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Pedophilia Is Linked to Reduced Activation in Hypothalamus and Lateral Prefrontal Cortex During Visual Erotic Stimulation

Martin Walter, Joachim Witzel, Christine Wiebking, Udo Gubka, Michael Rotte, Kolja Schiltz, Felix Bermpohl, Claus Tempelmann, Bernhard Bogerts, Hans Jochen Heinze, and Georg Northoff

Background: *Although pedophilia is of high public concern, little is known about underlying neural mechanisms. Although pedophilic patients are sexually attracted to prepubescent children, they show no sexual interest toward adults. This study aimed to investigate the neural correlates of deficits of sexual and emotional arousal in pedophiles.*

Methods: *Thirteen pedophilic patients and 14 healthy control subjects were tested for differential neural activity during visual stimulation with emotional and erotic pictures with functional magnetic resonance imaging.*

Results: *Regions showing differential activations during the erotic condition comprised the hypothalamus, the periaqueductal gray, and dorsolateral prefrontal cortex, the latter correlating with a clinical measure. Alterations of emotional processing concerned the amygdala–hippocampus and dorsomedial prefrontal cortex.*

Conclusions: *Hypothesized regions relevant for processing of erotic stimuli in healthy individuals showed reduced activations during visual erotic stimulation in pedophilic patients. This suggests an impaired recruitment of key structures that might contribute to an altered sexual interest of these patients toward adults.*

Key Words: Pedophilia, neural mechanism, hypothalamus, periaqueductal gray, dorsolateral prefrontal cortex, fMRI

AQ: 2

Pedophilia is a psychiatric disorder of high public concern, because 1–2 in 10 children have been sexually approached and abused by an adult (Fagan et al 2002; Freyd et al 2005). These patients are sexually attracted to prepubescent children and can be characterized by emotional immaturity and attentional deficits (Cohen et al 2002; Fagan et al 2002), although they show no sexual interest toward adults.

Case reports described changes in the prefrontal cortex and the medial temporal cortex in single pedophilic patients (Burns et al 2003; Dressing et al 2001; Mendez et al 2000). Together with the ventromedial hypothalamus, the periaqueductal gray (PAG), and the insula, these regions have been shown to be implicated in sexual arousal in healthy subjects, including its vegetative-autonomic and emotional and motivational components (Karama et al 2002; Mouras et al 2003; Redoute et al 2000; Stoleru et al 1999). In contrast, studies investigating deficits in neural correlates of sexual arousal in pedophilia have not yet been reported.

Our study aimed to test the hypothesis of whether pedophilic patients show altered neural activity in those brains regions implicated in sexual arousal. We addressed this question by studying 13 pedophilic patients and 14 closely matched healthy control subjects. With functional magnetic resonance imaging (fMRI), neural activity was recorded during visual presentation of erotic and non-erotic emotional pictures of adults.

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AQ: 1

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Methods and Materials

AQ: 3

Subjects

The group of pedophilic patients consisted of 13 male patients meeting the diagnostic criteria for pedophilia according to DSM-IV (American Psychiatric Association 2000). Unmedicated patients, in part under supportive psychotherapy, were recruited from the State Forensic Hospital Uchtspringe, Germany. Exclusion criteria were other psychiatric or neurological diseases, a history of alcoholism or drug abuse, and previous antiandrogenous medication.

All patients had committed sexual offenses involving child victims of < 10 years of age. The number of victims sexually assaulted by the offenders ranged from 1 to about 10 (mean 4.4, SD 2.7). Patients were scored in a routine procedure including a structured professional judgment (de Vogel et al 2004) according to the "Sexual Violence Risk 20"checklist (Boer et al 1997) and the "Multiphasic Sex Inventory (MSI)" (Nichols and Molinder 1984).

The control group was matched to the patient group for group size, age, years of education, and verbal and general intelligence. Except for one pedophilic patient, all subjects were right-handed.

The study was approved by the local ethics advisory board of the Medical School, Otto-von-Guericke-University Magdeburg, and written informed consent was obtained from all participants. All patients participated voluntarily without any benefits.

Paradigm

Subjects were asked to view a total of 256 erotic, emotional, and neutral photographs from the International Affective Picture System (IAPS; Lang et al 1997) that were projected on a mirror mounted on a standard headcoil. Erotic pictures depicting only adults were previously validated for sexual arousal with ratings by 21 healthy subjects. Erotic and emotional picture sets were matched for emotional arousal and valence, and all three picture types were presented in a randomized order across all eight runs, each picture lasting 5 sec (see also supplementary Figure 1). A button press at appearance of each picture was required to control subjects' vigilance in the scanner.

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To control for potential effects of preceding attention on emotional picture viewing (Bermpohl 2006), one-half of the pictures were preceded by an expectancy period of 4–6 sec. Following Kastner et al (1999), the type of the subsequently presented picture was indicated by presentation of specific white arrows on a dark background. In contrast, to control for general effects of the expectancy period, an ambiguous expectancy period was followed by random presentation of stimuli.

After the picture presentation, a fixation cross was presented for a variable duration of 8–10 sec (jitter steps of .5 sec) to make use of this interval variation in the data analysis (Sakai and Passingham 2003).

Reaction times of button presses were recorded during the fMRI scan. After the scan, subjective ratings of sexual and emotional intensity and valence were obtained for each participant with a visual analogue scale. Mean averages of reaction times and the three ratings were calculated for each stimulus type and compared with two sample t tests, setting the level of significance at $p < .05$.

Imaging

Data acquisition was conducted on a 1.5 Tesla General Electric Signa scanner (Signa, General Electric Medical System, Milwaukee, Wisconsin). Imaging procedures included collection of inversion recovery T1 weighted echo planar images coplanar with the functional images and echo planar functional images (402 volumes, 23 slices with 3.125-mm in-plane resolution, 5-mm thickness, 1-mm gap; T2* weighted gradient echo sequence: repetition time 2 sec, echo time 40 msec). Image processing and statistical analyses were carried out with SPM2 (Wellcome Department of Imaging Neuroscience, London; Friston et al 1995, 1998).

A total of 3160 (8 × 395) volume images were realigned to the first image to correct for head movement, mean-adjusted by proportional scaling, resliced, and normalized into standard stereotactic MNI space (Montreal Neurological Institute, isotrophic 3-mm resolution). Transformed data sets were smoothed with a Gaussian kernel of 8 mm (full-width half-maximum). Subject-specific low-frequency drifts in signals were removed by a high pass filter of 128 sec, and effects of separate picture viewing conditions were calculated with the General Linear Modelling implemented in SPM2. Group comparisons were tested with a two sampled t test in a random effects model. All whole brain analyses were performed at $p < .005$ uncorrected and a cluster threshold (k) of 10 contiguous voxels. Resulting clusters were entered into a region of interest (ROI) analysis. For correlation analysis, a simple regression of MSI sub scores of sexual contact with children with subjects' contrast images was performed on a whole brain level. For resulting regions, extracted percentage signal changes were tested with Spearman correlation with a two-sided $p < .05$.

Results

Previously matched for emotional valence and arousal values provided by the IAPS catalogue (Lang et al 1999), the behavioral data revealed significantly higher sexual arousal and emotional intensity ratings for erotic pictures than for non-erotic emotional pictures in both groups of healthy and pedophilic subjects, although these differences did not differ in extent from healthy subjects to control subjects. No significant group differences in ratings of both sexual arousal and emotional intensity of erotic and non-erotic emotional pictures or in reaction times were obtained between groups.

To elucidate neural correlates of sexual anomalies, we compared the contrast sexual arousal > emotional arousal between healthy and pedophilic subjects. Pedophilic patients showed significantly lower signal intensities (peak voxel x, y, z, Z scores) in the hypothalamus (−3, −3, −15; $Z = 2.74$), the dorsal midbrain with peak activation in the PAG (3, −30, −18; $Z = 3.34$), the dorsolateral prefrontal cortex (DLPFC) (−27, 42, 36; $Z = 3.18$), the right lateral parietal (60, −51, 6; $Z = 3.31$), the right ventrolateral (57, 27, 0; $Z = 3.34$), and the right occipital cortex (24, −78, 6; $Z = 3.43$) as well as the left insula (−33, 12, −3; $Z = 2.90$) for the sexual arousal condition than healthy subjects ($p < .005$ uncorrected, k ≥ 10 voxels, Figure 1, supplementary Table 1).

Signal differences in the hypothalamus and left DLPFC were observed in both the expected and the unexpected (i.e., ambiguous) mode when analyzed separately. The PAG, insula, and right ventrolateral and right parietal cortex showed differential activations only in the unexpected (i.e., ambiguous) mode, whereas a cluster in the left orbitofrontal cortex showed differential activation (−36, 30, −18; $Z = 2.83$) only found in the expected mode.

Correlation between clinical-behavioral measures and regional signal changes during sexual (compared with emotional) arousal revealed a significant negative relationship also at $p < .001$, uncorrected, between the MSI subscale for the sexual abuse of children and signal intensities in the DLPFC and the left occipital cortex. The higher the score for sexual abuse of children, the lower the signals obtained only during sexual arousal (see Figure 1 and supplementary Table 1).

To investigate neural correlates of emotional processing, signal changes during emotional pictures were compared with viewing of neutral pictures. Pedophilic patients revealed significantly less signal intensities (peak voxel x, y, z, Z-scores) in the dorsomedial prefrontal cortex (DMPFC) (−6, 66, 24; $Z = 3.63$), the retrosplenial cortex (12, −45, 3; $Z = 2.96$), and the left amygdala–hippocampal complex (−21, −21, −15 $Z = 3.52$) in the non-erotic emotional condition ($p < .005$ uncorrected, k ≥ 10 voxels).

When compared with neutral pictures, erotic pictures revealed similar patterns of differential activation, like the erotic > emotional picture contrast, but showed additional effects for the left amygdala and left parahippocampal gyrus corresponding to regions of the emotional > neutral contrast and further in the right parietal cortex (24, −60, 60; $Z = 3.41$; $p < .005$ uncorrected, k ≥ 10 voxels).

Discussion

Our results demonstrate, for the first time, abnormal neural activity in subcortical and cortical regions in pedophilia during sexual arousal. Subcortical regions like the hypothalamus and the dorsal midbrain are involved in the vegetative-autonomic component of sexual arousal in healthy subjects (Bancroft et al 2005; Ferretti et al 2005; Karama et al 2002). Although some caution regarding the level of significance or potential group differences in baseline perfusion rates is warranted, our findings indicate that pedophilic patients remain unable to recruit vegetative-autonomic regions during stimulation with sexually arousing stimuli of adults, which might account for their lack of sexual interest toward adults. This is further supported by observation of vegetative-autonomic (i.e., phallometric) abnormalities in pedophilia (Cohen et al 2002).

Subcortical regions involved in vegetative-autonomic processing are controlled by cortical regions like the DLPFC that modulate sexual arousal (Beauregard et al 2001). Reduced

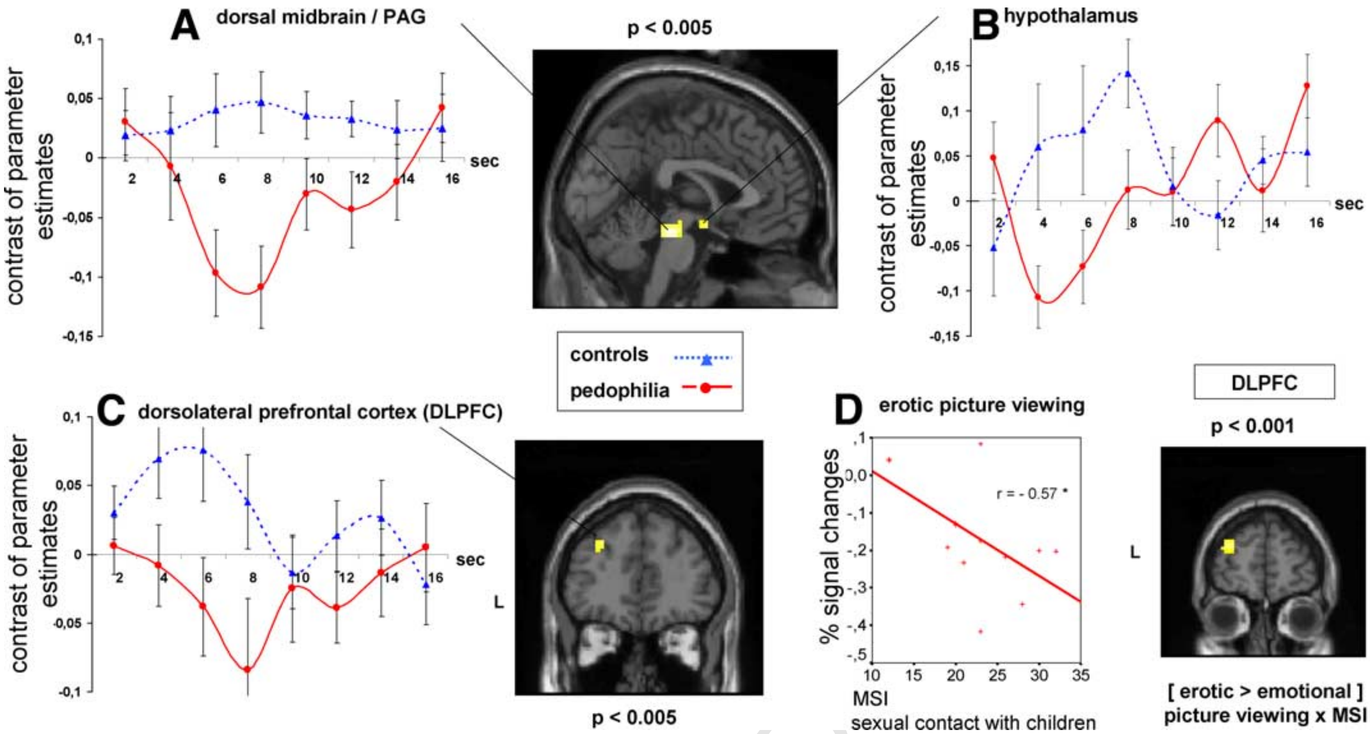

Figure 1. (A–C) Brain sections show regions with significantly greater signal changes in healthy control subjects for the contrast (erotic > emotional picture viewing) when compared with pedophilic patients ($p < .005$, k ≥ 10 voxels). The time course for this contrast is plotted over the next 16 sec (mean ± SEM, sampled time bin = 2 sec) after stimulus presentation for both groups. Erotic pictures lead to decreased signals in the dorsal midbrain and periaqueductal gray (PAG; **A**), the hypothalamus **(B)**, and the dorsolateral prefrontal cortex (DLPFC) **(C)** in pedophilic patients compared with control subjects. **(D)** In the left DLPFC, deactivations only during erotic picture viewing show that the stronger for pedophilic patients, the higher they score on the subscale for sexual contact with children in the multiphasic sexual inventory (MSI, $r = .57$, $p < .05$). The brain section shows voxels revealed by the simple regression of MSI scores and the contrast (erotic > emotional picture viewing) ($p < .001$, k ≥ 10 voxels).

activation in left DLPFC and correlation with a clinical measure of abuse thus suggest abnormal cortical control of sexual arousal in pedophilia. However, the relationship between cortical and subcortical regions (i.e., their functional and effective connectivity) (Morgane et al 2005) during sexual arousal needs to be investigated to further support this hypothesis. The specificity of these findings and their relation to abnormal sexual urges toward children remain to be investigated with corresponding pictorial stimuli of children, which is ethically problematic. Differences in patterns for the expected and the ambiguous mode signify the influence of attentional processes and underline the importance of further investigations.

We also observed reduced activation in the DMPFC , the hippocampus–amygdala complex, and the retrosplenial cortex (RSC) in pedophilic patients compared with healthy control subjects during non-erotic emotional stimulation. These regions have been associated with the emotional component of sexual arousal (Ferretti et al 2005; Karama et al 2002; Redoute et al 2000) as well as with emotional processing in general (Northoff et al 2000; Phan et al 2002). Altered neural activity in these regions might reflect some of the non-erotic emotional abnormalities observed in pedophilia, like lack of assertiveness and emotional immaturity. The relevance of an interaction of emotional and erotic processing, especially in the amygdala and parahippocampal gyrus, was further supported by the erotic > neutral picture contrast.

Neural differences contrast with our behavioral findings in pedophilic patients, which did not differ in their ratings of sexual arousal and emotional intensity from healthy subjects. This limits relation of neural findings to suppression or denial of adult stimuli, but it contradicts with characteristic clinical criteria and therefore complicates interpretation. Together with the clinical measures, such neural–behavioral dissociation suggests that the validity of the pedophilic patients' ratings might at least be questioned. Assessment of altered neural activation could therefore be considered a complementary tool to investigate the pedophilic patient's "true" feelings of sexual arousal.

In summary, we observed abnormal activation in subcortical (i.e., hypothalamus) and cortical (i.e., left DLPFC, DMPFC) regions in pedophilia during visual-erotic stimulation with adults. Because these regions are implicated in the vegetative-autonomic and emotional components of sexual arousal, our findings indicate possible neural correlates of lack of sexual interest toward adults in pedophilic patients. This might not only contribute to a better understanding of the pathophysiology of pedophilia but might also serve to establish future therapy and thus to lower public concern about this thus far rather neuroscientifically neglected psychiatric disorder.

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Supplementary material cited in this article is available online.

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AQ9— OK as revised? Alternatively, "…deactivations only during erotic picture viewing are stronger for pedophilic patients, scoring higher on the subscale for sexual contact with children…".

AQ1— In author affiliations section, is Uchtspringe the correct location for the State Hospital for Forensic Psychiatry? Please verify.

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AQ5— OK as revised: "…extracted percentage signal changes…"?

AQ6— Please provide reference entry for Lang et al 1999.

AQ7— OK as revised? Alternatively, "Because of the inherent ethical problems, the specificity of these findings…".

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