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Functional brain correlates of heterosexual paedophilia

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Although the neuronal mechanisms underlying normal sexual motivation and function have recently been examined, the alterations in brain function in deviant sexual behaviours such as paedophilia are largely unknown. The objective of this study was to identify paedophilia-specific functional networks implicated in sexual arousal. Therefore a consecutive sample of eight paedophile forensic inpatients, exclusively attracted to females, and 12 healthy age-matched heterosexual control participants from a comparable socioeconomic stratum participated in a visual sexual stimulation procedure during functional magnetic resonance imaging. The visual stimuli were sexually stimulating photographs and emotionally neutral photographs. Immediately after the imaging session subjective responses pertaining to sexual desire were recorded. Principally, the brain response of heterosexual paedophiles to heteropaedophilic stimuli was comparable to that of heterosexual males to heterosexual stimuli, including different limbic structures (amygdala, cingulate gyrus, and hippocampus), the substantia nigra, caudate nucleus, as well as the anterior cingulate cortex, different thalamic nuclei, and associative cortices. However, responses to visual sexual stimulation were found in the orbitofrontal cortex in healthy heterosexual males, but not in paedophiles, in whom abnormal activity in the dorsolateral prefrontal cortex was observed. Thus, in line with clinical observations and neuropsychological studies, it seems that central processing of sexual stimuli in heterosexual paedophiles may be altered by a disturbance in the prefrontal networks, which, as has already been hypothesized, may be associated with stimulus-controlled behaviours, such as sexual compulsive behaviours. Moreover, these findings may suggest a dysfunction (in the functional and effective connectivity) at the cognitive stage of sexual arousal processing.

Introduction

Paedophilia is a psychiatric disorder of high public concern characterized by intense sexually arousing urges and behaviours focused on sexual activity with a prepubescent child (American Psychiatric Association, 1994). Numerous studies have discussed the associations between behavioural disinhibition, frontal abnormalities, and impaired cognitive executive functioning. Although recent data from neuropsychological, sexual historical, plethysmographic, and neuroimaging investigations suggest that paedophilia is linked to early neurodevelopment perturbations (Cantor et al., 2004; Cohen et al., 2002), 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 (Krueger et al., 2005). Previous studies in healthy humans (Arnow et al., 2002; Beauregard et al., 2001; Bocher et al., 2001; Ferretti et al., 2005; Hamann et al., 2004; Holstege et al., 2003; Karama et al., 2002; Mouras et al., 2003; Park et al., 2001; Redoute et al., 2000; Stoleru et al., 1999; Paul et al., in press e-pub) 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 temporal cortex, the orbitofrontal cortex (OFC), the inferior and superior parietal lobules, the cingulate cortex, the anterior cingulate cortex (ACC), the insula, and the hypothalamus. These activation patterns are considered to represent the perceptual-cognitive, emotional, motivational, and physiological (autonomic and endocrinological) components of sexual arousal as proposed in a neurobehavioural and multifaceted model of neural mechanisms for sexual arousal (Redoute et al., 2000; Stoleru et al., 1999). Briefly, the cognitive component comprises a process of appraisal through which a stimulus is categorized as a sexual incentive and quantitatively evaluated as such. The emotional component includes the specific hedonic quality

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of sexual arousal, i.e., the pleasure associated with rising arousal and with the perception of specific bodily changes. The motivational component comprises the processes that direct behaviour to a sexual goal, including the perceived urge to express overt sexual behaviour. The autonomic and endocrinological components include various responses (e.g. cardiovascular, respiratory, and genital) leading the subject to a state of physiological readiness for sexual behaviour (Krueger et al., 2006). These four components are conceived to be closely interrelated and coordinated (Redoute et al., 2000).

Regarding deviant human sexual behaviour, several case reports on paedophilic patients and two group studies using voxel-based-morphometry described changes in the prefrontal cortex (PFC), the ventral striatum, the amygdala, and the medial temporal cortex (Mendez et al., 2000; Burns and Swerdlow, 2003; Schiffer et al., 2007; Schiltz et al., 2007). One group study using positron emission tomography (PET) also demonstrated a persistently decreased glucose metabolism in the right inferior temporal and superior ventral frontal gyrus (Cohen et al., 2002). Furthermore, two functional magnetic resonance imaging (fMRI) studies showed varying activations during different visual erotic stimulation paradigms (adult stimuli only and adult vs. child stimuli) in two groups of paedophilic forensic inpatient populations (heterosexual paedophiles and homosexual paedophiles). The results of one study comprised the hypothalamus, the periaqueductal gray, and the dorsolateral prefrontal cortex (Walter et al., 2007, for heterosexual paedophiles and adult stimuli), while those of the second study involved different parts of the PFC, the substantia nigra (SN), and the basal ganglia including caudate nucleus (CN), putamen, and pallidum (Schiffer et al., 2008, for homosexual paedophiles and adult vs. child stimuli).

The current study aimed to test for the first time the hypothesis that heterosexual paedophiles show altered neural activity in those brain regions implicated in sexual arousal, especially the OFC, the dorsolateral prefrontal cortex (DLPFC), the ACC, different limbic structures, including the cingulate gyrus, hypothalamus, and amygdala as well as the thalamus and parts of the basal ganglia. Therefore we used functional magnetic resonance imaging (fMRI) to compare neural activity patterns in a group of paedophile inpatients, who were exclusively attracted to female children, and heterosexually oriented control subjects, while viewing pictures of prepubescent girls and adult women in dressed/neutral vs. nude/sexually arousing mode.

Methods

Subjects

A group of eight unmedicated heterosexual paedophile patients, who met the DSM-IV (American Psychiatric Association, 1994) criteria for paedophilia and were exclusively attracted to female children, were recruited from two high-security forensic hospitals. All the patients had a history of at least two non-violent child molestations that were not limited to incest. They were additionally assessed in a routine procedure including the Multiphasic Sex Inventory (MSI) (Deegener, 1995), and the Minnesota Multiphasic Personality Inventory (MMPI-2) (Hathaway et al., 2001). Twelve healthy heterosexually oriented volunteers were recruited to match the patient group for age, handedness, socioeconomic stratum, and education level (Table 1). Of these participants, five paedophile patients and eight control subjects had participated in a previous morphometric study (Schiffer et al., 2007).

Each participant's sexual orientation was self-assessed using the Kinsey Scale (Kinsey et al., 1948). The Kinsey Scale attempts to measure sexual orientation on a seven-point scale from 0 (exclusively heterosexual) to 6 (exclusively homosexual). Only those who scored a 0 or 1 (exclusively or predominantly heterosexual) were included. Subjects with other disorders which might be related to neuropsychological impairment (significant physical or neurological illness, a history of head injury, neurodegenerative disorder, substance abuse or dependence in the last year, mental retardation) were excluded. Also excluded were controls with a personal or family history of psychiatric illness. Altogether four paedophiles and two control subjects were excluded: three due to a medium score on the Kinsey scale and three due to significant neuropsychological impairment. Neuropsychological performance was ascertained by various tests. The WIP (a reduced version of the German Wechsler Adult Intelligence Scale) was employed to assess global intelligence (Dahl, 1986). The Wisconsin Card Sorting Test (WCST-64) (Kongs et al., 2000) was used to 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 the information processing rate, alertness, and the visual-spatial working memory capacity. The psychiatric history of the paedophile sample, as ascertained by the Structured Clinical Interview for DSM IV Axis I and II Disorders (Wittchen et al., 1997), revealed a currently high rate of axis I comorbidity (37.5%–lifetime 62.5%) with foremost mood and anxiety disorders such as social phobia. The axis II comorbidity consisted primarily of cluster B (25%) and C (25%) disorders, such as avoidant and borderline personality

Table 1
Characteristics of Study Groups*

Characteristic	Group		
	Control (N=12)	Paedophilia (N=8)	Statistic
Demographic			
Age	36.1±7.5	38.4±9.4	$F_{1,18}$=0.32, p=0.577
Years of Education	12.81±2.47	11.15±1.73	$F_{1,18}$=9.31, p=0.003
(Last) Employment**	2.94±1.01	2.41±0.71	$F_{1,18}$=1,85, p=0.264
Cognitive and physical			
Full scale intelligence, *T*-Score	59.22±9.86	52.14±5.96	$F_{1,18}$=2.78, p=0.117
Visuo-spatial memory	5.78±1.09	5.00±0.58	$F_{1,18}$=2.88, p=0.111
Alertness	419.00± 100.35	350.86± 59.42	$F_{1,18}$=2.51, p=0.135
Executive functioning, T-Score	49.33±4.87	45.43±6.80	$F_{1,18}$=1.79, p=0.201
Handedness, N=(right/left)	N=(11/1)	N=(7/1)	
Weight, kg	81.67±15.82	77.29±16.01	$F_{1,18}$=0.299, p=0.593
Criminal			
Number of abused victims (court report)	–	6.41±3.67	
Length of stay in a forensic hospital (in years)	–	5.21±2.38	

* All data are given as mean±standard deviation unless otherwise indicated.
** (Last) Employment was classified as follows: 1=out of work; 2= vocational training; 3=help/unskilled worker; 4=employee/clerk; 5=senior staff.

disorders. All subjects gave informed consent to participate; 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.

Stimuli/Design

Functional imaging was performed as a block design. All subjects took part in two consecutive counterbalanced functional imaging sessions. Each session consisted of 14 epochs of two types of stimuli, one sexually arousing (7 epochs) and one neutral (7 epochs). In each session slides of nude girls or women were employed as sexually arousing stimuli, whereas the neutral stimuli were slides of a different group of dressed girls or women. Each epoch lasted 38.5 s and consisted of one slide with a photograph of one person only. In each session sexually arousing stimuli were alternated with neutral stimuli. Session and epoch order were counterbalanced between subjects to prevent any effects due to presentation order. All subjects were instructed to relax in the setting and to let the arousal occur. It was for this reason that we choose an epoch length that was comparatively long.

Erotic and non-erotic stimuli for the non-paraphilic group were taken from the International Affective Picture System (Lang et al., 2001) and had been 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 or art catalogues and were evaluated for potential sexual arousal and general attractiveness by another sample of paedophilic forensic inpatients in a preliminary study using 10 cm visual analogue scales (VAS; from ‘not at all’ to ‘extremely’). Only those pictures which yielded the highest ratings (i.e. sexual stimuli) or the lowest (i.e. neutral stimuli) in the preliminary study with heterosexual paedophiles were selected for the fMRI experiment. The use of these images was approved by the Ethics Committee of the Faculty of Medicine, University of Duisburg-Essen, Germany.

Individual sexual arousal was assessed immediately after functional imaging by subjective rating, using a VAS according to the Acute Sexual Experience Scale (ASES) (Krueger et al., 2003). In order to minimize falsified results due to social desirability processes or the awareness of the experimenter’s presence, subjects were again assured that all data were evaluated anonymously. The VAS ratings were therefore completed in a separate room.

MRI data acquisition and processing

All images were acquired using a conventional 1.5 T magnetic resonance scanner (Sonata, Siemens, Erlangen, Germany) with a phased array head coil. Thirty-six transversal T2* weighted slices were acquired using an echoplanar imaging technique (TR 3500 ms, TE 55 ms, flip angle 90°, FOV 220–240 mm, matrix 64) with 3 mm slice thickness and a 10% gap.

Statistical Data Analysis

For data analysis, Statistic Parametric Mapping software (SPM02, Welcome Department of Cognitive Neurology, London, UK) was used. The first three scans in each session were eliminated from data analysis to account for T1 relaxation effects. Prior to statistical analysis, images were realigned using sinc interpolation and normalized to a standard space (Montreal Neurological Institute, (Talairach and Tournoux, 1988)) utilizing trilinear interpolation. Images were smoothed with an isotropic Gaussian kernel with 9 mm full width half maximum. A voxel-by-voxel comparison according to the general linear model was used to calculate activation differences between the two alternating conditions. The model consisted of a boxcar function convolved with the haemodynamic response function and its corresponding temporal derivative. High-pass filtering with a cut off of 128 s and low-pass filtering with the haemodynamic response function was applied.

First-level analyses

Significant signal changes were assessed for each contrast (neutral vs. arousing) in each condition on a voxel-by-voxel basis (Friston, 1997). Areas of significant neural activation were identified for these contrasts by whole-brain analyses with a statistical threshold of $p<0.001$ (uncorrected), and with a spatial extent of at least 5 adjacent voxels. For visualization of neural activity, super threshold pixels were overlaid on the high-resolution T1-weighted single-subject images provided by SPM02. Contrasts within each condition led to parametric t-statistic maps for each subject, which were used in the second-level analyses.

Second-level analyses

Intra- and intergroup-specific effects in the activation patterns were assessed by a second-level analysis with condition or group as random effects factor. These were entered into a random effects model based on a paired or two-sample t test, respectively. To examine differences in the neural response to sexually arousing vs. neutral blocks, we first performed one-sample t tests using the single-subject contrast (parametric t-statistic) images of each subject. In addition, regression analyses were performed to identify regions that correlated with the sexual arousal ratings of each individual. Furthermore, for the paedophile group the MSI subscores of sexual contact with children were correlated with activation changes between the nude>dressed girls contrast. The correlation coefficients between percentage signal changes in the significantly activated clusters in each subject and the corresponding VAS ratings were calculated separately using bivariate Pearson correlations with a two-sided alpha of $p<.05$.

The processing specificity of the activation patterns induced by the stimuli of specific sexual interest was evaluated separately for each group. Therefore, we compared the two groups for the women>girls contrast and vice versa using paired t tests, as well as once during the women’s condition and once during the girls’

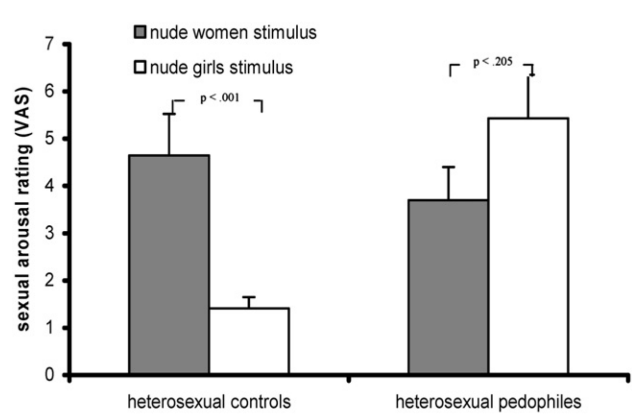

Fig. 1. Subjective ratings of visual stimuli by heterosexual controls ($N=12$) and heterosexual paedophiles ($N=8$). Each subject rated seven slides of nude boys and men using a 10 cm visual analogue scale. Data are presented as M±SEM.

Table 2
Brain regions activated in heterosexual control subjects ($N=12$) as demonstrated by random effects group analyses of the sexual block > neutral block contrast ($FDR_{corrected}$ $p<0.05$) in the women's and girls' condition, the women > girls contrast and vice versa, and the regression analyses with sexual arousal ratings, as regressor

Brain regions	Condition (nude > dressed women)							Condition (nude > dressed girls)						
	Lat.	BA	MNI coordinates			t Value	r_{corr}	Lat.	BA	MNI coordinates			t Value	r_{corr}
			x	y	z					x	y	z		
Sexual > Neutral Block Contrast														
Frontal Lobe														
OFC	L	47	−30	21	−24	11.83**								
	R	47	51	39	−9	6.80*		R	47	30	24	−18	6.10*	
	R	11	36	39	−12	9.81**								
DLPFC	R	46	51	39	3	8.46**		R	46	51	30	18	6.04*	
	L	6	−39	0	42	7.11*		R	8	48	18	45	5.34*	
Premotor cortex	L	6	−3	−9	72	9.36**								
	R	6	45	−18	63	6.39*		R	9	42	15	39	5.13	
ACC	L	32	−3	39	0	6.93*								
	L	32	−6	6	51	6.37*								
	R	24	3	39	6	6.30*								
Cingulate gyrus	L	24	−3	6	39	6.70*								
		32	−3	6	42	6.55*		R	32	12	21	39	5.90*	
Subcortical Regions														
Caudate head	L		−9	21	0	10.35**								
	R		6	9	−6	5.49*								
Putamen								R		24	−3	−3	9.05**	
								L		−18	−3	0	5.76*	
Amygdala	R		24	3	−18	4.71								
	L		−24	−3	−27	4.10								
Thalamus medial dorsal	L		−3	−12	9	6.78*								
	R		6	−15	9	5.81*								
Thalamus ventr. lat. post	R		21	−27	−3	8.88**								
SN	R		15	−21	−6	7.11*		L		−6	−15	−9	4.76	
Temporal Lobe														
Fusiform gyrus	L	37	−30	−45	−18	12.57**		R	37	30	−45	−18	6.29*	
	R	37	32	−36	−10	6.71*			19	33	−72	−12	6.60*	
	R	19	30	−75	−21	4.86		L	19	−21	−84	−21	6.53*	
Inferior temporal gyrus	R	19	48	−60	−6	7.18*								
Middle temporal gyrus	L	37	−48	−66	0	4.86								
Superior temporal gyrus	L	38	−48	15	−9	7.22*								
	R	38	51	21	−18	6.87*								
Parietal Lobe														
Postcentral gyrus	R	2	48	−33	39	7.30*								
	L	2	−45	−30	42	6.93*								
Parahippocampal gyrus	R	35	18	−27	−12	6.57*								
	L	37	−30	−45	−15	6.76*								
Precuneus	R	19	30	−78	33	7.55*								
	L	7	−9	−66	63	5.81*								
Inferior parietal lobule	L	40	−36	−48	54	6.42*								
Superior parietal lobule	R	7	24	−69	45	7.90*								
Occipital Lobe														
Middle occipital gyrus	L	18	−27	−87	−3	8.38*		L	19	−24	−99	12	5.19	
	R	18	27	−93	3	5.63								
Inferior occipital gyrus	R	19	45	−75	−12	14.39**		R	19	39	−78	−12	5.05	
	L	19	−36	−81	−9	6.30		L	18	−36	−84	−18	7.13*	
Superior occipital gyrus	R	39	36	−75	27	9.42**								
Cuneus	L	18	−21	−99	6	14.75**		L	17	−9	−90	3	4.56	
Sexual arousal ratings correlates														
OFC	R	11	32	36	−13	7.62**	−0.76**							
Fusiform gyrus	R	37	35	−31	−11	6.48*	.55*							

(continued on next page)

Table 2 (*continued*)

Brain regions	Condition (nude>dressed women)							Condition (nude>dressed girls)						
	Lat.	BA	MNI coordinates			t Value	r_{corr}	Lat.	BA	MNI coordinates			t Value	r_{corr}
			x	y	z					x	y	z		
Sexual arousal ratings correlates														
Precuneus	L	7	−11	−62	61	5.15*	.58*							
Inferior parietal lobule	L	40	−34	−45	52	5.85*	.61*							
Putamen								R		21	−2	−5	7.45**	.62*
Women>girls contrast														
OFC	L	47	−32	20	−21	9.63**								
ACC	L	32	−3	38	0	6.54*								
Caudate head	L		−11	23	2	8.94**								
Fusiform gyrus	L	37	−32	−44	−16	10.16**								
Postcentral gyrus	L	2	−44	−30	42	7.84*								
Parahippocampal gyrus	L	37	−30	−44	−13	7.46*								
Precuneus	L	7	−9	−66	65	5.11*								
Girls>women contrast								*No region*						

*$p<0.01$ (FDR corrected), **$p<0.05$ (FWE corrected); *$p<0.05$, ** $p<0.01$ (Pearson correlation).
BA, Brodmann area; DLPFC, dorsolateral prefrontal cortex;
OFC, orbitofrontal cortex; ACC, anterior cingulate cortex; SN, substantia nigra.

condition using two-sample *t* tests. All these contrasts refer solely to the nude>dressed condition. Finally to compare general activation patterns during visual sexual stimulation, the paedophile response in the nude>dressed girls contrast was subtracted from the activation maps of controls for the nude>dressed women contrast. For all second-level analyses, the statistical threshold was basically set to $p<0.05$ (FDR corrected) with a spatial extent of at least 10 adjacent voxels. Since cognitive performance is related to cortical activation, we matched the two groups for intelligence level (IQ) as it is the most valid factor of cognitive capacity. Nevertheless, regarding the differences in years of education (see Table 1), we also performed all intergroup analyses as analyses of covariance where years of education were inserted as a potentially confounding factor. Multiple testing (such as neuropsychological tests, voxel-based morphometry (VBM) and fMRI) runs the risk of inflating Type I error rates. In this study we therefore corrected for the number of analyses or hypotheses tested.

VAS ratings were analyzed by a two-factor ANOVA with repeated measures and with the stimulus condition as a within-subject factor. Additional effects of the stimulus conditions (girls vs. women) were assessed separately for paedophiles and controls using the Student's *t* test.

Results

Sexual arousal ratings

Subjects with both paraphilic and non-paraphilic heterosexual preferences rated the sexual stimuli as equivalently sexually arousing (no main effect of group affiliation: $F_{1,18}=1.207, p<0.286$). However, one significant interaction effect ($F_{1,18}=15.863$, $p<0.001$) indicated that both groups reported their preferred sexual stimuli to be more arousing than the non-preferred stimuli. Furthermore, the *t* statistics calculated separately for paedophiles and controls in the stimulus conditions (girls vs. women) revealed significant differences between the VAS ratings of heterosexual controls ($T=5224$; *df* 11; $p<0.001$). Even though paedophiles rated the nude women stimuli on average 1.84 points lower than nude girls, the difference failed to reach the significance level of $p<0.05$ ($T=-1397$; *df* 7; $p<0{,}205$) (Fig. 1).

Intragroup contrasts (one-sample t tests) and regression analyses

As shown in Table 2 (controls) and Table 3 (paedophiles) the activation patterns relating to the preferred sexual stimuli were

Table 3

Brain regions activated in heterosexual paedophiles ($N=8$) as demonstrated by random effects group analyses of the sexual block — neutral block contrast ($FDR_{corrected}$ $p<0.05$) in the women's and girls' condition, the women > girls contrast and vice versa, and the regression analyses with sexual arousal ratings, and MSI subscale sexual abuse of children as regressors

Brain regions	Condition (nude > dressed women)							Condition (nude > dressed Girls)						
	Lat.	BA	MNI coordinates			*t* Val.	r_{corr}	Lat.	BA	MNI coordinates			*t* value	r_{corr}
			x	*y*	*z*					*x*	*y*	*z*		
Sexual > Neutral Block Contrast														
Frontal lobe														
VLPFC	R	45	54	15	18	4.70		R	45	57	21	24	10.14*	
DLPFC	R	46	51	39	3	4.54		L	45	−42	18	15	10.33*	
								R	46	48	21	27	12.69**	
	L	8	−48	15	45	8.71		R	8	33	33	42	8.10*	
FPPFC								R	10	9	57	12	3.11	
ACC								L	24	−12	6	48	6.01	
Insula	L	13	−36	21	0	7.53		R	13	33	18	9	5.71	
Precentral gyrus									9	48	12	33	5.48	
Subcortical regions														
Caudate body								R		15	3	21	13.30**	
Putamen	L		−24	−3	6	10.11*								
			−21	9	3	6.44								
Amygdala								R		30	−3	−12	3.43	
Thalamus, medial dorsal								L		−3	−21	3	9.39*	
										−3	−6	6	4.85	
Hippocampus								L		−27	−36	−6	9.08*	
SN								L		−9	−21	−9	7.04	
Temporal lobe														
Fusiform gyrus	R	37	48	−45	−18	14.55**								
		37	39	−48	−18	6.34								
	L	37	−42	−54	−21	6.65		L	20	−33	−36	−21	7.92*	
									37	−48	−57	−15	6.65	
Inferior temporal gyrus	R	20	57	−63	−12	5.55		R	20	51	−51	−18	18.60**	
								L	37	−57	−60	−15	10.16	
Middle temporal gyrus								L	39	−45	−72	9	4.90	
									21	−60	−60	0	6.41	
								R	39	42	−78	9	16.70**	
Parietal lobe														
Postcentral gyrus	R	1	66	−18	24	8.16					-			
	L	2	−57	−27	42	7.64								
Parahippocampal gyrus								R	19	30	−48	−9	9.65*	
								L	36	−21	−39	−12	6.31	
Precuneus	L	19	−24	−78	33	6.73		R	19	30	−78	42	8.65	
Inferior parietal lobule	L	40	−51	−33	60	5.92		L	40	−36	−51	54	10.31*	
Superior parietal lobule								R	7	33	−57	60	7.25	
										24	−69	48	5.80	
Occipital lobe														
Middle occipital gyrus	L	18	−39	−90	3	10.94*		L	19	−45	−84	3	10.11*	
		19	−48	−60	−6	10.81*				−48	−63	−6	8.34*	
										−51	−69	−12	8.23*	
								R	19	39	−84	3	13.62**	
										45	−75	9	12.48**	
Inferior occipital gyrus	R	18	45	−81	−9	9.37*		R	19	39	−78	−12	12.42*	
	L	18	−36	−87	−15	9.18*		L	18	−33	−84	−12	7.52	
Sexual arousal ratings Correlates														
Fusiform gyrus	R	37	48	−45	−18	9.41**	.56*							
FPPFC								R	10	8	55	10	4.24	−0.67*
Fusiform gyrus								L	20	−33	−36	−23	6.87*	.62*
Inferior temporal gyrus								R	20	49	−50	−18	12.12**	.75**

(continued on next page)

Table 3 (*continued*)

Brain regions	Condition (nude>dressed women)							Condition (nude>dressed Girls)						
	Lat.	BA	MNI coordinates			*t* Val.	r_{corr}	Lat.	BA	MNI coordinates			*t* value	r_{corr}
			x	*y*	*z*					*x*	*y*	*z*		
MSI subscale sexual abuse of children														
Positive correlates														
ACC								L	24	−12	6	48	4.19	0.65*
Caudate body								R		16	4	19	9.31**	0.59*
Thalamus, medial dorsal								L		−3	−21	3	7.45*	0.55*
Fusiform gyrus								L	37	−48	−57	−19	6.98	0.51*
Negative correlates														
OFC								L	11	−42	36	−15	5.00	−0.64*
									11	−6	24	−15	4.85	−0.55*
DLPFC								L	9	−21	60	21	4.40	−0.67**
								R	9	18	54	39	3.32	−0.45*
FPPFC								L	10	−21	60	30	3.81	−0.49*
Women>girls contrast		*no region*												
Girls>women contrast														
DLPFC								R	8	33	33	42	8.10*	
Insula								R	13	33	18	9	5.71	
Thalamus, medial dorsal										−3	−6	6	4.85	
Hippocampus								L		−27	−36	−6	9.08*	
Middle occipital gyrus								L	19	−45	−84	3	10.11*	
								R	19	39	−84	3	13.62**	
Inferior occipital gyrus								L	18	−33	−84	−12	7.52	

* $p<0.01$ (FDR corrected), ** $p<0.05$ (FWE corrected); * $p<0.05$, ** $p<0.01$ (Pearson correlation).
BA, Brodmann area; VLPFC, ventrolateral prefrontal cortex; DLPFC, dorsolateral prefrontal cortex; FPPFC, frontopolar prefrontal cortex; SN, substantia nigra; ACC, anterior cingulate cortex; OFC, orbitofrontal cortex.

similar for both groups and included the occipitotemporal regions (BA's 18, 19, 20, 37), thus indicating general emotional visual and attention processing (Phan et al., 2002). Even though a significant signal change in the hypothalamus was not observed in either group, we found significant signal changes in several limbic structures including the amygdala and hippocampus, CN, SN, as well as in the medial dorsal nucleus of the thalamus, and the inferior temporal gyrus (see also Fig. 2A [controls] and 2B [paedophiles]) in both groups relating to the preferred sexual stimuli only. Interestingly, the two groups showed increased activity of the putamen only during the non-preferred stimuli. Furthermore, regarding the different intra-group analyses, at first glance it seems that compared to paedophiles, controls showed increased activation in bilateral OFC (BA 47) when viewing slides of nude vs. dressed women (Fig. 2C) as well as while viewing slides of nude vs. dressed girls (Fig. 2D). Interestingly, in paedophiles the more the OFC (BA 11), the DLPFC (BA 9), and the frontopolar prefrontal cortex (FPPFC; BA 10) are deactivated, the higher their scores on the MSI subscale for the sexual abuse of children (see Table 3, subsection 3, and Fig. 3C). In the same contrast, there was a positive correlation between the MSI subscale and activation increases in the ACC, ventral striatum (caudate body), the thalamus (medial dorsal nucleus), and the fusiform gyrus.

Paedophiles showed no more activation in response to women than girls (women>girls contrast) in any brain region, nor did the controls in response to girls than women (girls>women contrast). However controls showed significantly stronger BOLD responses to women than girls (women>girls contrast), including the OFC, the ACC, the ventral striatum (caudate head), the fusiform gyrus and several parietal regions (Table 2). The paedophiles activated the DLPFC, the insula, the thalamus (medial dorsal nucleus), the hippocampus as well as associative occipitotemporal cortices significantly more strongly in the girls than in the women's condition (Table 3).

Intergroup contrasts (paired and two sample tests)

Subsection 1 of Table 4 and Fig. 3A-red show the response increase of controls compared to paedophiles relating to the women stimuli (controls>paedophiles contrast). Significantly more activation was shown in the bilateral cingulate (BA 24), the right ACC (BA 24, 32, 33), and the left posterior cingulate gyrus (BA 30). Furthermore, we found activation differences in the bilateral superior temporal gyrus (BA 21, 38), as well as in the right cuneus (BA 7, 18), the left precuneus (BA 7, 31), the left lingual gyrus (BA 18), and the right fusiform gyrus (BA 19). Fig. 3A-blue shows the response increase of paedophiles compared to controls relating to girls stimuli (paedophiles>controls contrast). Only three regions showed increased activation in the paedophile group: The bilateral hippocampus, the bilateral fusiform gyrus (BA 37), and the right Pulvinar of the thalamus (see also subsection 2 of Table 4).

In the next step, differences between paedophiles and controls in the basal processing of visual sexual stimuli were examined in a direct statistical manner by means of one *overall* comparison, including the activation map of each group relating to their preferred sexual stimuli (see Table 4, subsections 3 and 4). Compared to controls, paedophiles showed more activation only in the right DLPFC (BA 46) (see also Fig. 3B — blue). As shown in Fig. 3B —red, on the other hand, controls showed more activation in the reverse contrast (con-

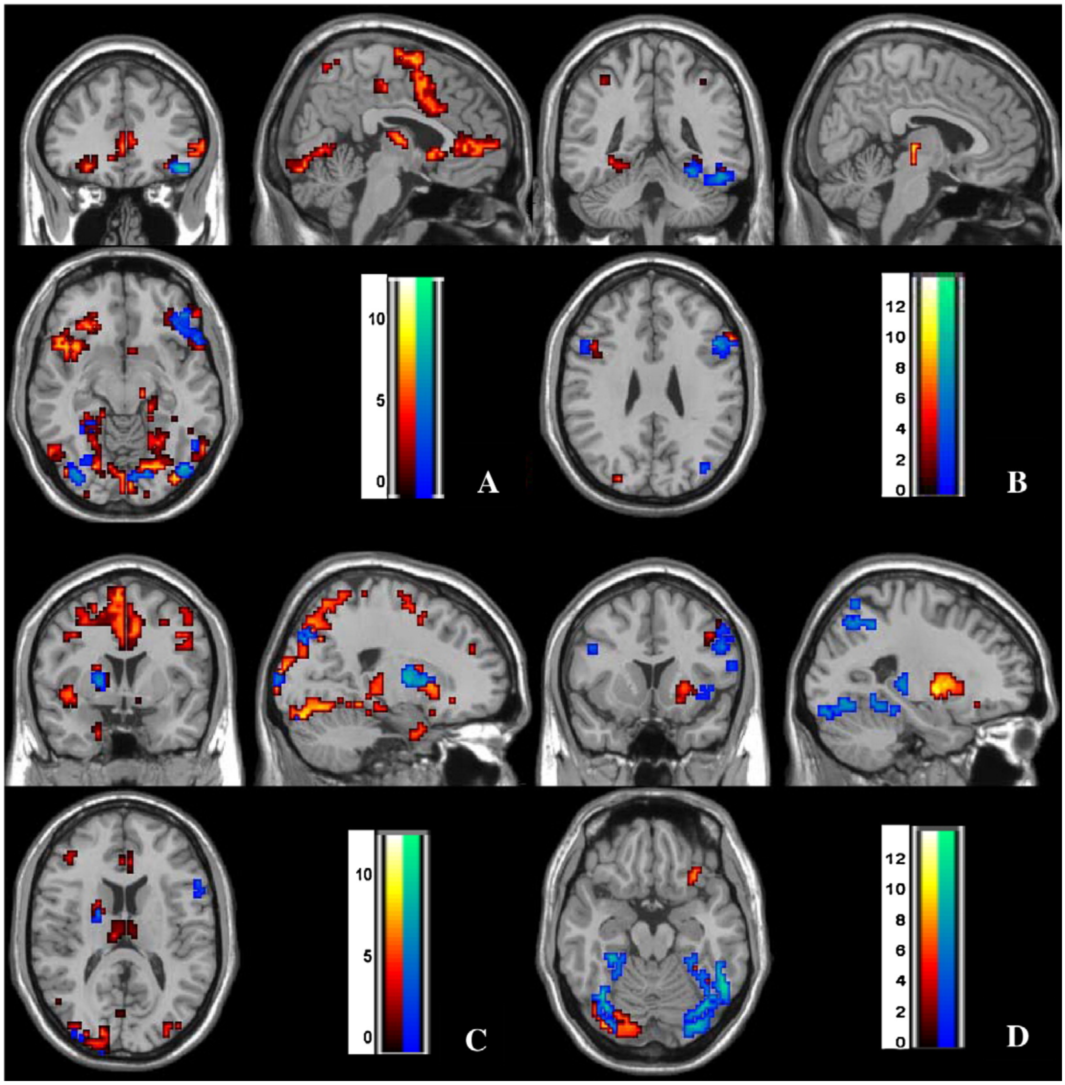

Fig. 2. Regional maps of activation in heterosexual *controls* and *paedophiles* for the Sexual Block–Neutral Block contrast in various conditions. (A) Red = Activation map of heterosexual *controls* in the women's condition, Blue = Correlation map of activation and the corresponding sexual arousal ratings; statistical threshold FDR $p<0.05$ (corrected for multiple comparisons) for a minimum of 5 adjacent voxels (MNI coordinates $-5\times35\times-10$ mm). (B) Red = Activation map of heterosexual *paedophiles* in the girls' condition, Blue = Correlation map of activation and the corresponding sexual arousal ratings; statistical threshold FDR $p<0.05$ (corrected for multiple comparisons) for a minimum of 5 adjacent voxels (MNI coordinates: $-6\times-43\times28$ mm) (C) Regional maps of activation in heterosexual *controls* (red) and *paedophiles* (blue) for the Sexual Block–Neutral Block contrast in the women's condition; statistical threshold FDR $p<0.05$ (corrected for multiple comparisons) for a minimum of 5 adjacent voxels (MNI coordinates: $-21\times4\times14$ mm). (D) Regional maps of activation in heterosexual *controls* (red) and *paedophiles* (blue) for the Sexual Block–Neutral Block contrast in the girls' condition; statistical threshold FDR $p<0.05$ (corrected for multiple comparisons) for a minimum of 5 adjacent voxels (MNI coordinates: $24\times13\times-18$ mm).

trols > paedophiles) in the bilateral OFC (BA 47), the bilateral cingulate gyrus (BA 32) and the ACC (BA 24), as well as in the FPPFC (BA 10). Additionally, significant activation differences were found in various parts of the bilateral premotorcortex (BA 6), and the left paracentral lobule (BA 31).

Finally, we addressed the question of the extent to which the differences in brain functioning might be attributable to paedophilia, the presence of comorbid disorders or differences in education levels. Due to the small subgroup size of the various comorbid disorders, it was impossible to statistically control for the influence of all disorders in a direct manner, and for an analysis of covariance metric variables would have been required. Alternatively, the results were controlled for the influence of the most common comorbid symptoms or syndromes as measured by the MMPI-2 scores, such as depression, social and phobic anxiety, shyness, self-assurance, self-confidence and also for antisocial characteristics. The results were not significantly modified by controlling for any of these variables.

Discussion

The current investigation aimed to test the hypothesis that heterosexual paedophiles show altered neural activity in those brain regions implicated in sexual arousal. In contrast to a previous report (Walter et al., 2007), we therefore used functional magnetic resonance imaging (fMRI) to compare the neural activity patterns of a group of eight paedophile inpatients, who were *exclusively* attracted to female children, and 12 heterosexually oriented control subjects with regard

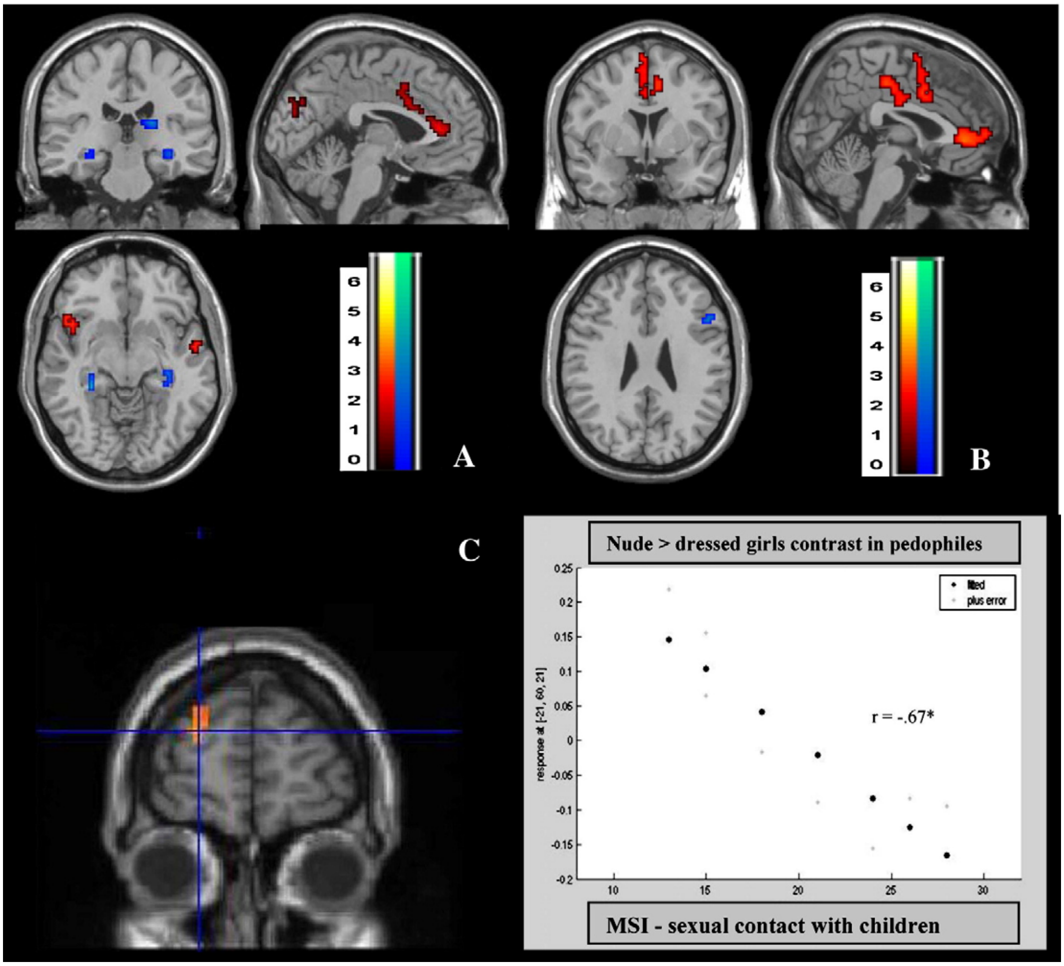

Fig. 3. Regional maps of activation contrasts between paedophiles and controls during sexual visual stimulation (cond. 1 — girls; cond. 2 — women); statistical threshold FDR $p<0.05$ (corrected for multiple comparisons) for a minimum of 5 adjacent voxels. A (red): heterosexual controls>heterosexual paedophiles in condition 2 (women); (blue): heterosexual paedophiles>heterosexual controls in condition 1 (girls) (MNI coordinates $2\times-25\times-9$ mm). B: regional maps of activation contrasts between paedophiles in the girls' condition>controls in the women's condition (blue) during sexual visual stimulation and reversed (red); statistical threshold FDR $p<0.05$ (corrected for multiple comparisons) for a minimum of 5 adjacent voxels (MNI coordinates: $-3\times3\times27$ mm). C: in the left DLPFC, deactivation takes place only during the preferred sexual stimuli (girls) and the more marked this deactivation is in paedophilic patients, the higher they score on the subscale for sexual contact with children in the multiphasic sexual inventory (MSI, $r=-0.67$, $p<0.05$). The brain section shows voxels revealed by the simple regression analysis of MSI scores and the contrast (nude>dressed girls, $p<0.001_{\text{uncorrected}}$, $k\geq 10$ adjacent voxels).

to their *preferred sexual stimuli*, i.e. prepubescent girls for the former and adult women for the latter, in dressed/neutral vs. nude/sexually arousing mode. This paradigm demonstrates for the first time the specific neural activity in subcortical and cortical regions in paedophilia during sexual arousal and reveals the differences in the orbito- and prefrontal networks compared to heterosexual controls. These results integrate and extend the evidence from previous studies, at the same time clarifying the neural circuit that subserves the processing of erotic visual stimuli in humans in respect to different sexual orientations or paedophilic abberrations.

In the first part of the study we analyzed the responses of both groups (intra-group contrasts) relating to their preferred sexual stimuli (sexual>neutral block contrast). These are in line with previous reports (Mouras et al., 2003; Redoute et al., 2000; Stoleru et al., 2003; Stoleru et al., 1999; Bocher et al., 2001; Arnow et al., 2002) demonstrating the different activation components of sexual arousal processes in healthy humans as proposed in the neurobehavioural model of sexual arousal by Stoleru and Redoute (Redoute et al., 2000; Stoleru et al., 1999). The findings show that the brain response of heterosexual males to heterosexual stimuli is largely comparable to that of heterosexual paedophiles to heteropaedophilic stimuli. Increased activation was observed in several limbic structures (amygdala, cingulate gyrus and hippocampus), SN, CN, as well as in the ACC, the medial dorsal nucleus of the thalamus, and associative cortices (inferior temporal, and inferior occipital gyri). Apart from the perceptual-cognitive component, this activation pattern represents all the components (emotional, motivational, and physiological [autonomic and endocrinological]) of sexual arousal as proposed in the neurobehavioural model for sexual arousal mentioned above. We interpret the findings of the present study in the light of that model.

There is evidence that the activation of the right OFC, which was only activated in healthy heterosexual controls, not in paedophiles, is correlated with the cognitive component of the proposed model (Redoute et al., 2000). The fact that healthy heterosexuals activated the right OFC in both the women's and the girls' condition may not represent a specific sexual arousal process but may be an indication of the categorization and evaluation processes of the stimuli in terms

Table 4
Brain regions activated in the each preferred stimulus condition as demonstrated by random effects group analyses of the paedophiles (P)> controls (C) contrast and vice versa, respectively ($FDR_{corrected}$ $p<0.05$)

Contrast	Brain regions	Lat.	BA	MNI coordinates			t value
				x	y	z	
C>P (women condition)	Cingulate gyrus	L	24	−9	12	33	5.58
	ACC	R	24	3	36	9	5.28
			32	3	15	27	4.26
			33	6	21	21	3.92
	Posterior cingulate gyrus	L	30	−6	−54	3	3.89
	Superior temporal gyrus	L	21	−48	15	−9	4.95
		R	38	54	−3	−12	4.93
	Cuneus	R	7	21	−81	30	4.29
			18	9	−75	30	4.07
	Precuneus	L	7	−9	−66	30	4.76
			31	−12	−57	30	4.54
	Lingual gyrus	L	18	−6	−63	0	4.76
	Fusiform gyrus	R	19	24	−78	−18	4.21
P>C (girls condition)	Hippocampus	L		−27	−36	−6	7.65*
		L		−33	−27	−12	4.16
		R		30	24	−9	3.29
	Fusiform gyrus	L	37	−36	−39	−12	5.40
		R	37	51	−60	−21	4.62
	Thalamus, Pulvinar	R		18	−24	15	5.08
C>P (each preferred stimulus condition)	OFC	R	47	30	21	−24	6.05
			47	45	33	−12	4.41
		L	47	−30	15	−30	4.47
	FPPFC	R	10	6	57	3	4.64
	Cingulate gyrus	R	32	3	−15	39	4.86
			32	6	3	42	4.47
		L	32	−3	6	39	4.56
	ACC	L	24	−3	38	0	5.38
		R	24	3	42	3	5.07
	Premotor cortex	R	6	42	−18	63	4.76
		L	6	−30	−15	69	4.61
	Paracentral lobule	L	31	−3	−24	48	4.68
P>C (each preferred stimulus condition)	DLPFC	R	46	48	18	27	4.74

*$p<0.01$ (FDR corrected).
BA, Brodmann area; ACC, anterior cingulate cortex; OFC, orbitofrontal cortex; FPPFC, frontopolar prefrontal cortex; DLPFC, dorsolateral prefrontal cortex.

of sexual incentiveness (Beauregard et al., 2001). In this sense, these findings may suggest a dysfunction in paedophiles regarding the appraisal process through which a stimulus is categorized as a sexual incentive. This may in turn be due to substance alterations in paedophiles in the same region as indicated by previous reports (Burns and Swerdlow, 2003; Mendez et al., 2000; Schiffer et al., 2007). Frontal cortices are involved in the appraisal of stimuli, but they are also central in the consideration of future consequences of current acts, in learning from punishment and behavioural inhibition (Knutson and Cooper, 2005). Thus, in line with clinical observations, central processing of sexual stimuli in heterosexual paedophiles may be mediated by a disturbance in OFC network activity, which according to an earlier hypothesis may be associated with stimulus-controlled behaviours such as sexual compulsive behaviours (Bradford, 2001). It would seem to make sense, therefore, to consider whether paedophiles display fewer frontally-mediated inhibitory processes during sexual arousal than do healthy males. Possibly, the hippocampus, which in paedophiles merely showed increased BOLD response in the girls' condition, may play a role in deviant sexual orientation, as it may moderate memory aspects of experienced sexual arousal and thereby compensates the lack of present OFC-related appraisal and evaluation processes of the stimuli. However, the relationship between cortical and subcortical connectivity during sexual arousal needs to be further investigated to support this hypothesis.

Another important structure is the amygdala, which receives multimodal sensory input, as well as input from the hippocampal formation, the thalamus and association cortices, and relays processed information to the ventral striatum, hypothalamus, autonomic brain stem areas (e.g. the substantia nigra), and the PFC. The current findings regarding amygdala activations in these two groups may support the neurobehavioural model where the amygdala participates in the evaluation of emotional content of the complex perceptual information associated with the visual processing of erotic stimuli. Additionally, a significant increase in activation in the associative temporo-occipital areas was also observed during erotic picture viewing compared to neutral picture viewing.

The ACC and the PFC play a role in the evaluation of motivational/emotional information and in the initiation of goal-directed behaviour (Beauregard et al., 2001; Park et al., 2001; Stoleru et al., 1999), since these areas are specifically related to the monitoring and the control of emotionally driven behaviours. The anterior region of the cingulate is subdivided into "affect" and "cognition" components – the former having extensive connections with the amygdala and periaqueductal grey – that assess the motivational content of the internal and external stimuli and regulate context-dependent behaviours often involved in responses associated with affect (Devinsky et al., 1995). According to this neurobehavioural view, the activation of the ACC may reflect the maintenance of correspondence between the sexual response and the affective value of the stimulus (Ferretti et al., 2005).

Vice versa, activation patterns in both groups during non-preferred sexual stimuli are also largely comparable. This is characterized by a lack of subcortical (CN, SN, thalamus, hippocampus, amygdala), parahippocampal, anterior cingulate, and insula activation as compared to the response pattern relating to their preferred sexual stimuli. Interestingly, in this study the putamen appears to be a marker for the opposite sexual interest in both groups, as it showed increased activity only during those conditions. The putamen is hypothesized to be part of the "motor loop" because it receives information from the sensorimotor cortex and then sends it indirectly back to the premotor regions of the frontal cortex. The functional alterations in the putamen and OFC in paedophiles are possibly due to morphological substance defects, which have also been found in these brain areas in a comparable sample (Schiffer et al., 2007). However, it is more likely that the putamen activation in both groups during the non-preferred stimuli condition is associated with inattention processes (Teicher et al., 2000).

The observed differences in activation patterns contrast with the behavioural findings in paedophilic patients, who did not differ from healthy subjects in their ratings of sexual arousal for the adult stimuli. This limits the relation between paedophilia and neural findings of suppression or denial of adult stimuli and contradicts characteristic clinical criteria. Together with the clinical measures, such neural-behavioural dissociation suggests that the validity of the paedophilic patients` ratings should at least be questioned. In this respect, one of the limitations of this study is that only self-report measures of sexual arousal are used. A phallometric measure of sexual arousal would be ideal, or at least some other objective measure of autonomic arousal, such as galvanic skin response, heart beat, etc., to objectify sexual arousal processes. Nevertheless, the interpretation of the self-report measures of paedophiles regarding adult stimuli as questionable is also supported by the intergroup contrast maps which were created in the next step of the analyses for the groups relating to their preferred sexual stimuli. The response increases in controls as compared to paedophiles (controls>paedophiles contrast) for the women's condition, as well as the overall comparison of the two groups during their preferred sexual stimuli (controls>paedophiles), revealed significantly stronger BOLD responses in the bilateral and left posterior cingulate cortex, right ACC, VMPFC, OFC, and associative temporal cortices including the fusiform gyrus in the controls. Thus, paedophiles showed less activation in regions representing the cognitive, emotional, motivational, and physiological components of the model, indicating that they were not sexually aroused by adult heterosexual stimuli and contradicting their sexual arousal ratings of adult stimuli. The assessment of alterations in neural activation due to deviant sexual stimuli might therefore be considered as a complementary tool for investigating the paedophilic patients' real cognitions and/or emotions of experienced sexual arousal.

Surprisingly, the paedophiles>controls contrast for the girls' condition revealed differences only in thalamic, hippocampal, and fusiform activity, possibly due to the small sample size. In contrast, brain regions that are more strongly implicated in sexual arousal such as the insula, cingulate, anterior cingulate, and inferior temporal gyri, or inferior and superior parietal lobules, as revealed in the controls>paedophiles contrast in the women's condition, showed no activation increases. Interestingly, the overall comparison of the two groups during their preferred sexual stimuli (paedophiles>controls) only revealed one significant overactivation of the right DLPFC in paedophiles. Subcortical regions involved in vegetative-autonomic processing are controlled by cortical regions like the DLPFC that modulate sexual arousal (Beauregard et al., 2001). Increased activation of the right DLPFC, on the one hand, and negative correlation between the activation in the left DLPFC and a clinical measure of abuse, on the other hand, suggest abnormal prefrontal processing of sexual arousal in paedophilia.

The lack of hypothalamic activation, which is associated with the physiological component of sexual arousal, in either group in any condition is possibly due to an understated sexual valence of the stimuli used. In a previous study we were able to demonstrate that activation increases in the hypothalamus in heterosexual subjects when inducing sexual arousal via erotic *videos* as opposed to sexually neutral videos (Paul et al., in press).

Taken together, the current results demonstrate that the brain response of heterosexual males to heterosexual stimuli is comparable to that of heterosexual paedophiles to heteropaedophilic stimuli. In both groups only erotic stimuli corresponding to the specific sexual interest led to a brain activation pattern characteristic of sexual arousal, suggesting a uniform neurofunctional correlate for sexual arousal, independent of individual sexual interests. Conversely, the brain response to the non-preferred sexual stimuli is also similar in both groups, with the absence of characteristic sexual arousal activation and conspicuous putamen activity. However, responses to visual sexual stimulation in the OFC were only found in healthy heterosexual males but not in paedophiles, who showed abnormal DLPFC activity. These findings may suggest a dysfunction (i.e. dysfunctional and ineffective connectivity) at the cognitive stage of sexual arousal processing. Thus, in line with clinical observations, central processing of sexual stimuli in heterosexual paedophiles may be mediated by a disturbance in the OFC loop, which, as has already been hypothesized, may be associated with stimulus-controlled behaviours such as sexual compulsive behaviours. These data may provide a basis for the development of more sophisticated diagnostic tools and new therapeutic approaches to the treatment of paedophilia.

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