Association between brain structure and phenotypic characteristics in pedophilia

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\section*{Abstract}

Studies applying structural neuroimaging to pedophiles are scarce and have shown conflicting results. Although first findings suggested reduced volume of the amygdala, pronounced gray matter decreases in frontal regions were observed in another group of pedophilic offenders. When compared to non-sexual offenders instead of community controls, pedophiles revealed deficiencies in white matter only. The present study sought to test the hypotheses of structurally compromised prefrontal and limbic networks and whether structural brain abnormalities are related to phenotypic characteristics in pedophiles. We compared gray matter volume of male pedophilic offenders and non-sexual offenders from high-security forensic hospitals using voxel-based morphometry in cross-sectional and correlational whole-brain analyses. The significance threshold was set to \( p < .05 \), corrected for multiple comparisons. Compared to controls, pedophiles exhibited a volume reduction of the right amygdala (small volume corrected). Within the pedophilic group, pedosexual interest and sexual recidivism were correlated with gray matter decrease in the left dorsolateral prefrontal cortex \(( r = -.64)\) and insular cortex \(( r = -.45)\). Lower age of victims was strongly associated with gray matter reductions in the orbitofrontal cortex \(( r = .98)\) and angular gyrus bilaterally \(( r = .70 \text{ and } r = .93)\). Our findings of specifically impaired neural networks being related to certain phenotypic characteristics might account for the heterogeneous results in previous neuroimaging studies of pedophilia. The neuroanatomical abnormalities in pedophilia seem to be of a dimensional rather than a categorical nature, supporting the notion of a multifaceted disorder.

\section*{1. Introduction}

Despite a prevalence of sexual fantasies or sexual contact involving prepubescent children between 3\% and 9\% in the male population (Seto, 2009) and an estimated lifetime prevalence of pedophilia among men around 5\% (Mokros et al., 2012), studies assessing the brains of pedophiles through neuroimaging techniques are still scarce.

Functional brain abnormalities in pedophilic subjects under visual sexual stimulation have been revealed by functional magnetic resonance imaging (fMRI). During sexual excitement, altered activity has been demonstrated in regions such as dorsolateral prefrontal cortex (DLPFC), orbitofrontal cortex (OFC), middle temporal gyrus, cingulate cortex, and insula (Schiffer et al., 2008a,b; Poeppl et al., 2011), however without particular overlap across studies. Moreover, there is evidence that pedophilia might be linked to reduced activation in the hypothalamus, periaqueductal gray, dorsolateral and ventrolateral prefrontal cortex (VLPFC), the lateral parietal and occipital cortex as well as in the insula in response to erotic stimuli depicting adults (Walter et al., 2007). Although these results evidently differ, a recent fMRI study suggests that, at least in pedophilic men who admit their sexual interest in prepubescent children, neuroimaging of functional brain response patterns to erotica might be a promising tool to objectify the diagnosis with high levels of sensitivity and specificity (Ponseti et al., 2012).

Aside from functional abnormalities, sexual attraction to children has also been associated with structural cerebral changes. First

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results suggested reduced volume of the amygdala and related diencephalic structures such as hypothalamus, innominative substance, bed nucleus striae terminalis, and septal region (Schiltz et al., 2007). In contrast, pronounced gray matter (GM) decreases in the lateral OFC, posterior cingulate cortex (PCC), retrosplenial cortex (RSC), medial temporal lobe, middle temporal gyrus, ventral striatum, and cerebellum were observed in another group of pedophilic offenders (Schiffer et al., 2007). These differences in GM emerged from comparisons of pedophilic offenders from forensic hospitals with healthy subjects from the community which may reduce the specificity of the findings (Cantor et al., 2008). Hence, it is quite possible that at least some of these findings of impaired GM in pedophilia can be attributed to general criminality rather than to the disorder itself. Surprisingly but in line with this notion, pedophiles revealed deficiencies in white matter (WM) only when compared to other offenders (who had not committed any sexual offenses, however) instead of community controls (Cantor et al., 2008). These structural differences were located in the fronto-occipital fasciculus and in the right arcuate fasciculus and interpreted as a network disconnection syndrome of cerebral regions crucial for recognizing sexually relevant stimuli. Taken together, some of the inconsistent results in past imaging studies might be explained by the choice of comparison groups.

In the light of the previous contradictory findings, the present study sought to test the hypotheses of structurally compromised frontostrial (Schiffer et al., 2007) and limbic-diencephalic (Schiltz et al., 2007) networks related to sexual preference for prepubescents by applying voxel-based morphometry (VBM) in an independent sample of pedophilic offenders while controlling for unspecified factors such as general criminality or chronic stress by the use of non-sexual offenders as a comparison group. In addition, we aimed to ascertain whether structural brain abnormalities might be related to specific phenotypic characteristics in pedophiles.

2. Materials and methods

2.1. Participants

Nine male pedophilic patients (diagnosed according to both DSM-IV-TR and ICD-10 criteria) and 11 male non-sexual offenders were recruited from three high-security forensic hospitals and characterized as follows: mean (M) IQ (Formann and Piswanger, 1970) = 92 ± 18 standard deviation (SD) vs. M = 100 ± 19 SD, t(18 d.f.) = 92, p = .37; age: M = 45 years ± 8 SD vs. 29 years ± 6 SD, t(18 d.f.) = 5.01, p < .001; handedness (Oldfield, 1971): non-right-handed 22% vs. 27%, p > .99 in a two-sided Fisher exact test. According to self-reports using the Sell Assessment of Sexual Orientation (Sell, 1996), the majority of participants (N = 13) were categorized as primarily heterosexual. All of the subjects who were categorized as primarily homosexual (N = 7) were from the pedophilic group. All pedophilic offenders had relatively high scores on the Screening Scale for Pedophilic Interests (SSPI) (Seto and Lalumière, 2001; Seto et al., 2004), a measure for identifying pedophilic interest among child molesters, which also predicts sexual offense recidivism: M = 4.22 ± .83 SD. For the pedophilic participants, the mean age of their youngest victim was 7 years ± 3 SD (range: 2–13). According to their files, six pedophilic patients had abused more than one child. For two pedophiles, only female victims were reported, one pedophilic participant had both female and male victims, the remaining pedophilic patients had exclusively abused male prepubescents. No incest offenses were documented in the records. The criminal convictions of the control participants ranged from driving without driver’s license to attempted homicide, but mainly consisted of property offenses. Exclusion criteria were psychiatric medication, alcohol or drug abuse, schizophrenia, bipolar disorder, obsessive–compulsive disorder, and attention deficits. All participants provided written informed consent to the study protocol approved by the ethics committee of the School of Medicine at the University of Regensburg, Germany.

2.2. Brain imaging

High-resolution brain images were acquired on a 1.5 T MR scanner (MAGNETOM Sonata, Siemens Medical Solutions, Erlangen, Germany), adopting a 3D magnetization-prepared rapid acquisition with gradient echo sequence: repetition time 1970 msec, echo time 3.93 msec, flip angle 15°, 256 sagittal slices, voxel size 1 mm × 1 mm × 1 mm. Data were analyzed by means of VBM8 (http://dbm.neuro.uni-jena.de/vbm/), implemented as a toolbox in SPM8 (Wellcome Trust Centre for Neuroimaging, London, UK). After segmentation and normalization into standard stereotactic space of the Montreal Neurological Institute (MNI), images were smoothed using an isotropic Gaussian kernel of 8 mm full width at half maximum. First, differences in GM between pedophilic and non-sexual offenders were assessed by a two-sample t-test. Second, we used separate general linear models entering SSPI scores and victim age, respectively, as regressors in order to obtain correlations of GM reductions with strong pedosexual interest including higher likelihood of reoffending and with proneness to preferably young prepubescents, respectively, among child offenders. Age, handedness and IQ were included as covariates in all analyses to remove possibly confounding effects. The data were initially thresholded at p < .005, uncorrected. We applied a threshold of p < .05, corrected across the whole brain for multiple comparisons using the family-wise error (FWE) rate. For regions that had been reported to be structurally altered by two previous studies (Schiffer et al., 2007; Schiltz et al., 2007), a small volume correction, using a sphere of 16 mm radius around the respective maxima, was performed (see supplementary material for an overview of the regions). If not stated otherwise, regions are reported at p < .05, FWE corrected for multiple comparisons across the whole brain. When a brain area survived FWE correction for multiple comparisons after small volume correction (SVC), this is indicated by SVC. If a region which has not been previously reported was significant at p < .05 corrected on one hemisphere and p < .005 uncorrected on the other, both are reported (Elliott et al., 2000). Due to the non-isotropic smoothness of VBM data, results received non-stationarity correction. Cluster correlation coefficients (Pearson’s r) were calculated by means of SPSS (PASW Statistics 18, release version 18.0.0, SPSS, Inc., 2009; Chicago, IL, http://www.spss.com) after extracting data based on the regression design matrices with MarsBar (Brett et al., 2002). Brain regions were macroanatomically labeled by reference to the probabilistic Harvard-Oxford atlas (Desikan et al., 2006) included within FSLView v3.1 (http://www.fmrib.ox.ac.uk/fsl/). For a more precise allocation, we made use of the cytoarchitectonic maps of the human brain provided by the Anatomy Toolbox (Eickhoff et al., 2005, 2006c, 2007).

3. Results

Voxel-based comparisons of GM between pedophilic and non-sexual offenders revealed substance reductions (peak voxel location in Montreal Neurological Institute (MNI) space: x, y, z; Z score) among pedophiles in the centromedial nuclei group (CM) of the right amygdala (x = 30, y = −12, z = −12; Z = 3.38; SVC) extending into the laterobasal nuclei group (LB) and the cornu ammonis (CA) of the hippocampus (Amunts et al., 2005) (see, Fig. 1). This effect in the amygdala region also remained significant when not covarying for age, suggesting its independence from influences of age (differences). However, when additionally controlling for the
left insular cortex and the left DLPFC, whereas preference for lower aged children is affiliated with GM loss in the OFC and angular gyri bilaterally. The contradictory findings of previous research in the neuroimaging of pedophilia might therefore not only be due to different control groups but also due to exploring different patient samples representing distinct features of pedophilia. For instance, the correlation analyses presented herein revealed associations between variables indicative of exclusive pedophilia (higher SSPI scores and younger victim age) and GM alterations in both OFC and insula, which have been reported to distinguish between pedophilic perpetrators exclusively attracted to prepubescents and healthy controls (Schiffer et al., 2007). Hence, GM changes in both regions may be specific for an exclusive interest in prepubescent children and therefore not be seen in samples possibly also including subjects attracted to both prepubescents and adults (e.g., Schiltz et al., 2007; Cantor et al., 2008).

The replication of right-sided amygdalar deficits within the present study may be regarded as evidence for structural amygdala impairment as a general feature of pedophilia. It has to be considered that pedophilic and non-sexual offenders differed with respect to age. However, the observed group differences in amygdala volume can unlikely be attributed to the pedophilic participants being older, since (1) age was controlled in the analyses and (2) the amygdalohippocampal area shows a relative preservation during aging (Good et al., 2001). As previously shown (Schiltz et al., 2007), such volume reduction of the amygdala is neither age-dependent nor progressive and thus unlikely the consequence of degenerative atrophy over time. It rather seems to reflect a pre-existing condition, potentially arisen at the prepubertal period of life, possibly as early as in fetogenesis. The hypothesis of early neurodevelopmental perturbations as a risk factor for pedophilia is also supported by neuropsychological abnormalities in affected individuals, such as lower IQ and impaired visuospatial memory abilities (Cohen et al., 2002; Cantor et al., 2004; Blanchard et al., 2007). Also an increased rate of non-right-handedness among pedophilic subjects has been seen in line with an (non-specific) association between pedophilia and events occurring early in brain organization, since handedness might already be determined at the fetal stage (Cantor et al., 2004). It might be interjected that reduced amygdalar GM in the pedophilic patients is a neurostructural correlate of different scores of psychopathy, a condition that is associated with sexual promiscuity (Hare and Neumann, 2008). Although we applied no measures of psychopathy, this assumption unlikely pertains to our sample, as it has previously been shown that GM loss of the amygdala in pedophilic perpetrators is independent from psychopathy scores (Schiltz et al., 2007). Moreover, amygdala volume is bilaterally reduced in psychopaths (Yang et al., 2009), whereas unilateral right-sided reduction was observed in the present and a previous sample of pedophilic patients (Schiltz et al., 2007). Lateralized damage to the temporal lobe might rather result in changes of sexual preference, as seen in Klüver–Bucy syndrome (Lilly et al., 1983). Especially right-sided lesions tend to influence sexual function, which matches well with the lateralization of amygdalar GM loss to the right side in the present sample of pedophiles.

Needless to say, it is implausible that anatomical amygdalar deficits cause sexual preference for children in a direct manner. However, they might represent an organic substrate that increases the risk for the development of pedophilic behavior. The amygdala plays a pivotal role in sexual maturation especially during puberty (Romeo et al., 2002; Bramen et al., 2011). Structural impairment of this region may therefore represent the neuroanatomical basis for a deficient devaluation process of pre-existing infantile erotic interest in other children that normally culminates at puberty (Freund and Kuhn, 1993). The resulting lack in sexual attraction to adults

( relativelarge) number of predefined regions of interest, it did not survive correction for multiple comparisons. Pedophilic interest predicting sexual recidivism was correlated with left-sided volume loss in the transition zone between insula and parietal operculum (OP1 [Eickhoff et al., 2006a,b]) (x = −44, y = −22, z = 18; Z = 4.53) and the left DLPFC (x = −36, y = 29, z = 9; Z = 3.14). The corresponding cluster correlation coefficients were r = −.45 and r = −.64, respectively (see, Fig. 2). Lower age of victims in contrast was associated with GM decrease in the OFC (x = 3, y = 26, z = −29; Z = 4.64) as well as in the left (x = −40, y = −58, z = 21; Z = 3.89) and right (x = 36, y = −57, z = 19; Z = 4.00; p < .005 uncorrected) angular gyrus (PGa [Caspers et al., 2006, 2008]). Here, GM amount especially in the OFC was strongly linearly dependent on victim age (r = .98) (see, Fig. 3), but also the left and right angular gyrus showed a linear relationship of comparable strength (r = .70 and r = .93, respectively) with victim age (see, Fig. 4).

4. Discussion

We found structural changes of prefrontal, parietal, insular and limbic brain areas in pedophilic offenders. The evidence of reduced GM in the right (but not left) amygdala confirms previous research (Schiltz et al., 2007). Moreover, the results provide several new insights. While alterations in the right amygdala might discern pedophiles from non-pedophiles, certain phenotypic characteristics seem to correlate with specific GM changes within pedophilic individuals. Strong pedophilic fixation is linked to reduced GM in the

Fig. 1. Gray matter (GM) reduction in pedophiles compared to non-pedophiles. The only significant cluster comprising the right amygdala (p < .05 corrected) is superimposed on an average GM template in Montreal Neurological Institute (MNI) space. Thresholded at p < .005, uncorrected.
and a sexual preference for prepubescents would then also be reflected in amygdalar activity. Accordingly, the amygdala of (homosexual) pedophiles responds more intensely to visual sexual stimuli depicting children than to adult erotic content (Schiffer et al., 2008a). Also, compared to non-pedophilic individuals, pedophiles exhibit stronger activation of the amygdala and adjacent structures in the medial temporal lobe when stimulated with pictures of nude prepubescents (Sartorius et al., 2008; Poepppl et al., 2011). Such sexual salience attribution to inappropriate stimuli might be the result of amygdala dysfunction during sexual maturation, which resonates well with the importance of the amygdala for the detection of socially and emotionally relevant cues (Ball et al., 2007; Schiffer et al., 2008a).
the positive correlation between GM amount in the OFC (functionally diverse structure (Kurth et al., 2010) that is essential with pedophilic interest. The insula is a phylogenetically old and anterior sequence (Craig, 2011). In the same vein, it is involved in and appears to integrate all salient neural activity in a posterior-to-

ordinates ($x, y, z$). Thresholded at $p < .005$, uncorrected. The scatter plot exemplifies the positive correlation between GM amount in the OFC ($r = .98$) and victim age.

Bzdok et al., 2011) and its involvement in the functional neuroanatomy of sexual arousal (Stolérü et al., 2012). Furthermore, the amygdala is structurally, connectionally, and functionally partitioned into different nuclei (Bzdok et al., in press). The centromedial and laterobasal nuclei, where we found reduced GM in pedophiles, are implicated in mediating behavioral and autonomic responses (Pessoa, 2010), in the modulation of attention to salient environmental stimuli (Barbour et al., 2010) (CM), and in the associative processing of environmental information and the integration with self-relevant cognition (LB) (Bzdok et al., in press). Hence, these processes may be impared in pedophiles during sexual maturation, impeding the development of normal mating behavior.

The centromedial nucleus of the right amygdala is functionally connected to the insular cortex on the opposite hemisphere (Bzdok et al., in press), where we observed a linear GM decrease associated with pedophilic interest. The insula is a phylogenetically old and functionally diverse structure (Kurth et al., 2010) that is essential for subjective feelings, emotion, and self-awareness (Craig, 2002) and appears to integrate all salient neural activity in a posterior-to-

anterior sequence (Craig, 2011). In the same vein, it is involved in mediating sexual arousal (Stolérü et al., 2012). In pedophiles, the insular cortex shows higher activation in response to sexual ma-

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Fig. 3. Linear relationship between victim age and gray matter (GM) in the orbito-frontal cortex (OFC) of pedophilic offenders. Statistical parametric map (SPM) is superimposed on an average GM template in Montreal Neurological Institute (MNI) space. Brain slices are shown at local maxima of the respective cluster at MNI co-

ordinates ($x, y, z$). Thresholded at $p < .005$, uncorrected. The scatter plot exemplifies the positive correlation between GM amount in the OFC ($r = .98$) and victim age.

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The DLPFC is not only involved in exerting cognitive control but also, more specifically, in moral reasoning (Greene et al., 2004). Together with cortical midline structures, amygdala, OFC, and angular gyrus, it constitutes a neural network critical for social cognitive and moral judgment processing (Raine and Yang, 2006; Forbes and Grafman, 2010). Especially the angular gyrus is engaged in morality and empathy (Bzdok et al., 2012). It is intriguing that, according to our results, the more impaired pedophilic individuals’ brain regions related to moral cognition (OFC and angular gyrus) are, the younger their victims’ age is. Although this relation is most coherent, it seems to be of the utmost significance in the context of pedophilia as a paraphilic disorder when considering the role of the angular gyrus in sexual arousal. There is strong evidence that healthy male sexual arousal is accompanied by a deactivation of the angular gyrus (Redouté et al., 2000; Moulier et al., 2006; Mouras et al., 2008). Even though GM reduction does not necessarily result in decreased activity, deficits in the angular region might condition a sexual hyperexcitability to inadequate objects, i.e.,
children. Besides, GM decreases in this area of the inferior parietal cortex could also account for known neuropsychological abnormalities in pedophiles such as lower IQs and deficits in recall memory (Cohen et al., 2002; Cantor et al., 2004; Blanchard et al., 2007), given its leading part in arithmetic and semantic processing as well as memory processes (Seghier, in press). More precisely, neuroimaging studies have demonstrated strong IQ/GM correlations for the angular gyrus in men (Haier et al., 2005) and have moreover disclosed its functional relevance for cued recall and episodic memory retrieval (Sestieri et al., 2011; Hayama et al., 2012). In general, the association of structural brain deficits with victim age is in line with prior research which showed that pedophilic men who sexually abused particularly young children are less discriminating with regard to victim gender (Levenson et al., 2008; Carlstedt et al., 2009) and may show more mental health problems (Kalichman, 1991; Firestone et al., 2005).

It has recently been shown that both pedophilic and non-pedophilic child offenders suffer from executive dysfunction, particularly concerning response inhibition (Tost et al., 2004; Schiffer and Vonlaufen, 2011), pointing to a dysfunction in the orbitofrontal cortex (Schiffer and Vonlaufen, 2011). Consistent with this assumption, we found orbitofrontal defects in pedophilic offenders to be the more pronounced, the younger their victims were. Orbitofrontal lesions can not only lead to neurological symptoms but also involve pedophilic behavior (Burns and Swedlow, 2003; Mendez and Shapira, 2011). Furthermore, such behavior violating socially established rules may quite originate from early-onset damage to the prefrontal cortex (i.e., before the age 16 months) (Anderson et al., 1999), although such defects may be subtle in pedophiles. The lack in proper processing of emotional information associated with orbitofrontal damage (Bechara, 2004) could well explain the emotional and cognitive distortions in child sex offenders including distorted beliefs about children’s sexuality (Mihailides et al., 2004). In addition, damage to the OFC results in insensitivity to future consequences of one’s own actions (Bechara et al., 1994), which fits well with our observation that in pedophiles OFC volume linearly decreases with the age of their victims.

It should be acknowledged that the sample size of the present study was relatively small. Accordingly, we cannot exclude the possibility that other effects than the reported ones were overlooked due to limited statistical power. On the other hand, the statistical significance of our findings (stringently controlled for false positives), based on a small sample corroborates the quantitative strength of the observed results. In this context, it has recently been suggested that significant findings from small samples should not be easily dismissed but taken more seriously than equivalent results in very large studies (Friston, 2012). Nevertheless, it seems worthwhile to attempt replicating the present findings. A replication might preferably be undertaken with self-referred pedophilic men from the community since, as a second limitation, the present study investigated only delinquent pedophiles who were inpatients at secure institutions. Despite the employment of non-sexual offenders as a control group in order to control the factors incarceration and general criminality, this may have influenced the results.
Taken together, we delineated structurally impaired neural networks in pedophilia, including amygdala, insula, DLPCF, angular gyri, and OFC. These neuroanatomical deficits might account for distinct features of pedophilia such as strong pedophilic fixation, sexual recidivism, and low victim age. The observed relationship of specific GM reductions with certain phenotypic characteristics might account for the heterogeneous findings in previous neuroimaging of pedophilia. Furthermore, it suggests that neuroanatomical abnormalities in pedophilia are of a dimensional rather than a categorical nature, supporting the notion of a multifaceted disorder.

Conflict of interest

None of the authors reports any actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations within three years of beginning the work submitted that could inappropriately influence, or be perceived to influence, their work.

Contributors

T. B. Poeppel, J. Nitschke, P. Santtila, M. Osterheider and A. Mokros designed the study. T. B. Poeppel, J. Nitschke, M. W. Greenlee and A. Mokros gathered the data, which T. B. Poeppel, M. Schecklmann, B. Langguth and A. Mokros analyzed. T. B. Poeppel and A. Mokros wrote the article, which J. Nitschke, P. Santtila, M. Schecklmann, B. Langguth, M. W. Greenlee and M. Osterheider revised before submission.

Disclosure

All authors reported no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jspychires.2013.01.003.

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