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Association between brain structure and phenotypic characteristics in pedophilia

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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 gyri bilaterally ($r = .70$ 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.

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, innominate 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 frontostriatal (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 unspecific 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, $t(18\ \text{d.f.}) = .92$, $p = .37$; age: M = 45 years ± 8 SD vs. 29 years ± 6 SD, $t(18\ \text{d.f.}) = 5.01$, $p < .001$; 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

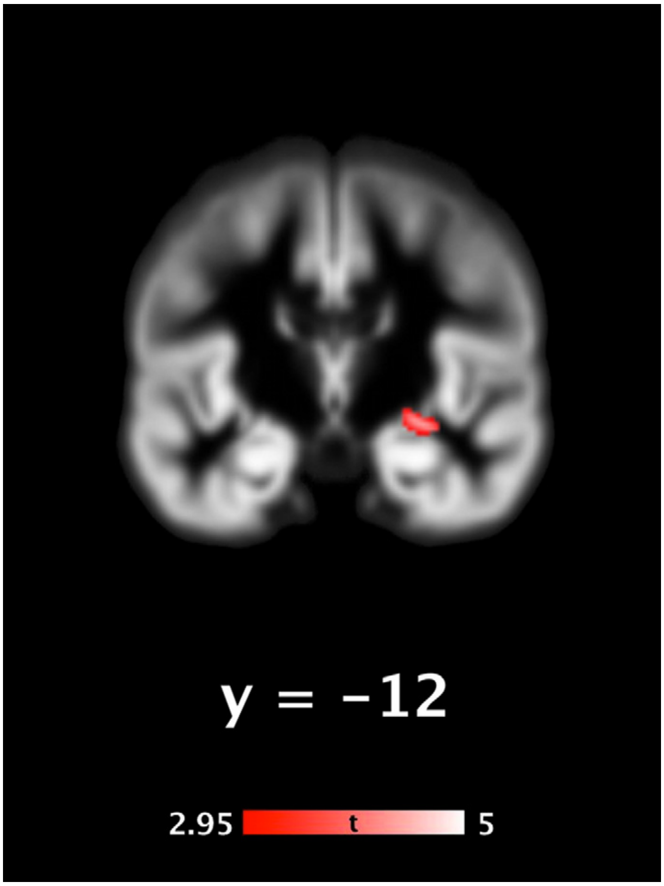

Fig. 1. Gray matter (GM) reduction in pedophiles compared to non-pedophiles. The only significant cluster comprising the right amygdala ($p < .05$ corrected) is superimposed on an average GM template in Montreal Neurological Institute (MNI) space. Thresholded at $p < .005$, uncorrected.

(relatively large) 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 (OP 1 [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 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 covaried out 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 Kuban, 1993). The resulting lack in sexual attraction to adults

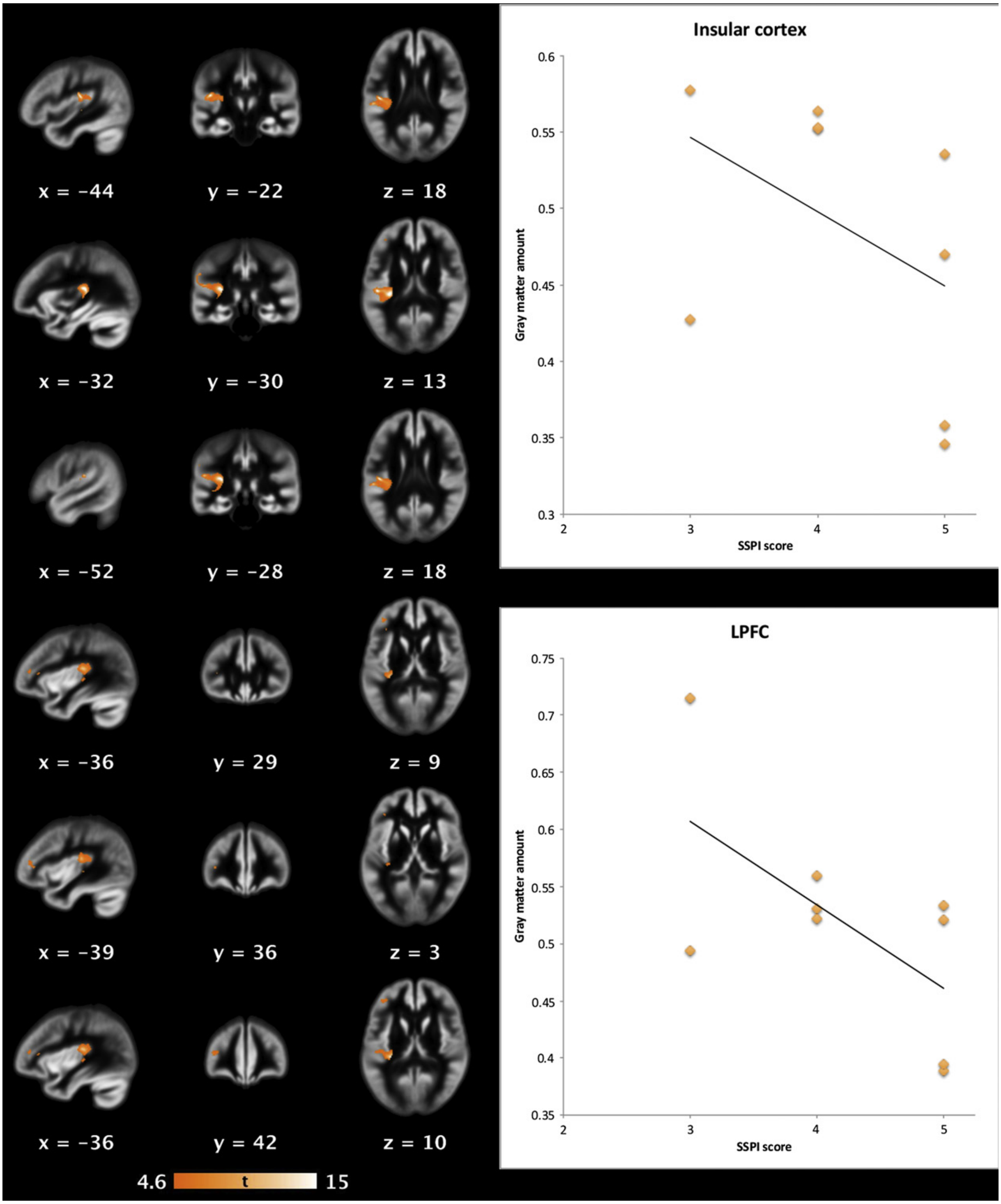

Fig. 2. Inverse relationship between pedophilic interests and gray matter (GM) in pedophilic offenders. Significant clusters in the left operculo-insular cortex and the left dorsolateral prefrontal cortex (DLPFC) are superimposed on an average GM template in Montreal Neurological Institute (MNI) space. Brain slices are shown at local maxima of the respective clusters at MNI coordinates (*x*, *y*, *z*; insula: upper three rows, DLPFC: lower three rows). Thresholded at $p < .005$, uncorrected. The scatter plot exemplifies the negative correlation between GM amount in the left insula ($r = -.45$) as well as in the left lateral prefrontal cortex (LPFC; $r = -.64$) and pedosexual interest (SSPI scores) as measured by a Screening Scale for Pedophilic Interests (SSPI [Seto and Lalumière, 2001; Seto et al., 2004]).

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; Poeppl 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;

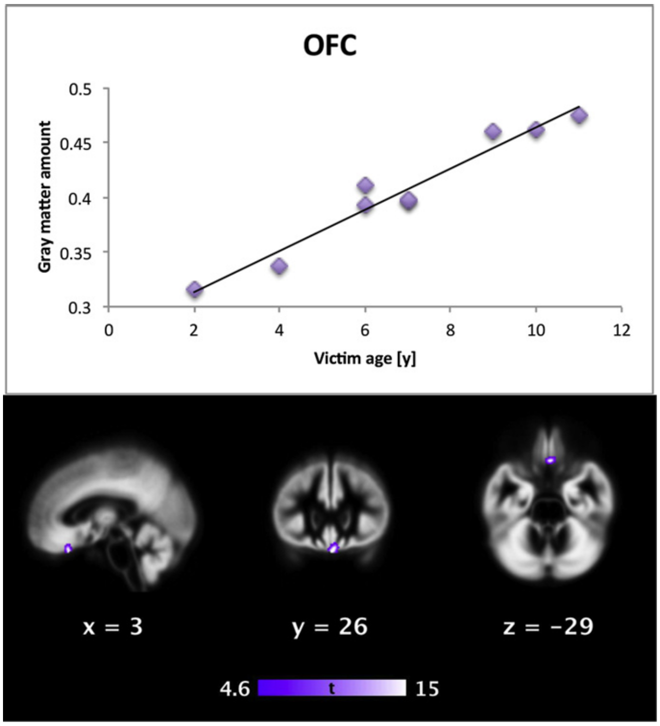

Fig. 3. Linear relationship between victim age and gray matter (GM) in the orbitofrontal cortex (OFC) of pedophilic offenders. Statistical parametric map (SPM) is superimposed on an average GM template in Montreal Neurological Institute (MNI) space. Brain slices are shown at local maxima of the respective cluster at MNI coordinates (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 (Stoléru 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 impaired 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 (Stoléru et al., 2012). In pedophiles, the insular cortex shows higher activation in response to sexual material containing prepubescents than to erotic pictures of adults (Schiffer et al., 2008a,b; Poeppl et al., 2011). In addition, decreased insular activity during visual stimulation with adult erotica (Walter et al., 2007; Poeppl et al., 2011) and increased activity in the insula during sexual arousal in general (Poeppl et al., 2011) has been shown in pedophilic perpetrators when compared with non-pedophiles. These findings indicate a dysfunction in pedophiles' insular cortex, that might be based on the macroscopic structural GM alterations that have been revealed in the present sample of pedophiles and had already been announced by Schiffer et al. (2007). We here disclosed the inverse relationship of insular GM amount with an objective, file-based index of pedosexual interest (SSPI), a measure that is positively associated with sexual arousability to children in pedosexual offenders as measured through penile plethysmography (Seto et al., 2003). This finding suggests that the observed neuroanatomical abnormalities are of a dimensional nature and depend on the degree of pedophilic interest affiliated with sexual recidivism. That the insular GM alterations vary among pedophilic offenders might explain why functional and structural anomalies in this region have not been observed in every sample of pedophiles investigated so far when compared to non-pedophiles. In summary, given the importance of the insular cortex for emotion processing and sexual arousal, the substance reduction associated with pedophilic fixation reported herein may account for dysfunctional sexual excitement elicited by inappropriate (child) stimuli.

Similarly, GM volume in the left DLPFC was inversely correlated with pedosexual interest and recidivism. No structural impairment in pedophiles has been reported in this region up to now (Schiffer et al., 2007; Schiltz et al., 2007; Cantor et al., 2008). In contrast, functionally altered responses have been described repeatedly (Walter et al., 2007; Schiffer et al., 2008a,b). In particular, abnormal activity in the left DLPFC seems to distinguish pedosexual arousal from normal sexual excitement (Schiffer et al., 2008a). Moreover, the neurofunctional correlates of pedophiles' sexual disinterest in adults comprise deactivation of the left DLPFC (Walter et al., 2007). Basically, the lateral prefrontal cortex (LPFC) is involved in the processing of visual sexual stimuli (Ferretti et al., 2005; Brunetti et al., 2008). It also plays a pivotal role in the categorization of visual stimuli (Freedman et al., 2001) and is capable of encoding category-based reward information (Pan et al., 2008). In the context of pedophilia as a sexual deviation, GM reduction in the DLPFC correlating with pedophilic interest might contribute to an improper classification and consequently dysfunctional processing of visual sexual stimuli. However, there is also some evidence that the DLPFC is implicated in the inhibition of sexual arousal (Beauregard et al., 2001), thus exercising cognitive control over arising (sexual) emotions. Its structural impairment may hence imply a deficiency of conscious inhibitory mechanisms, entailing limited ability to suppress pedosexual arousal. This notion seems particularly reasonable in the face of the GM reduction correlating with SSPI scores, which in turn were demonstrated to predict offense recidivism among pedophilic perpetrators (Seto et al., 2004). Moreover, it may be inferred that morphologic abnormalities in the DLPFC are not specifically related to abnormal sexual interests but some more general cognitive dysfunction that accounts for acting on the pedosexual urges.

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.,

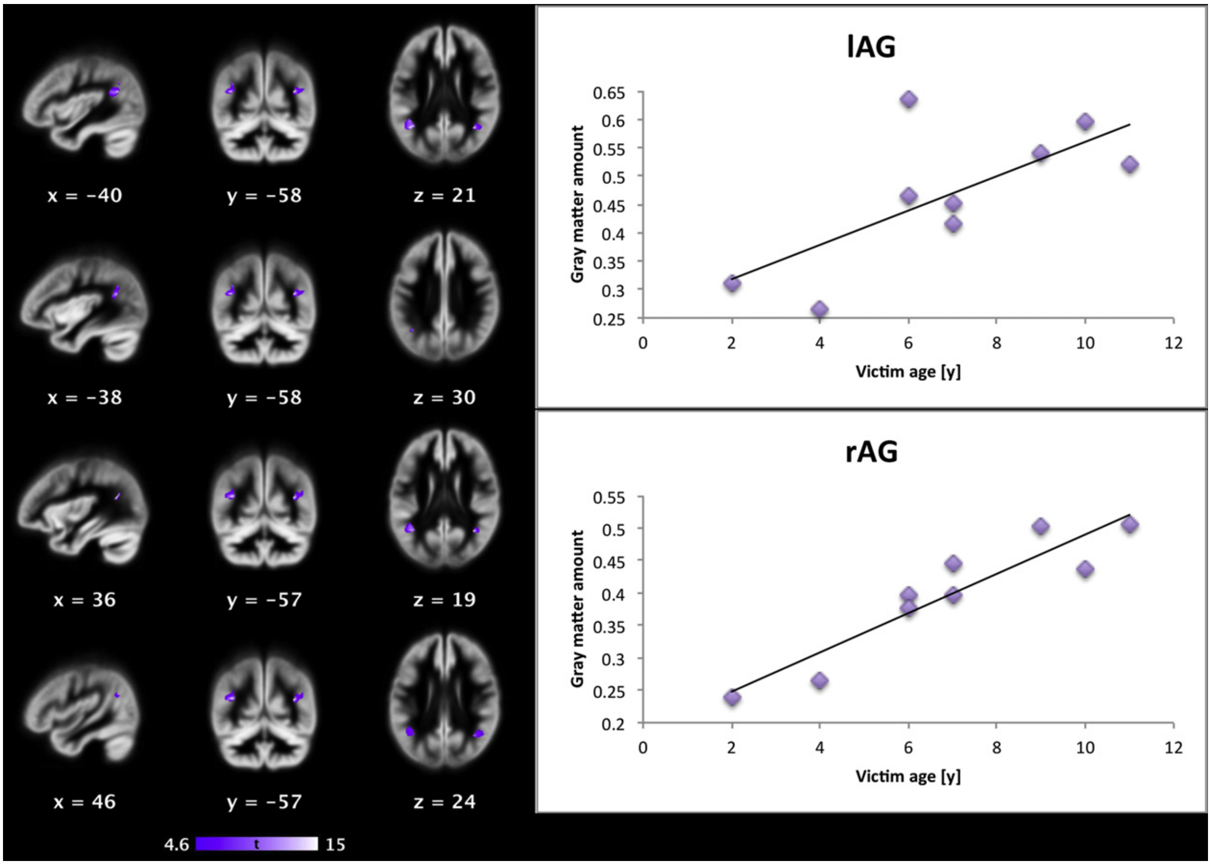

Fig. 4. Linear relationship between victim age and gray matter (GM) in the left and right angular gyrus (lAG, rAG) of pedophilic offenders. Statistical parametric map (SPM) is superimposed on an average GM template in Montreal Neurological Institute (MNI) space. Brain slices are shown at local maxima of the respective clusters at MNI coordinates *x*, *y*, z; lAG: rows 1 and 2, rAG: rows 3 and 4). Thresholded at $p < .005$, uncorrected. The scatter plot exemplifies the positive correlation between GM amount in the lAG ($r = .70$) as well as the rAG ($r = .93$) and victim age.

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 Swerdlow, 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, DLPFC, 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. Poeppl, J. Nitschke, P. Santtila, M. Osterheider and A. Mokros designed the study. T. B. Poeppl, J. Nitschke, M. W. Greenlee and A. Mokros gathered the data, which T. B. Poeppl, M. Schecklmann, B. Langguth and A. Mokros analyzed. T. B. Poeppl 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.

Role of the funding source

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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.jpsychires.2013.01.003.

References

Amunts K, Kedo O, Kindler M, Pieperhoff P, Mohlberg H, Shah NJ, et al. Cytoarchitectonic mapping of the human amygdala, hippocampal region and entorhinal cortex: intersubject variability and probability maps. Anatomy and Embryology 2005;210:343–52.
Anderson SW, Bechara A, Damasio H, Tranel D, Damasio AR. Impairment of social and moral behavior related to early damage in human prefrontal cortex. Nature Neuroscience 1999;2:1032–7.
Ball T, Rahm B, Eickhoff SB, Schulze-Bonhage A, Speck O, Mutschler I. Response properties of human amygdala subregions: evidence based on functional MRI combined with probabilistic anatomical maps. PLoS One 2007;2:e307.
Barbour T, Murphy E, Pruitt P, Eickhoff SB, Keshavan MS, Rajan U, et al. Reduced intra-amygdala activity to positively valenced faces in adolescent schizophrenia offspring. Schizophrenia Research 2010;123:126–36.
Beauregard M, Lévesque J, Bourgouin P. Neural correlates of conscious self-regulation of emotion. The Journal of Neuroscience: The Official Journal of the Society for Neuroscience 2001;21:RC165.
Bechara A. The role of emotion in decision-making: evidence from neurological patients with orbitofrontal damage. Brain and Cognition 2004;55:30–40.
Bechara A, Damasio AR, Damasio H, Anderson SW. Insensitivity to future consequences following damage to human prefrontal cortex. Cognition 1994;50:7–15.
Blanchard R, Kolla NJ, Cantor JM, Klassen PE, Dickey R, Kuban ME, et al. handedness, and pedophilia in adult male patients stratified by referral source. Sexual Abuse: A Journal of Research and Treatment 2007;19:285–309.
Bramen JE, Hranilovich JA, Dahl RE, Forbes EE, Chen J, Toga AW, et al. Puberty influences medial temporal lobe and cortical gray matter maturation differently in boys than girls matched for sexual maturity. Cerebral Cortex 2011;21:636–46.
Brett M, Anton JL, Valabregue R, Poline JB. Region of interest analysis using an SPM toolbox. Abstract presented at the 8th International Conference on Functional Mapping of the Human Brain, Sendai, Japan. Available on CD-ROM in NeuroImage 2002;16(2).
Brunetti M, Babiloni C, Ferretti A, Del Gratta C, Merla A, Olivetti Belardinelli M, et al. Hypothalamus, sexual arousal and psychosexual identity in human males: a functional magnetic resonance imaging study. European Journal of Neuroscience 2008;27:2922–7.
Burns JM, Swerdlow RH. Right orbitofrontal tumor with pedophilia symptom and constructional apraxia sign. Archives of Neurology 2003;60:437–40.
Bzdok D, Laird AR, Zilles K, Fox PT, Eickhoff SB. An investigation of the structural, connectional, and functional subspecialization in the human amygdala. Human Brain Mapping, in press.
Bzdok D, Langner R, Caspers S, Kurth F, Habel U, Zilles K, et al. ALE meta-analysis on facial judgments of trustworthiness and attractiveness. Brain Structure & Function 2011;215:209–23.
Bzdok D, Schilbach L, Vogeley K, Schneider K, Laird AR, Langner R, et al. Parsing the neural correlates of moral cognition: ALE meta-analysis on morality, theory of mind, and empathy. Brain Structure & Function 2012;217:783–96.
Cantor JM, Blanchard R, Christensen BK, Dickey R, Klassen PE, Beckstead AL, et al. Intelligence, memory, and handedness in pedophilia. Neuropsychology 2004;18:3–14.
Cantor JM, Kabani N, Christensen BK, Zipursky RB, Barbaree HE, Dickey R, et al. Cerebral white matter deficiencies in pedophilic men. Journal of Psychiatric Research 2008;42:167–83.
Carlstedt A, Nilsson T, Hofvander B, Brimse A, Innala S, Anckarsäter H. Does victim age differentiate between perpetrators of sexual child abuse? A study of mental health, psychosocial circumstances, and crimes. Sexual Abuse: A Journal of Research and Treatment 2009;21:442–54.
Caspers S, Eickhoff SB, Geyer S, Scheperjans F, Mohlberg H, Zilles K, et al. The human inferior parietal lobule in stereotaxic space. Brain Structure & Function 2008;212:481–95.
Caspers S, Geyer S, Schleicher A, Mohlberg H, Amunts K, Zilles K. The human inferior parietal cortex: cytoarchitectonic parcellation and interindividual variability. NeuroImage 2006;33:430–48.
Cohen LJ, Nikiforov K, Gans S, Poznansky O, McGeoch P, Weaver C, et al. Heterosexual male perpetrators of childhood sexual abuse: a preliminary neuropsychiatric model. The Psychiatric Quarterly 2002;73:313–36.
Craig AD. How do you feel? Interoception: the sense of the physiological condition of the body. Nature Reviews Neuroscience 2002;3:655–66.
Craig AD. Significance of the insula for the evolution of human awareness of feelings from the body. Annals of the New York Academy of Sciences 2011;1225:72–82.
Desikan RS, Ségonne F, Fischl B, Quinn BT, Dickerson BC, Blacker D, et al. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. NeuroImage 2006;31:968–80.
Eickhoff SB, Amunts K, Mohlberg H, Zilles K. The human parietal operculum. II. Stereotaxic maps and correlation with functional imaging results. Cerebral Cortex 2006b;16:268–79.
Eickhoff SB, Heim S, Zilles K, Amunts K. Testing anatomically specified hypotheses in functional imaging using cytoarchitectonic maps. NeuroImage 2006c;32:570–82.
Eickhoff SB, Paus T, Caspers S, Grosbras MH, Evans AC, Zilles K, et al. Assignment of functional activations to probabilistic cytoarchitectonic areas revisited. NeuroImage 2007;36:511–21.
Eickhoff SB, Schleicher A, Zilles K, Amunts K. The human parietal operculum. I. Cytoarchitectonic mapping of subdivisions. Cerebral Cortex 2006a;16:254–67.
Eickhoff SB, Stephan KE, Mohlberg H, Grefkes C, Fink GR, Amunts K, et al. A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. NeuroImage 2005;25:1325–35.
Elliott R, Friston KJ, Dolan RJ. Dissociable neural responses in human reward systems. The Journal of Neuroscience: The Official Journal of the Society for Neuroscience 2000;20:6159–65.
Ferretti A, Caulo M, Del Gratta C, Di Matteo R, Merla A, Montorsi F, et al. Dynamics of male sexual arousal: distinct components of brain activation revealed by fMRI. NeuroImage 2005;26:1086–96.
Firestone P, Dixon KL, Nunes KL, Bradford JM. A comparison of incest offenders based on victim age. The Journal of the American Academy of Psychiatry and the Law 2005;33:223–32.
Forbes CE, Grafman J. The role of the human prefrontal cortex in social cognition and moral judgment. Annual Review of Neuroscience 2010;33:299–324.
Formann AK, Piswanger K. Der Wiener Matrizentest. Ein Rasch-skalierter sprachfreier Intelligenztest. Weinheim: Beltz Test Gesellschaft; 1970.
Freedman DJ, Riesenhuber M, Poggio T, Miller EK. Categorical representation of visual stimuli in the primate prefrontal cortex. Science 2001;291:312–6.
Freund K, Kuban M. Toward a testable developmental model of pedophilia: the development of erotic age preference. Child Abuse & Neglect 1993;17:315–24.

Friston K. Ten ironic rules for non-statistical reviewers. NeuroImage 2012;61:1300–10.

Good CD, Johnsrude IS, Ashburner J, Henson RN, Friston KJ, Frackowiak RS. A voxel-based morphometric study of ageing in 465 normal adult human brains. NeuroImage 2001;14:21–36.

Greene JD, Nystrom LE, Engell AD, Darley JM, Cohen JD. The neural bases of cognitive conflict and control in moral judgment. Neuron 2004;44:389–400.

Haier RJ, Jung RE, Yeo RA, Head K, Alkire MT. The neuroanatomy of general intelligence: sex matters. NeuroImage 2005;25:320–7.

Hare RD, Neumann CS. Psychopathy as a clinical and empirical construct. Annual Review of Clinical Psychology 2008;4:217–46.

Hayama HR, Vilberg KL, Rugg MD. Overlap between the neural correlates of cued recall and source memory: evidence for a generic recollection network? Journal of Cognitive Neuroscience 2012;24:1127–37.

Kalichman SC. Psychopathology and personality characteristics of criminal sexual offenders as a function of victim age. Archives of Sexual Behavior 1991;20:187–97.

Kurth F, Zilles K, Fox PT, Laird AR, Eickhoff SB. A link between the systems: functional differentiation and integration within the human insula revealed by meta-analysis. Brain Structure & Function 2010;214:519–34.

Levenson JS, Becker J, Morin JW. The relationship between victim age and gender crossover among sex offenders. Sexual Abuse: A Journal of Research and Treatment 2008;20:43–60.

Lilly R, Cummings JL, Benson DF, Frankel M. The human Klüver–Bucy syndrome. Neurology 1983;33:1141–5.

Mendez M, Shapira JS. Pedophilic behavior from brain disease. The Journal of Sexual Medicine 2011;8:1092–100.

Mihailides S, Devilly GJ, Ward T. Implicit cognitive distortions and sexual offending. Sexual Abuse: A Journal of Research and Treatment 2004;16:333–50.

Mokros A, Osterheider M, Nitschke J. Pedophilia. Prevalence, etiology, and diagnostics. Der Nervenarzt 2012;83:355–8.

Moulier V, Mouras H, Pélégrini-Issac M, Glutron D, Rouxel R, Grandjean B, et al. Neuroanatomical correlates of penile erection evoked by photographic stimuli in human males. NeuroImage 2006;33:689–99.

Mouras H, Stoléru S, Moulier V, Pélégrini-Issac M, Rouxel R, Grandjean B, et al. Activation of mirror-neuron system by erotic video clips predicts degree of induced erection: an fMRI study. NeuroImage 2008;42:1142–50.

Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 1971;9:97–113.

Pan X, Sawa K, Tsuda I, Tsukada M, Sakagami M. Reward prediction based on stimulus categorization in primate lateral prefrontal cortex. Nature Neuroscience 2008;11:703–12.

Pessoa L. Emotion and cognition and the amygdala: from “what is it?” to “what’s to be done?”. Neuropsychologia 2010;48:3416–29.

Poeppl TB, Nitschke J, Dombert B, Santtila P, Greenlee MW, Osterheider M, et al. Functional cortical and subcortical abnormalities in pedophilia: a combined study using a choice reaction time task and fMRI. The Journal of Sexual Medicine 2011;8:1660–74.

Ponseti J, Granert O, Jansen O, Wolff S, Beier K, Neutze J, et al. Assessment of pedophilia using hemodynamic brain response to sexual stimuli. Archives of General Psychiatry 2012;69:187–94.

Raine A, Yang Y. Neural foundations to moral reasoning and antisocial behavior. Social Cognitive and Affective Neuroscience 2006;1:203–13.

Redouté J, Stoléru S, Grégoire MC, Costes N, Cinotti L, Lavenne F, et al. Brain processing of visual sexual stimuli in human males. Human Brain Mapping 2000;11:162–77.

Romeo RD, Richardson HN, Sisk CL. Puberty and the maturation of the male brain and sexual behavior: recasting a behavioral potential. Neuroscience and Biobehavioral Reviews 2002;26:381–91.

Sartorius A, Ruf M, Kief C, Demirakca T, Bailer J, Ende G, et al. Abnormal amygdala activation profile in pedophilia. European Archives of Psychiatry and Clinical Neuroscience 2008;258:271–7.

Schiffer B, Krueger T, Paul T, de Greiff A, Forsting M, Leygraf N, et al. Brain response to visual sexual stimuli in homosexual pedophiles. Journal of Psychiatry & Neuroscience 2008a;33:23–33.

Schiffer B, Paul T, Gizewski E, Forsting M, Leygraf N, Schedlowski M, et al. Functional brain correlates of heterosexual paedophilia. NeuroImage 2008b;41:80–91.

Schiffer B, Peschel T, Paul T, Gizewski E, Forsting M, Leygraf N, et al. Structural brain abnormalities in the frontostriatal system and cerebellum in pedophilia. Journal of Psychiatric Research 2007;41:753–62.

Schiffer B, Vonlaufen C. Executive dysfunctions in pedophilic and nonpedophilic child molesters. The Journal of Sexual Medicine 2011;8:1975–84.

Schiltz K, Witzel J, Northoff G, Zierhut K, Gubka U, Fellmann H, et al. Brain pathology in pedophilic offenders: evidence of volume reduction in the right amygdala and related diencephalic structures. Archives of General Psychiatry 2007;64:737–46.

Seghier ML. The angular gyrus: multiple functions and multiple subdivisions. The Neuroscientist: A Review Journal Bringing Neurobiology. Neurology and Psychiatry 2013;19:43–61.

Sell RL. The Sell assessment of sexual Orientation: background and scoring. Journal of Gay, Lesbian, & Bisexual Identity 1996;1:295–310.

Sestieri C, Corbetta M, Romani GL, Shulman GL. Episodic memory retrieval, parietal cortex, and the default mode network: functional and topographic analyses. The Journal of Neuroscience: The Official Journal of the Society for Neuroscience 2011;31:4407–20.

Seto MC. Pedophilia. Annual Review of Clinical Psychology 2009;5:391–407.

Seto MC, Harris GT, Rice ME, Barbaree HE. The Screening Scale for Pedophilic Interests predicts recidivism among adult sex offenders with child victims. Archives of Sexual Behavior 2004;33:455–66.

Seto MC, Lalumière ML. A brief screening scale to identify pedophilic interests among child molesters. Sexual Abuse: A Journal of Research and Treatment 2001;13:15–25.

Seto MC, Murphy WD, Page J, Ennis L. Detecting anomalous sexual interests in juvenile sex offenders. Annals of the New York Academy of Sciences 2003;989:118–30.

Stoléru S, Fonteille V, Cornélis C, Joyal C, Moulier V. Functional neuroimaging studies of sexual arousal and orgasm in healthy men and women: a review and meta-analysis. Neuroscience and Biobehavioral Reviews 2012;36:1481–509.

Tost H, Vollmert C, Brassen S, Schmitt A, Dressing H, Braus DF. Pedophilia: neuropsychological evidence encouraging a brain network perspective. Medical Hypotheses 2004;63:528–31.

Walter M, Witzel J, Wiebking C, Gubka U, Rotte M, Schiltz K, et al. Pedophilia is linked to reduced activation in hypothalamus and lateral prefrontal cortex during visual erotic stimulation. Biological Psychiatry 2007;62:698–701.

Yang Y, Raine A, Narr KL, Colletti P, Toga AW. Localization of deformations within the amygdala in individuals with psychopathy. Archives of General Psychiatry 2009;66:986–94.