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ORIGINAL PAPER

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Abnormal amygdala activation profile in pedophilia

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Abstract Despite considerable public interest research in neurobiological correlates of pedophilia is scarce. Since amygdala activation is central for emotional valuation, arousal, and salience, we investigated the activation profile of this structure in 10 male subjects with pedophilia (exclusively attracted to boys), all convicted sex-offenders and sentenced to forensic psychiatric treatment along with ten male heterosexual matched controls. We used a sexually non-explicit functional Magnetic Resonance Imaging (fMRI) paradigm with images of men, women, boys or girls randomly embedded in neutral target/non-target geometrical symbols. We applied statistical parametric mapping (SPM2) and SPSS 14 for image processing and analysis. While controls activated significantly less to pictures of children compared to adults, the activation profile was reversed in subjects with pedophilia, who exhibited significantly more activation to children than adults. The highest activation was observed for boys in the patient group, and for women in control participants. Our data show enhanced activation to children's pictures even in an incidental context and suggest the provocative hypothesis that a normally present mechanism for reduced emotional arousal for children relative to adults is reversed in pedophilia, suggesting a neural substrate associated with deviant sexual preference in this condition. More extensive research in this field would be of benefit for both the victims and the offenders.

Key words fMRI · pedophilia · striato-limbic pathway · amygdala

Introduction

Pedophilia has generated a great deal of public attention and is a highly emotionally charged issue. Despite the brain's role as the "master organ" governing sexual function [30] research in neurobiological correlates of pedophilia is scarce [9]. "With several hundred convicted pedophiles behind bars in the United States, it is surprising that there have been no imaging studies of their brains" [36].

While the etiology of pedophilia is not clear, there is consensus that a deviant arousal pattern often begins with puberty [1, 12]. Although a causal relationship between abnormal brain functioning and pedophilia has not been proven, associations have been noted between a variety of relatively non-specific or global measures of brain function and pedophilia. There is evidence, for example, for an association between pedophilia and both lower cognitive capacity and increased rates of left handedness, which has been suggested to reflect a consequence of neurodevelopmental perturbation or head injuries before the age of 13 [2, 6]. Results of quantitative EEG studies also yielded evidence for neurophysiological instability of the dominant hemisphere with dysregulation of interhemispheric relationships. These EEG data

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had been recorded during rest, verbal and visuospatial conditions in 52 pedophiles who had demonstrated a definite phallometric response to erotic stimuli [11]. Howard et al. demonstrated in another quantitative EEG study that pedophiles with penile plethysmographic responsiveness to videos of children failed to produce an increase in contingent negative variation (CNV) amplitude while viewing images of adults. Since CNV had been proposed to reflect central arousability, it was suggested as a possible measure of deviant sexual desire [19].

Disturbances in central serotonin neurotransmission have also been suggested as a possible neurobiological basis of paraphilias [21, 33]. While preliminary neuropsychological data show pronounced deficits in cognitive domains associated with prefrontal and motor processing loops, this does not hold true for cognitive domains without a comparable high frontal association [7, 42]. This supports the hypothesis that disturbances in striato-thalamo-cortical networks may also be relevant for the formation of pedophilic urges and behaviors [42]. Such focus on the striato-cortical pathway is further supported by a very recent voxel based morphometry study where pedophiles showed decreased gray matter portions within the striatum and the orbitofrontal cortex [40].

Functional imaging studies investigating brain activation by sexual arousal in healthy heterosexual males have reported frontal and temporal paralimbic as well as subcortical involvement including the claustrum, putamen, ventral striatum, caudate nucleus and amygdala [10, 35].

There is no doubt about the importance of the amygdala for processing the emotional relevance of sensory stimuli [44], especially as it affects human sexual behavior [14]. It is involved in the enhancement of long-term memory of emotionally arousing events [5], unconscious emotional fearful learning [31, 32], and emotional processing of fearful targets [15, 39].

Considering the amygdala as a relevance detector in emotion processing [13, 38] we expected a significant difference in activation patterns among pedophile sex-offenders (attracted to boys; while viewing boys) compared to normal heterosexual control subjects.

Materials and methods

Participants

The present fMRI study examined ten male subject with pedophilia (i.e. pedophiles (ICD-10: F 65.4) attracted to boys), all convicted sex offenders and sentenced to forensic psychiatric treatment because of a negative prognosis along with age and education matched heterosexual controls.

All subjects, pedophiles and heterosexual controls, had provided written informed consent and the study had been approved by the local ethics committee. All pedophiles were inmates of forensic security hospitals following their conviction. Their therapists had judged them as still dangerous and unable to control their pedophile behavior. They all fulfilled ICD-10 criteria for pedophilia (F65.4), and admitted their sexual abuse of boys. A history of additional sexual abuse of girls was an exclusion criterion. Misused boys were between the age of 8–13 years, the average hospital stay of pedophiles was 9 (±3.5) years.

Table 1 Demographic data heterosexual controls and pedophiles

	Controls ± SD	Pedophiles ± SD	t^a	P^a
Age (*y*)	35.3 ± 8.3	33.1 ± 8.9	0.57	0.57
Years of education (*y*)	9.2 ± 0.4	9.0 ± 0.0	1.50	0.17
IQ (MWT-B)	98 ± 6	91 ± 9	2.05	0.06
BDI-II	5.8 ± 6.4	18.1 ± 10.6	3.14	0.01
HZI	17.5 ± 10.9	17.7 ± 11.3	0.04	0.97
Brown ADD-Scales	21.2 ± 25.1	26.2 ± 19.9	0.49	0.63
BIS	13.8 ± 2.9	14 ± 2.9	0.88	0.88

MWT-B multiple-choice word test, *BDI-II* beck depression inventory, second edition, *HZI* Hamburg obsession compulsion inventory (sum score), *Brown ADD-Scales* Brown attention-deficit disorder scales, *BIS* Barrat impulsiveness scale
[a]*t* tests, two-tailed

Healthy control subjects were recruited through advertisements in local newspapers in Mannheim, Germany. The ads called for German speaking, heterosexual males, without a school diploma or with only minimal education, to serve as controls in a nuclear magnetic resonance study, where images of low erotic content would have to be watched and judged inside a MR scanner. "The examination will be paid (50 Euro) and will be safe, there will be no X-ray exposure and no drugs will be given."

Controls were matched for age, IQ and educational level, (Table 1), with IQ determined by the multiple-choice word test (MWT-B) [25]. All participants were right-handed and had been screened to exclude psychiatric comorbidity using the beck depression inventory (BDI-II) [18], the Hamburg obsession compulsion inventory (HZI, to exclude OCD) [23], the Brown attention-deficit disorder scales (ADD) [4], the Barrat impulsiveness scale (BIS) [34] and the psychiatric health questionnaire (PHQ-D, German version) [26]. Additionally, all participants were screened by interview and chart review (for the inmates) for somatic comorbidity. Alcohol use was assessed with the Alcohol Use Disorders Identification Test (AUDIT) [37]. Fulfilling the criteria of alcohol abuse or dependency (ICD 10: F10.1 or 10.2) was an exclusion criterion. None of the participants was taking illegal drugs. All participants were medication free, had no somatic diseases, no brain disorders and none of the healthy subjects had ever attended a psychiatrist. All healthy subjects were judged as heterosexual by means of a clinical interview and paraphilias were ruled out by screening with the Multiphasic Sex Inventory (MSI) [8].

fMRI design

Image acquisition

Images were acquired with a Siemens Vision plus 1.5 Tesla scanner (Siemens Medical Solutions, Erlangen, Germany). Echo-planar images, optimized for blood oxygenation-level dependent (BOLD) functional imaging were acquired as 24 ascending slices in an oblique transversal orientation with 5 mm thickness and 1 mm gap covering the whole cerebral cortex. A standard Siemens EPI sequence (TE = 60 ms, $\alpha = 90°$) was used. In plane resolution was 3.43 mm × 3.43 mm (FOV = 220 mm × 220 mm, matrix size = 64 × 64). The shot repetition time TR was 2,700 ms.

A whole brain high resolution T1-weighted scan was performed as an anatomical reference (3D magnetization prepared rapid gradient echo (MPRAGE) with an isotropic resolution of 1 mm and an acquisition time of 9 min).

Stimulus presentation

We developed a paradigm based on the hypothesis that subjects with pedophilia will show an increased activation in brain regions relevant for unconscious emotional processing even when they are confronted with sexually non-explicit stimuli (boys in swimsuits). The event-related fMRI paradigm was designed as an odd-ball paradigm, with objects of no sexual interest defined as targets (colored circles) and emotionally relevant stimuli (e.g. boys in swimsuits) both embedded in the context of other objects defined as non-targets. Since the participants were asked to focus on the defined targets (i.e. colored circles) the paradigm was set up to explore unconscious emotional processing.

Five-hundred stimuli were presented in two runs, including 48 targets (colored circles with different size), 392 neutral non-targets (colored squares with different size) and 15 images of boys or girls as well as 15 of men or women, all wearing swimsuits or underwear. Images of boys, girls, men and women were chosen from German mail-order catalogues available free of charge. We decided not to use sexually explicit images inter alia for ethical reasons. Intervals between stimuli (ISI) were pseudorandomized and varied between 300 and 3,000 ms, with stimuli presented for 1,000 ms. Between the stimuli a centered white cross on a black screen was shown. One fMRI run took 12 min. Two runs were conducted with a small time gap to relax. In randomized order, one run comprised only images of males (men and boys), the other only images of females (women and girls). The occurrence of the stimulus events in the experimental time scale was logged into a file for post hoc analysis. All participants were instructed using a standardized procedure and a standardized text. Additionally, their understanding of the instruction was tested. Instructions were as follows: "Images of circles will be presented. Circles will be of different color and size and there will be other images as well. Whenever you spot a circle, press the button located by your forefinger. Whenever you see something else, press the button by your middle finger. Between presentations you will be shown a white cross against a black background. Do not press any button then."

Self-assessment manikin (SAM)—rating [24] of the four image categories (boys, girls, men, women) was assessed for the dimensions "valence" and "arousal", and additionally, in a modified version for "sexual arousal" (9 point scale, 1–9). For the valence rating scale, 1 indicates unpleasant; 9, pleasant. For the arousal rating scale, 1 indicates calm; 9 arousing, and for the sexual arousal rating scale, 1 indicates sexually non-exciting; 9, sexually exciting. SAM rating was performed immediately after the fMRI scan presenting the same images of boys, girls, women and men in swimsuits that had been used in the fMRI paradigm on a computer screen.

As pedophiles did not deny sexual abuse of boys, and as clinical interview and MSI inventory in the control group revealed no paraphilic sexual orientation, we predicted that pedophiles would judge pictures of boys about as arousing as heterosexual male controls the pictures of adult females.

Data analysis

Image pre-processing and subsequent analyses were conducted using statistical parametric mapping (SPM2; http://www.fil.ion.ucl.ac.uk/spm) and SPSS 14 (SPSS Inc, Chicago, IL). The first four volumes of the functional data were discarded to minimize the influence of T1 in the time series. The remaining functional volumes were then realigned to the first volume and spatially normalized to a standard EPI template in the montreal neurological institute (MNI) space. Data were subsequently smoothed with an isotropic Gaussian kernel (FWHM = 9 mm). Time series were filtered in the time domain using a high pass filter. All EPI images were carefully inspected for regions of signal dropout in the amygdala and caudate nucleus due to changes in magnetic susceptibility. For this purpose functional activation maps were also superimposed on the individual co-registered EPI images. The predictors used within the general linear model (GLM) were created based on information on the presentation time in the individual log files and convolved with a canonical hemodynamic response function.

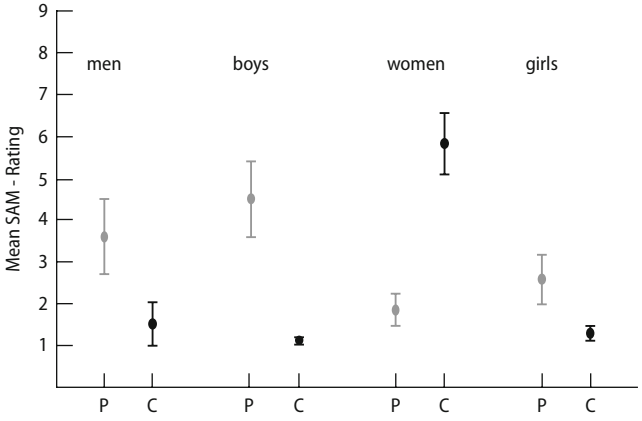

Fig. 1 Sexual arousal SAM-ratings for pedophiles attracted to boys (*P*) and heterosexual controls (*C*). Mean sexual arousal self-assessment manikin (SAM)-rating [24] (*standard error* indicated) of the four image categories presented during the fMRI scan. Self-Assessment Manikins were rated from 1 indicating no sexual arousal to 9 indicating maximal sexual arousal

Statistical maps were obtained for each subject. This first level analysis included the contrast of emotional versus geometrical figures for each individual stimulus category (man, woman, girl, boy). In a second level analysis these contrast images of both pedophiles and controls were included in a one-sample *t*-test (emotional versus geometrical stimuli), which yielded activations in both amygdalae (see Fig. 1). The coordinates of the global maxima in both amygdalae were determined by performing a ROI analysis using the WFU pick atlas [28] with masks taken from the AAL toolbox [43]. In all contrast images the beta values at these coordinates (MNI left −27, −3, −24; right 30, 3, −24) were then entered in an ANOVA with the factors hemisphere, group and stimulus class.

Results

In our group of pedophiles viewing boys mean sexual arousal—as reported by SAM rating—was 4.5 ± 2.8 and did not differ ($P = 0.27$) from mean sexual arousal of controls viewing women (5.8 ± 2.3), see Fig. 2 Results of the dimensions "valence" and "arousal" are presented in Table 2.

ANOVA demonstrated a significantly different profile of amygdala activation for the different stimuli between diagnostic groups (group * contrast interaction $F = 3.6$, $P = 0.015$). The means of the dependent variable (β values of amygdalae contrast images) are demonstrated as a graph in Fig. 3. No significant laterality effect was evident (hemisphere * group * contrast interaction). Post-hoc testing revealed that the group difference in activation profile was due to relatively more activation in the right amygdala for boys and girls in pedophiles compared to controls (significant results for the following contrasts (means are visualized in Fig. 3): boy > geo: $t = -3.04$, $P = 0.007$, girl > geo: $t = -3.38$, $P = 0.003$.). As demonstrated in Fig. 4, ANOVA showed a significant group * contrast interaction ($F = 10.5$, $P = 0.001$)

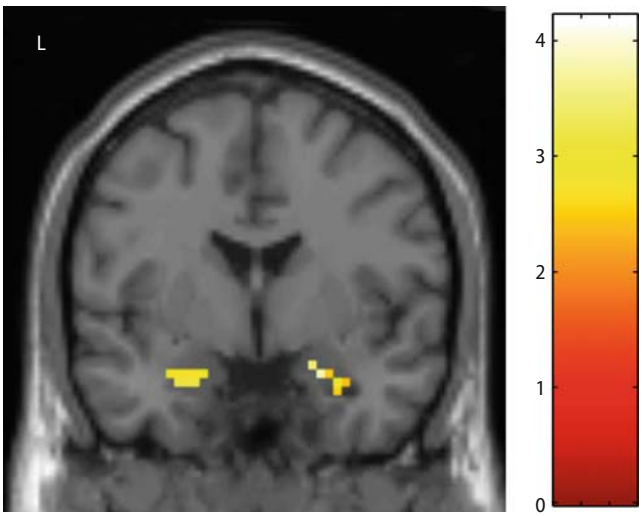

Fig. 2 Contrast image of emotional versus geometrical figures for all participants. Contrast images of the first level analysis of all participants were included in a one-sample *t* test (emotional versus geometrical stimuli). The resulting *t*-values are graphically shown (thresholded at $P < 0.005$ and uncorrected for multiple comparisons). The computed β-values of the left and right amygdala are presented in Fig. 3

when children versus adults were contrasted in pedophiles and controls. Again no significant laterality effect was evident (hemisphere *group *contrast interaction). Figure 4 illustrates that relative to adults, controls show less amygdala activation and pedophiles more activation while viewing children.

Although BDI scores were significantly higher in forensic inmates, this does not imply that they had clinically manifest depression. All probands underwent a semi-structured clinical interview with no proband fulfilling criteria of a major depressive episode. Including BDI values as a covariate in the ANOVA analysis showed no significant result for BDI and did not change the above findings.

Discussion

To the best of our knowledge the current data represent the first demonstration of altered brain activation in pedophiles in a visual stimulation paradigm. Pedophiles that were attracted to boys showed significant amygdala activation while viewing pictures of boys in swimsuits.

The behavioral meaning of the significantly greater relative activation of the amygdala in pedophilic sex-offenders compared with heterosexual controls offers at least two interpretations: It could mirror fearful emotion or sexual arousal or even a combination of fear and sexual arousal. Since the amygdala

Table 2 Results of the SAM rating dimensions "valence" and "arousal"

	Men		Boys		Women		Girls	
	Valence	Arousal	Valence	Arousal	Valence	Arousal	Valence	Arousal
Pedophiles	6.4 ± 2.3	2.8 ± 2.4	7.0 ± 1.9	3.2 ± 2.3	4.8 ± 2.4	2.2 ± 1.3	5.5 ± 2.5	2.2 ± 1.4
Controls	5.1 ± 3.0	1.3 ± 0.6	5.1 ± 3.0	1.1 ± 0.3	8.1 ± 1.1	4.9 ± 2.4	5.2 ± 2.9	1.4 ± 0.6

Means and standard deviation of valence and arousal of the four image categories presented during the fMRI scan as assessed by self-assessment manikin (SAM)-rating [24]. For the valence rating scale, 1 indicates unpleasant; 9, pleasant. For the arousal rating scale, 1 indicates calm; 9 arousing

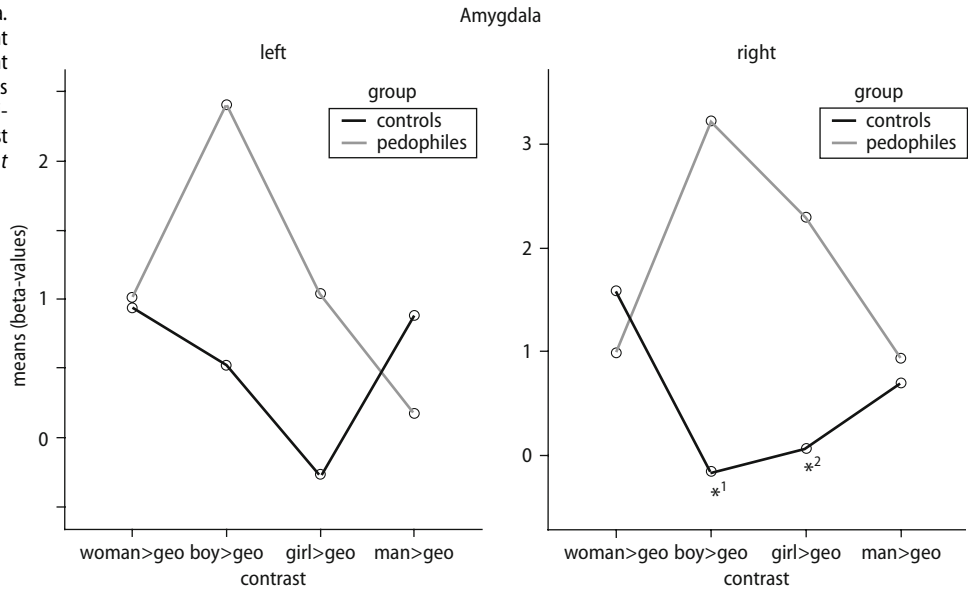

Fig. 3 Means of the β values of the amygdala. Means of the β values of left and right sided amygdala (MNI left −27, −3, −24; right 30, 3, −24) for all possible emotional versus geometrical contrasts. ANOVA reveals significance for left sided group and for contrast *group interaction. *[1]: $P = 0.007$ (post hoc *t* test). *[2]: $P = 0.003$ (post hoc *t* test)

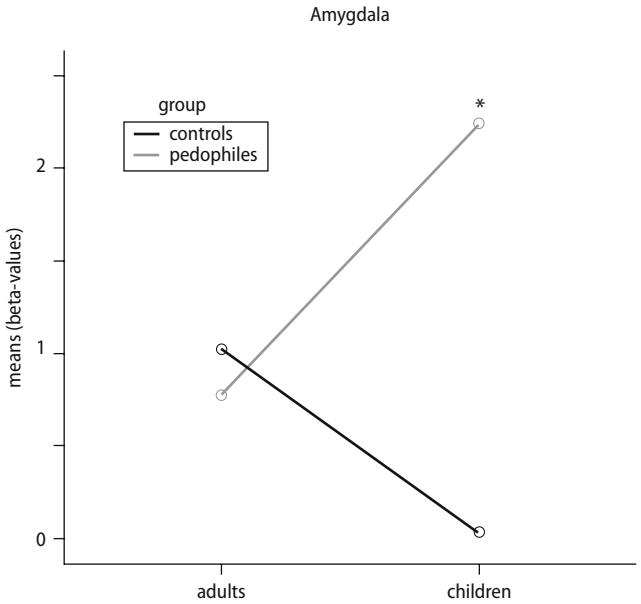

Fig. 4 Means of the β values of the amygdala: adult versus children contrast. Means of the beta values of the amygdala for children or adult versus geometrical contrasts. *$P = 0.001$ (post hoc ANOVA, group * contrast interaction, see results section)

is a critical structure for processing the emotional relevance of sensory stimuli, significant amygdala activation in pedophiles while viewing pictures of boys could mirror fearful emotions induced by the interpretation of this visual stimulus as legally and socially forbidden. An additional indirect indication for a fearful emotional reaction in pedophiles due to their illegal and penalized sexual preference may be the absence of a significantly higher amygdala response in controls while viewing women compared to their viewing man or children.

On the other hand, the observed relative activation may also reflect responsiveness to sexually salient stimuli. This interpretation is supported by the results of the SAM-ratings. Although answers in SAM-ratings by the pedophiles might be unreliable due to the forensic setting, it is interesting to note that SAM-ratings for sexual arousal between controls viewing women and sex-offenders viewing boys were similar. Following Hariri [16], cognitive evaluation of the stimuli leads to an attenuated amygdala response, suggesting a potentially less conscious evaluation in pedophiles. Additionally, the relatively high valence rating of pedophiles viewing boys (see Table 2) can be taken as an argument in favor of the salience or desire interpretation and against a fearful emotional reaction.

The results may also indicate that amygdala-mediated emotional salience in healthy adults is reduced for unfamiliar children, relative to unfamiliar adults. Although amygdala activation, as discussed, does not map unambiguously on emotional domains, this reduction makes ethological sense both regarding threat-related processing (a child is less likely to pose a salient threat than an adult) and regarding sexual emotions (as healthy adults are not sexually attracted to prepubertal children). In subjects with pedophilia, this pattern was completely reversed: while comparable activations were observed for adults, significantly stronger amygdala activity was observed for children (see Fig. 4). While again, this could reflect both a fear-related (as subjects are being currently penalized for criminal behaviour related to their sexual preference) and a appetitive (attraction to children) response, the fact that increased activation was also observed for girls, which are not sexually preferred and not related to SAM arousal ratings, suggests the intriguing speculation that in pedophilia, a mechanism present in healthy controls that reduces emotional salience of unfamiliar children may be impaired. This would underline the view that homosexual pedophilia is not a strictly categorized biological entity, but a more dimensional diagnosis.

In a very recent volumetric MR study a prominent total amygdala volume reduction as well as a local gray matter deficit in a group of pedophilic offenders was stated [41]. Both reductions were significant on the right side, which corresponds to the somewhat more pronounced functional differences of the right amygdala in our own study. The lateralisation is not surprising since emotional memory of men seems to be more right sided [27]. Certainly, a correlation of an increased activity in the amygdala and its volume loss does not imply a causal relationship. Two speculations are possible: A primary morphological alteration within this region is associated with a functional overactivation, or -the other way round- a chronic functional overactivation, which seems to be possible in our case, since stimuli are ubiquitous, leads to a volume loss, for example through excessive glutamatergic overactivation.

It should be emphasized that pedophile sex-offenders showed significant amygdala activation (reflecting an enhanced emotional answer) while stimulated by fairly ubiquitous visual stimuli showing children. This could reflect limbic activation (and/or an impaired mechanism of reduced emotional salience) that escapes cognitive control.

As pedophilia is characterized by socially deviant, repetitive, highly arousing sexual fantasies, urges and activities, it shares some phenomenological similarities with obsessive-compulsive disorders (OCDs), which are also characterized by inadequate urges and poorly inhibited, repetitive behavior. Serotonergic modulation can also ameliorate paraphilic sexual behavior [21, 22]. Indeed the amygdala is a brain region of serotonergic modulation. Volunteers receiving citalopram showed decreased amygdala responses to masked presentations of threat [17]. Anxious children and adolescents with diagnosed general anxiety disorder (GAD) accompanied with a strong amygdala activity before intervention

responded well to SSRI treatment [29]. Finally, animal models of anxiety disorders using c-Fos expressions (a human proto-oncogene belonging to the immediate early gene family of transcription factors) also identified the region of the basolateral nucleus of the amygdala as a likely candidate region of primary anxiolytic action of SSRIs [20]. Consequently, the hypothesis that SSRI treatment as well as classical medical treatments, such as luteinizing hormone-releasing-hormone agonists [3], might lead to a reduction of pedophilic behavior and a decrease of amygdala activation should be tested in future studies.

Since there is a shortage of fMRI studies in sex-offenders and neurobiological research could serve as an important tool to further our understanding of the conditions underlying this deviant behavior the present study can offer first valuable insights despite its small sample size and preliminary nature. Undoubtedly, further research in this field would be beneficial for both victims and offenders.

In conclusion, we suggest that in pedophilia, a mechanism present in healthy controls that reduces emotional salience of unfamiliar children may be impaired. It seems plausible that the limbic system and the striato-thalamo-cortical network are at least a part of the anatomical and functional correlate of this mechanism.

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