexual block–neutral block contrast in boys and men condition for homosexual control subjects ( $n = 12$ ) and activated brain regions as demonstrated by a regression analysis with sexual arousal ratings as regressor**

Brain regions	Sexual > neutral block contrasts*													
	Condition; nude > dressed boys						Condition; nude > dressed men							
	Lat.	BA	MNI coordinates			T	$r_{corr}$	Lat.	BA	MNI coordinates			T	$r_{corr}$
Frontal lobe														
Inferior frontal gyrus								R	46	48	51	12	4.10	
										54	42	12	3.58	
Temporal lobe														
Fusiform gyrus	<b>R</b>	<b>37</b>	<b>48</b>	<b>-48</b>	<b>-15</b>	<b>4.45</b>	<b>0.68†</b>	R	19	45	-67	-18	5.26	
	L	37	-45	-60	-21	3.12			37	48	-48	-15	4.56	
								L	37	-45	-78	-12	4.70	
										-48	-48	-21	4.68	
Inferior temporal gyrus	L	37	-45	-72	-3	3.52								
Parietal lobe														
Precuneus	R	7	27	-51	48	3.42		R	19	36	-81	33	5.45	
	L	7	-21	-60	57	3.74			7	27	-57	54	3.36	
Superior parietal lobule	R	7	33	-51	54	3.42		R	7	15	-66	63	3.49	
										21	-69	57	3.27	
Occipital lobe														
Middle occipital gyrus	R	19	51	-75	-3	3.93		R	19	33	-84	15	3.26	
			45	-81	3	4.09				42	-84	3	4.01	
	L	18	-39	-90	0	3.93		L	19	-45	-78	-12	5.29	
		19	-45	-84	3	3.42				-33	-90	3	4.23	
Inferior occipital gyrus	R	19	42	-75	-9	4.44		R	19	42	-75	-12	6.36‡	
	L	18	-36	-87	-9	4.28								
Lingual gyrus	L	18	-45	-84	-6	4.25								
Superior occipital gyrus								R	19	36	-75	27	3.88	

MNI = Montreal Neurological Institute; Lat = laterality; BA = Brodmann's area; R = right; L = left.

\*Values in bold are significantly correlated with sexual arousal ratings in the Statistic Parametric Mapping regression analyses.

† $p < 0.01$  (false discovery rate corrected or Pearson correlation).

‡ $p < 0.05$ .

**Table 3: Brain regions activated as demonstrated by a random effects group analysis of the sexual block–neutral block contrast in boys and men condition for homosexual pedophiles ( $n = 11$ ) and brain regions activated as demonstrated by regression analyses with sexual arousal ratings as regressor**

Brain regions	Sexual > neutral block contrasts*												
	Condition; nude > dressed boys						Condition; nude > dressed men						
	Lat.	BA	MNI coordinates			T	$r_{corr}$	Lat.	BA	MNI coordinates			T
		x	y	z					x	y	z		
<b>Frontal lobe</b>													
Inferior frontal gyrus	R	46	51	39	15	8.20†		L	46	-48	42	12	3.31‡
			57	33	12	7.07†							
			51	39	6	4.34‡							
		47	36	27	-18	6.11†							
			24	33	-6	4.78‡							
		9	51	15	27	4.43‡							
Superior frontal gyrus		<b>11</b>	<b>24</b>	<b>42</b>	<b>-15</b>	<b>3.75‡</b>	<b>0.68†</b>						
Middle frontal gyrus	L	<b>9</b>	<b>-51</b>	<b>15</b>	<b>33</b>	<b>6.63†</b>	<b>0.72†</b>	R	46	48	18	27	3.48‡
		46	-42	33	18	4.99‡							
	R	8	57	9	42	4.98‡							
		9	51	12	36	4.89‡							
Anterior cingulate gyrus	R	<b>25</b>	<b>3</b>	<b>15</b>	<b>-6</b>	<b>5.27‡</b>	<b>0.84†</b>	R	25	3	12	-6	4.41‡
	L	<b>25</b>	<b>-3</b>	<b>12</b>	<b>-6</b>	<b>6.07‡</b>	<b>0.83†</b>	L	25	-3	12	-6	4.54‡
	R	32	3	30	-9	3.90‡							
<b>Subcortical regions</b>													
Caudate head	R		6	18	0	3.21‡	0.87†						
Medial globus pallidus	R		18	-6	-9	5.79‡							
Lateral globus pallidus	R		27	-18	-3	5.48‡							
Putamen	R		27	3	-6	3.82‡							
Substantia nigra	L		-9	-21	-12	4.06‡							
	R		12	-21	12	3.48‡							
<b>Temporal lobe</b>													
Fusiform gyrus†	R	37	48	-45	-15	6.82†		R	37	48	-42	-15	5.37‡
								L	<b>37</b>	<b>-36</b>	<b>-57</b>	<b>-18</b>	<b>3.85‡</b>
													<b>0.87†</b>
Superior temporal gyrus	R	<b>38</b>	<b>30</b>	<b>15</b>	<b>-33</b>	<b>4.88‡</b>	<b>0.76†</b>						
	L	<b>38</b>	<b>-39</b>	<b>18</b>	<b>-36</b>	<b>5.01‡</b>	<b>0.80†</b>						
Middle temporal gyrus	L	39	-54	-72	9	8.51†		L	19	-36	-84	15	3.19‡
	R	<b>21</b>	<b>51</b>	<b>6</b>	<b>-21</b>	<b>6.10‡</b>	<b>0.86†</b>						
<b>Parietal lobe</b>													
Precuneus	R	7	30	-51	51	7.00†							
Superior parietal lobule	R	7	33	-54	60	6.88†		R	7	39	-60	57	3.27‡
								L	7	-30	-66	57	3.91‡
								L	36	-36	-36	-18	3.94‡
Parahippocampal gyrus													
Postcentral gyrus	R	2	54	-24	54	6.71†							
<b>Occipital lobe</b>													
Middle occipital gyrus	L	19	-42	-87	9	9.29†		L	19	-39	-78	6	4.19‡
			-36	-87	18	8.51†				-36	-87	9	3.47‡
	R	19	48	-72	6	8.21†							
		18	36	-90	0	6.38†							
Inferior occipital gyrus								L	19	-36	-81	-9	5.38‡
									18	-42	-87	-6	3.08‡

MNI = Montreal Neurological Institute; Lat. = laterality; BA = Brodmann's area; L = left; R = right.

\*Values in bold are significantly correlated with sexual arousal ratings in the Statistic Parametric Mapping regression analyses.

† $p < 0.01$  (false discovery rate corrected or Pearson correlation).‡ $p < 0.05$ .

sexually arousing stimulus conditions (the boys condition in pedophiles/C and the men condition in control subjects/B) showed similarities in the 2 groups regarding the occipitotemporal (Brodmann's areas [BA] 18, 19, 20, 37) and prefrontal cortices, which indicates general emotional, visual and attention processing (Table 2 for control subjects; Table 3 for pedophiles). However, compared with pedophiles, homosexual control subjects generally showed less activation during presentation of the respective stimuli, with less activated areas at the same threshold and lower  $z$  values in the activated areas. A significant signal change in the hypothalamus was not observed for either group. Further significant signal

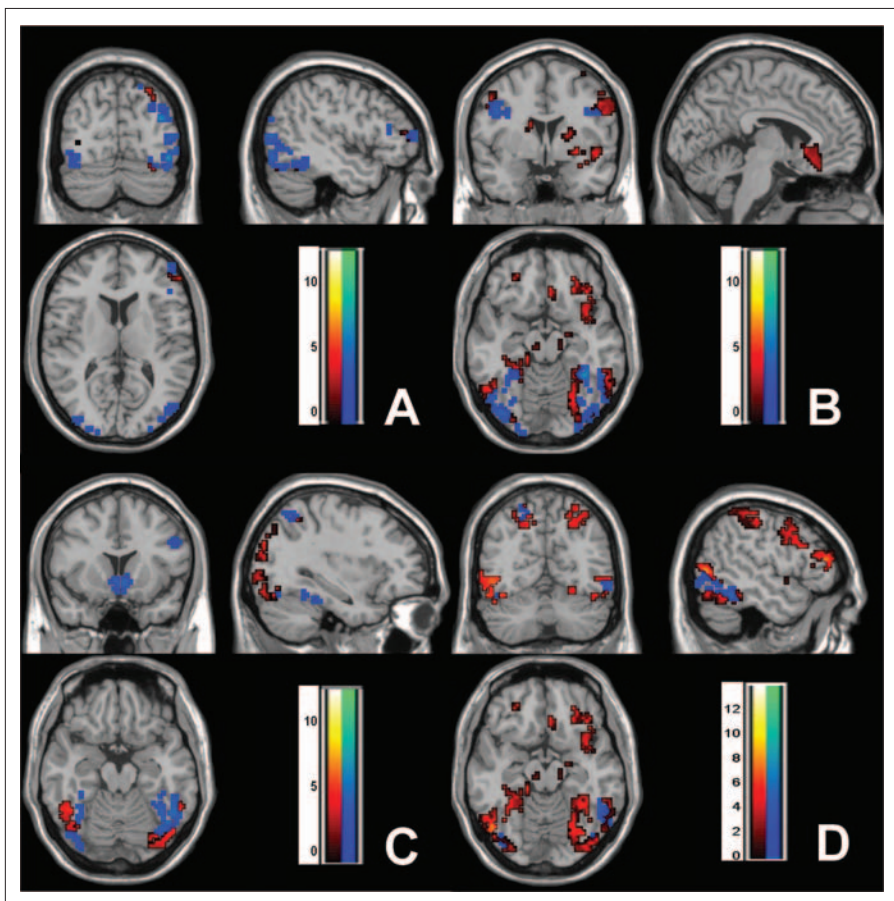
changes in the substantia nigra and in several regions of the limbic system, including the nucleus caudatus and thalamus, were found in pedophiles but not in control subjects (Fig. 2A for control subjects and Fig. 2B for pedophiles; both are in red shading). With regard to conditions A and C (nude > dressed boys), when compared with pedophiles, control subjects showed increased activation in the bilateral fusiform gyrus (BA 37), the left inferior temporal gyrus (BA 37), the superior parietal lobule (BA 7) and the bilateral precuneus (BA 7) as well as in the inferior and middle occipital regions, but not in the frontal lobe (Table 2, Fig. 2D blue shading). By contrast, in pedophiles, condition D (nude > dressed men) led to increased activation of the inferior (BA 46) and middle (BA 46) frontal gyri as well as the bilateral anterior cingulate gyrus (BA 25) and others (see Table 3, Fig. 2C blue shading). The regression analysis with sexual arousal rating as regressor revealed comparable correlation patterns in homosexual control subjects and pedophiles; these included the inferior frontal and fusiform gyrus, the precuneus, the superior parietal lobule and the middle occipital gyus. Interestingly, subcortical regions and the anterior cingulate gyrus, which were significantly activated in pedophiles, did not show any relation to sexual arousal (Table 3).

The activation differences in pedophiles for the boys versus men contrast (C > D, threshold  $p_{\text{uncorrected}} < 0.001$ , ) revealed significant positive differences in activation in the inferior (BA 47) and middle (BA 9) frontal gyri (with maxima at  $48 \times 39 \times 15$ ,  $t = 3.96$ ; and  $-57 \times 6 \times 39$ ,  $t = 3.62$ ), the bilateral insula (BA 13) (with maxima at  $-42 \times -3 \times 15$ ,  $t = 5.53$ ; and  $42 \times -3 \times -6$ ,  $t = 5.13$ ), the left parahippocampal gyrus (BA 36) (with a maximum at  $-27 \times -39 \times -12$ ,  $t = 5.68$ ) and the left precuneus (BA 7) (with a maximum at  $-15 \times -60 \times 51$ ,  $t = 3.77$ ). Further activation differences were observed in several occipitotemporal regions, including inferior (BA 19), middle (BA 39) and superior (BA 38) temporal gyri as well as the middle occipital gyrus (BA 19). Additional activation was documented in the right amygdala (with a maximum at  $20 \times -23$ ,  $t = 3.95$ ).

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#### Intergroup contrasts

Fig. 3A (blue shading) shows the pedophiles > control subjects contrast in the boys condition (C > A). Significantly



**Fig. 2:** Intragroup contrast maps. Regional maps of activation in homosexual control subjects and pedophiles for the sexual block versus neutral block contrast in the boys and men conditions. (A) Red = activation map of homosexual control subjects in the men condition. Blue = correlation map of activation and the corresponding sexual arousal ratings; statistical threshold  $p_{\text{uncorrected}} < 0.001$  for a minimum of 5 adjacent voxels (MNI coordinates:  $46 \times 75 \times 11$  mm). (B) Red = activation map of homosexual pedophiles in the boys condition. Blue = correlation map of activation and the corresponding sexual arousal ratings; statistical threshold  $p < 0.05$  (FDR corrected) for a minimum of 5 adjacent voxels (MNI coordinates:  $4 \times 2 \times -14$  mm). (C) Regional maps of activation in homosexual control subjects (red) and pedophiles (blue) for the sexual block versus neutral block contrast in the men condition; statistical threshold  $p_{\text{uncorrected}} < 0.001$  for a minimum of 5 adjacent voxels (MNI coordinates:  $32 \times 13 \times 18$  mm). (D) Regional maps of activation in homosexual control subjects (blue) and pedophiles (red) for the sexual block versus neutral block contrast in the boys condition; statistical threshold  $p < 0.05$  (FDR corrected) for a minimum of 5 adjacent voxels (MNI coordinates:  $50 \times 63 \times -14$  mm). MNI = Montreal Neurological Institute; FDR = false discovery rate.

increased activation was seen in the bilateral anterior cingulate (BA 24, 32) (with maxima at  $6 \times 30 \times 0$ ,  $t = 4.70$ ;  $3 \times 30 \times -9$ ,  $t = 4.40$ ; and  $-6 \times 39 \times 3$ ,  $t = 3.74$ ) as well as in the ventromedial prefrontal cortex (BA 10) (with a maximum at  $3 \times 54 \times 0$ ,  $t = 3.82$ ). Conversely, the control subjects > pedophiles contrast in the men condition (B > D) only displayed increased blood oxygenation level-dependent responses in the caudate nucleus (with maxima at  $12 \times 18 \times 15$ ,  $t = 3.97$ ; and  $9 \times 9 \times 18$ ,  $t = 3.88$ ) (Fig. 3A, red shading).

Finally, we examined the differences between pedophiles and control subjects in the basal processing of visual sexual stimuli. We explored varying activation patterns during sexual arousal in a direct statistical comparison with one overall comparison including both groups under different conditions (i.e., the conditions that were sexually arousing for the respective subjects). We analyzed basic differences in sexual arousal patterns, documenting the C versus B contrast (homosexual pedophiles in the boys condition > homosexual control subjects in the men condition) and the reverse contrast B > C. Although the B > C contrast showed no significant signal increases, the C > B contrast revealed significant activations in the left fusiform gyrus (BA 20) (with a maximum at  $30 \times -33 \times -21$ ,  $t = 4.19$ ) as well as in the left dorsolateral prefrontal cortex (BA 46) (with maxima at  $-36 \times 36 \times 15$ ,  $t = 3.83$ ; and  $-42 \times 33 \times 21$ ,  $t = 3.71$ ) (Fig. 3B, red shading).

Finally, we addressed the question of the extent to which the differences in brain functioning are attributable to pedophilia or to the presence of a comorbid disorder. Because subgroup sizes for the different comorbid disorders were small, it was impossible to statistically control for the influence of all disorders in a direct manner, and for an analysis of covariance, metric variables were needed. Alternatively, the

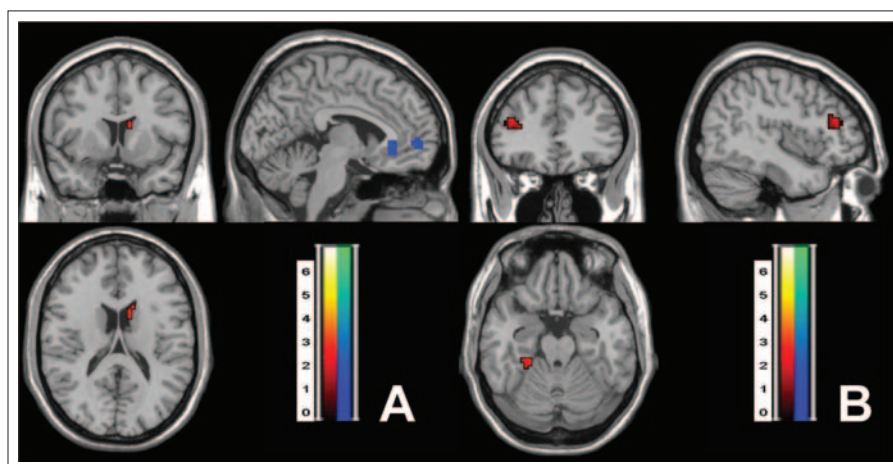
results were controlled for the influence of the most common comorbid symptoms or syndromes as measured by the Minnesota Multiphasic Personality Inventory-2 (depression, social and phobic anxiety, shyness, self-assurance, self-confidence and antisocial characteristics). The results were not significantly modified by controlling for these variables.

## Discussion

Recent investigations have focused on the cerebral mechanisms controlling sexual arousal and penile erection in healthy male subjects.<sup>9,14,19</sup> However, the neurobiological mechanisms underlying paraphilic sexual behaviour are still largely unknown. In this experimental fMRI study, we analyzed the processing of visually induced sexual arousal in homosexual pedophilic patients and homosexual control subjects. In contrast to sexually neutral stimuli, the presentation of sexually arousing pictures of homosexual and pedophile content led to an activation of brain areas known to be involved in processing visual stimuli with emotional content, including occipitotemporal and prefrontal cortices, in both groups. However, during the presentation of the respective sexual stimuli, the thalamus, globus pallidus, substantia nigra and striatum, corresponding to key areas mediating sexual arousal and behaviour, showed significant activation in pedophiles, but not in control subjects.

### *Neuronal response pattern to visual sexual stimulation in pedophiles and control subjects*

Homosexual pedophiles and homosexual control subjects rated the respective sexual stimuli as more physically arousing



**Fig. 3:** Intergroup contrast maps. Regional maps of activation contrasts between pedophiles and control subjects for visual sexual stimulation;  $p < 0.05$  (FDR corrected) for a minimum of 5 adjacent voxels. **(A)** Red = homosexual control subjects versus homosexual pedophiles in the men condition. Blue = homosexual pedophiles versus homosexual control subjects in the boys condition (MNI coordinates  $4 \times 9 \times 18$  mm). **(B)** Regional maps of activation contrasts for sexual visual stimulation between pedophiles in condition 1 (boys) and control subjects in condition 2 (men) (blue) and reversed (red); statistical threshold  $p < 0.05$  (FDR corrected) for a minimum of 5 adjacent voxels (MNI coordinates:  $-44 \times 35 \times -21$  mm). FDR = false discovery rate; MNI = Montreal Neurological Institute.

than the opposite stimuli, but they did not significantly differ in the level of arousal when the stimuli of primary sexual interest were presented. The results for the sexual > neutral block contrast in the boys condition, together with the appendant regression analyses with sexual arousal ratings in homosexual pedophiles, confirmed an activation pattern previously reported in heterosexual males.<sup>9,16,18,19</sup> This includes activation in occipitotemporal regions, in the prefrontal cortex (BA 9, 11, 46 and 47) and in relevant subcortical (limbic) areas such as the striatum, globus pallidus, substantia nigra and medial temporal cortex. Thus, except for the thalamus, this activation pattern comprised large parts of the reward system,<sup>47</sup> which has recently been considered in a neurobehavioural and multifaceted model of neural mechanisms during sexual arousal.<sup>18,19</sup> This model includes cognitive, emotional, motivational and physiologic (autonomic and endocrinological) components. Cerebral areas that have been found to be linked to the cognitive mechanism include the "attentive" network involving the orbitofrontal cortex and the superior parietal lobules as well as motor imagery in the inferior parietal lobules. The motivational component is stored in the caudal part of the anterior cingulate cortex related to motor preparation processes. The autonomic mechanism involves the hypothalamus, the insula and the rostral part of the anterior cingulate cortex. Thus pedophiles' activation patterns during presentation of the respective sexual stimuli fit into this previously described, multifaceted model of neural processing during sexual arousal in healthy male subjects.

Similarly, activation in the occipitotemporal and prefrontal regions for the sexual > neutral block contrast during the men condition in homosexual control subjects parallels previous reports on heterosexuals.<sup>9,16,18,19</sup>

However, the activation pattern in the control subjects was less intense and did not include activation of the relevant subcortical regions of the brain as observed in pedophiles and as reported in previous studies.<sup>48,49</sup> This may lead to the assumption that there is a generally lower sexual arousal level in healthy male homosexuals, which is confirmed by the psychometric data on sexual arousal ratings in this group. Reasons for the weaker activation pattern may include abated reactivity to visual sexual stimuli in the form of pictures, as has been observed in other imaging studies in a comparable context.<sup>13,15,50</sup> However, this issue will need further clarification. In addition, homosexual pedophiles may respond more strongly to the respective erotic stimuli than homosexual nonpedophiles because the former may have less opportunity to view erotic stimuli of interest. It is also possible that the stimuli depicting nude men were not sufficiently arousing to produce an equivalently large difference between the nude and the dressed conditions. Certainly, more profound sexual arousal and cerebral activation patterns would have been found in all subjects if we had used film excerpts instead of pictures, as observed in previous studies.<sup>13,15,50</sup> However, for legal, moral and ethical reasons, it is not feasible to employ pornographic videos showing sexual activities involving children.

Another issue to be discussed is the fact that only subjective evaluations of sexual arousal were employed in the

current study owing to ferromagnetic incompatibility of measurement tools with MRI. However, a series of previous studies on the sexual physiology of humans has demonstrated that even subjective ratings can achieve a high degree of accuracy in regard to the self-estimation of sexual arousal.<sup>44,51</sup> Thus MRI-compatible techniques for measurement of penile tumescence or other psychophysiological parameters in men, as used by Ferretti and colleagues,<sup>12</sup> might be very useful in future investigations, but subjective estimations of sexual arousal are probably equally valid.

#### *Neuronal processing of relevant and irrelevant sexual stimuli in pedophiles and control subjects and specificity of activation patterns*

Intragroup contrasts, as calculated between the boys and men conditions in the pedophile group, showed activation increases in the insula region, prefrontal cortex (BA 9, 47), parahippocampal gyrus, precuneus, some occipitotemporal regions and amygdala, indicating processes of sexual arousal with the deviant stimulus in pedophiles. Thus these data support the view that autonomic and endocrine control of sexual behaviour is mediated by the hypothalamus, whereas activation of the amygdala seems to be related to the appraisal process through which erotic stimuli are evaluated as sexual incentives.<sup>10</sup> Indeed, the amygdaloid complex receives multimodal sensory input, as well as input from the hippocampal formation, the thalamus and the association cortices, and relays processed information to the ventral striatum, the hypothalamus, the autonomic brainstem areas and the prefrontal cortex.<sup>12</sup>

The intergroup contrast for the boys condition resulted in signal increases only for the pedophile group. Significant activation differences were documented merely for the anterior cingulate cortex (BA 24, 32) and the frontopolar cortex (BA 10), but not for the hippocampus, thalamus or hypothalamus. The anterior cingulate cortex (ACC) is involved in attention processes and also modulates autonomic and endocrine functions, including secretion of gonadotropin-releasing hormone and epinephrine.<sup>52</sup> Activation increases in the ACC, especially in BA 24, as well as in different thalamic nuclei and in the ventromedial prefrontal cortex (BA 10), seemed to be correlated with markers of sexual arousal<sup>9,18</sup> and were also reported in a single-case fMRI study of a homosexual pedophile.<sup>35</sup> In addition, anterior cingulate and prefrontal cortices mediate the evaluation of motivational-emotional information and the initiation of goal-directed behaviour.<sup>10,19</sup> However, the direct statistical comparison of the 2 groups using the sexual > neutral block contrasts in the men condition revealed only 1 significant signal difference, namely, in the caudate nucleus for the control subjects, which has been reported to be responsible for the control of behavioural programs.<sup>53</sup> Finally, we analyzed whether there are basic differences in the sexual arousal patterns of subjects with paraphilic sexual interests. We performed 2 analyses, in which homosexual pedophiles and nonpedophile homosexual control subjects were contrasted in the conditions that were sexually arousing for the respective subjects. Compared

with the presentation of nude boys in the pedophile group, the presentation of nude men in the control subjects did not lead to significantly stronger activation in any brain region. The reverse contrast (pedophiles > control subjects) depicted activation in the fusiform gyrus and the left dorsolateral prefrontal cortex (BA 46) only, which may indicate that there was more cognitive participation in the evaluation of the stimuli. However, these data need to be carefully interpreted because control subjects generally showed weaker activation.

Taken together, these results augment the evidence from previous studies on sexual deviance, adding new information on the neural circuit subserving the processing of erotic visual stimuli in subjects with aberrant sexual interests. However, these data are only suggestive of the biologic differences in sexual processing between homosexual pedophiles and nonpedophile homosexual control subjects because different factors, such as social influences, need to be taken into account when explaining differing results in comparative studies. Another aspect concerns the weaker activation level in homosexual control subjects, which may be due to the quality of the stimuli used to induce sexual arousal. Future studies should also include a preliminary study to evaluate sexual stimuli for the control subjects. Even though we aimed to eliminate the differences in education level statistically, groups of subjects under investigation should be carefully matched regarding education level and social conditions (in our study, pedophiles living in a high-security forensic hospital were compared with homosexual control subjects living independently). Although homosexual control subjects did not show any sexual arousal during presentation of nude boys in the current investigation (Fig. 1B), future studies should also evaluate pedophile tendencies in control subjects because they might partially influence the intergroup effects.

In summary, we investigated central processing of sexual stimuli in homosexual pedophiles and nonpedophile homosexual control subjects. In pedophiles, compared with homosexual control subjects, activation patterns during visual sexual stimulation seem to refer more strongly to subcortical regions that are possibly involved in the context of processing reward signals and also play an important role in addictive and stimulus-controlled behaviour. Because the between-group differences may also partly be due to the generally weaker activation levels in homosexual control subjects, this issue will need further investigation in future studies. Such studies, together with the current data, may increase our understanding of the neurobiology of pedophilia and other sexual disorders, thus providing a basis for the development of more sophisticated diagnostic tools and new therapeutic approaches to the treatment of pedophilia.

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**Contributors:** Drs. Schiffer, Krueger, Forsting, Leygraf, Schedlowski and Gizewski designed the study. Drs. Schiffer, Paul, Gizewski and Mr. de Greiff acquired the data, which Drs. Schiffer and Gizewski analyzed. Dr. Schiffer wrote the article, and Drs. Krueger, Paul, Forsting, Leygraf, Schedlowski, Gizewski and Mr. de Greiff revised it. All authors gave final approval for the article to be published.

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