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Diminished fronto-limbic functional connectivity in child sexual offenders☆

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A R T I C L E I N F O

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A B S T R A C T

Background: Child sexual abuse and neglect have been related to an increased risk for the development of a wide range of behavioral, psychological, and sexual problems and increased rates of suicidal behavior. Contrary to the large amount of research focusing on the negative mental health consequences of child sexual abuse, very little is known about the characteristics of child sexual offenders and the neuronal underpinnings contributing to child sexual offending.
Methods and sample: This study investigates differences in resting state functional connectivity (rs-FC) between non-pedophilic child sexual offenders (N = 20; CSO-P) and matched healthy controls (N = 20; HC) using a seed-based approach. The focus of this investigation of rs-FC in CSO-P was put on prefrontal and limbic regions highly relevant for emotional and behavioral processing.
Results: Results revealed a significant reduction of rs-FC between the right centromedial amygdala and the left dorsolateral prefrontal cortex in child sexual offenders compared to controls.
Conclusion & recommendations: Given that, in the healthy brain, there is a strong top-down inhibitory control of prefrontal over limbic structures, these results suggest that diminished rs-FC between the amygdala and the dorsolateral prefrontal cortex and may foster sexual deviance and sexual offending. A profound understanding of these concepts should contribute to a better understanding of the occurrence of child sexual offending, as well as further development of more differentiated and effective interventions.

1. Introduction

Child sexual offending (CSO) is a widespread, global problem affecting millions of children worldwide, despite the United Nations having declared in the Rights of the Child, in 1989, in Article 19 and 34, to prevent child sexual abuse (Barth et al., 2013; Stoltenborgh et al., 2011). Child sexual offenses are among the crimes that evoke the most public concern and occur across most ethnic, religious, and socio-economic groups. The subsequent short- and long-term health consequences are severe, ranging from post-traumatic stress disorder (PTSD) to depression and anxiety disorders, as well as including an increase in suicidal behavior (Hornor, 2010; Joiner et al., 2007). Comprehensive meta-analyses estimated the general prevalence of child sexual abuse (CSA) to be more than 10% (Pereda et al., 2009;

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Stoltenborgh et al., 2011). About 3% of boys and 9% of girls are victims of severe sexual abuse and forced intercourse (Finkelhor et al., 2014; Häuser et al., 2011). Despite these high prevalence rates and the urgent need to prevent these crimes, little is known about neurobiological underpinnings of CSO and the mechanisms leading to CSO (Kärgel et al., 2015). Even if pedophilia is known as the major risk factor for committing CSO, pedophilia is neither sufficient nor necessary for CSO (Seto, 2008; Seto et al., 2006). Investigations among convicted child sexual abusers show that about 50% of all offenses are committed by non-pedophilic CSO (Maletzky and Steinhauser, 2002). Reliable authoritative numbers are a pressing need, currently there are only speculations about the proportion of non-preference specific CSO, as most CSO are not reported (Hanson et al., 1999). According to Blanchard et al. (2006), most sexual offenses against children are committed by non-pedophilic perpetrators. These offenses tend to be more violent and intrusive in comparison to those of pedophilic perpetrators (Kingston et al., 2007). Studies focusing on the underlying mechanisms of CSO in perpetrators without a sexual preference for children are scarce. Sexual violence may occur as a result of complex interrelated factors (Thakker and Ward, 2012). Violence in general (Davidson et al., 2000), and sexual violence in particular (Howells et al., 2004; Ward and Beech, 2006), often arise as a consequence of impaired regulation of emotions (Gillespie et al., 2012; Langton and Marshall, 2000; Ward and Hudson, 2000). Furthermore, there is a broad body of literature arguing that an impaired ability to regulate negative affective states contributes as a causal factor to the process of sexual offending (Hanson and Harris, 2000).

On a neural level, studies on brain functioning identified the interplay of limbic structures, in particular the amygdala and the prefrontal cortex (PFC) to be crucial in the regulation of emotional (Davidson et al., 2000; Dörfel et al., 2014; Gillespie et al., 2012; Lee et al., 2012; Paschke et al., 2016) and sexual behavior (Beauregard et al., 2001; Georgiadis and Kringelbach, 2012; Klucken et al., 2016; Stoléru et al., 2012). It is assumed that the PFC ensures that amygdala-driven emotional and sexual responses are elicited in a socially appropriate manner (Kärgel et al., 2015; Rosenbloom et al., 2012) but the definite role of the different prefrontal substructures are not completely understood. The role of the amygdala as an integrative center for emotional and sexual behavior has been supported through studies linking its activity to aberrant emotional (Etkin and Wager, 2007; Kamphausen et al., 2013) and sexual processing (Baird et al., 2004; Mohnke et al., 2014; Schiltz et al., 2007; Walter et al., 2008), as well as sexual offending (Kärgel et al., 2015; Poeppl et al., 2014). The amygdala is not a homogenous structure, but a complex entity comprised of three major subdivisions: a basolateral, a superficial, and a centromedial complex, consisting of the central and the medial nucleus (CMA; Amunts et al., 2005; Roy et al., 2009). The CMA plays a decisive role in directing behavioral responses (Ko et al., 2015) through projections to the brainstem and cortical and striatal regions (Davis, 1997; Roy et al., 2009), including organizing sexual behavior (Gillespie et al., 2012). Several researchers argue a significant role of the medial nucleus in the control of reproductive behavior (Dominguez et al., 2001; Kondo, 1992; Newman, 1999). Emerging evidence is supporting a prominent role for the CMA in reward-directed behavior (Parker et al., 2014; Robinson et al., 2014) as sexual activity. Furthermore, the CMA is anatomically connected to the hypothalamus, which is also critically involved in directing not only sexual (Poeppl et al., 2015), but also aggressive behavior (Falkner and Lin, 2014). Moreover, Beauregard et al. (2001) suggested that the amygdala is crucial in the modulation of endocrine and autonomic responses through projections from the CMA to the hypothalamus. Recent models argue that altered CMA functioning is involved in emotion regulation deficits in individuals with higher levels of psychopathic traits (Moul et al., 2012). In particular, a diminished functional and structural connectivity between the amygdala and the PFC has been suggested as a neurobiological feature of psychopathy (Motzkin et al., 2011). Based on anatomical landmarks (Öngür et al., 2003) and functional specificity (Bechara, 2004), the relevant prefrontal areas involved in emotion regulation can broadly be divided into the orbitofrontal (OFC), the dorsolateral (dlPFC), the ventrolateral and a medial PFC. While anatomical tracing studies have demonstrated strong reciprocal connections between the amygdala and the OFC, ventrolateral PFC and dorsomedial PFC (Ghashghaei et al., 2007), the dlPFC probably exerts its main influence over limbic structures indirectly through the OFC (Gillespie et al., 2012; Phillips et al., 2008). These regions are assumed to play an important role for the control of sexual motivation, arousal and behavior (Beauregard et al., 2001; Leon-Carrion et al., 2006; Toates, 2009) as well as impulsive violence (Davidson et al., 2000). The orbitofrontal cortex (OFC) occupies the ventral surface of the frontal part of the brain as the most inferior part of the brain (Fuster, 1997). The OFC plays a central role in emotion regulation. Lesions in the OFC and adjacent PFC regions produce syndromes characterized by impulsivity and aggression (for more details see Rolls, 2004). (Gillespie et al., 2012) emphasized the importance of the OFC in understanding the association of emotion regulation and cognition because of its strong connection to the amygdala. The OFC and interconnected structures, particularly the amygdala, are crucial for the successful regulation of emotional states. An inhibitory connection from regions of the prefrontal cortex, probably the OFC, to the amygdala is assumed for being the underlying mechanism to suppress negative emotions, and also plays a key role in impulsive violence (Davidson et al., 2000) and compulsive sexual behavior (Schmidt et al., 2017). Stoléru et al. (2012), postulated the OFC as being highly relevant for the suppression of sexual arousal and hypothesized amygdala, OFC and medial PFC, among others, as the neural substrate of sexual arousal. In Georgiadis and Kringelbach (2012), the amygdala and the orbital and ventromedial cortices are associated with sexual desire and sexual excitation. Alterations of the functional connectivity between OFC and amygdala were also found in CSO (Kärgel et al., 2015). The role of the dlPFC in the control of behavior remains a topic of ongoing controversy (Mars and Grol, 2007) The dlPFC is situated in the frontal lobe and associated with cognitive executive function (Baena et al., 2010) and comprises primary Brodmann's areas 9 and 46 but also 8-9, 9–45, 46–10, and 46–45 (Rajkowska and Goldman-Rakic, 1995 for an overview; Miller and Cohen, 2001). It was often associated with the mere maintenance of information by guiding attention to internal representation of sensory stimuli and motor plans (Curtis and D'Esposito, 2003) and is thought to contribute to emotion regulation through the process of reappraisal (Golkar et al., 2012), and goal directed behavior (Ballard et al., 2011). But also linked to sexual arousal (Beauregard et al., 2001; Leon-Carrion et al., 2006), hypersexuality (Schmidt et al., 2017) and impulsivity (Ko et al., 2015; Yang and Raine, 2009) in the way to exert executive control on motivational and emotional behaviors (Delgado et al., 2008) Lee et al. (2012) found that the functional connectivity (fc) between the dlPFC and amygdala, to be relevant for the regulation of negative emotion, which in turn may represent a causal factor for sexual offending (Ward, 2014). In line with these findings, distorted connectivity between dlPFC and amygdala was linked to a heightened risk for violent behavior (Davidson et al., 2000), impulsivity (Ko et al., 2015), hypersexual behavior (Schmidt et al., 2017), sexual offense recidivism (Poeppl et al., 2013), severe deficits in emotion regulation, and impulsive aggression (New et al., 2007). Thus the amygdala is a key structure in eliciting emotions whilst the task of the PFC is to control the output of the amygdala. Problems of emotional regulation are seen as a risk factor in CSO.

Most studies related to child sexual offending are conducted on pedophilic offenders and many studies did not account for the effects of offense and sexual preference. A growing body of literature suggests that CSO, rather than pedophilia, is related to deficits in executive functioning and emotion regulation (Kärgel et al., 2016, 2015; Poeppl et al., 2013). Therefore, this study aimed to investigate resting state functional connectivity in clinically carefully assessed non-pedophilic child sexual offenders in the amygdala network, highly relevant for

Table 1
Characteristics of study groups.

Matching parameter	CSO-P (N = 20)		HC (N = 20)		CSO-P vs. HC	
Sexual orientation (hetero-/homo/bisexual)	16/2/2		16/2/2			
Handedness (r/l/amb)	18/1/1		18/1/1			
	Mean	**SD**	**Mean**	**SD**	**t-value**	**p-value**
Age	38.25	8.54	45.20	11.16	1.128	.266
WAIS IQ estimates	90.5	13.51	102.77	23.89	1.833	.075

Caption: Handedness was assessed using an adapted 10-item version of the German Edinburgh Handedness Inventory. Total intelligence score was extrapolated from the four subtests of the short version of the German WAIS using the following formula: [point scale points (*vocabulary*) + point scale points (*similarities*)]*3.0 + [point scale points (*block design*) + point scale points (*matrix reasoning*)]*2.5. Differences between groups were assessed using a two-sample *t*-test. Abbr.: CSO-P = non-paedophiles with a history of child sex offending. HC = healthy controls. r = right, l = left, amb = ambidextrous. SD = standard deviation. N = number of subjects in group.

regulation of emotion, behavior, and sexual arousal. Especially we expect differences in functional connectivity between amygdala and regions in the prefrontal cortex related to emotion regulation. This research is aimed to contribute towards a better understanding of the relationship between aberrant functional connectivity and deviant sexual behavior, as well as informing preventive and therapeutic approaches to CSO.

2. Methods

2.1. Participants

Participants were assessed within the framework of a German multisite research project called "Neural Mechanisms Underlying Pedophilia and Sexual Offending Against Children" (NeMUP; www.nemup.de). From the total NeMUP sample of more than 400 participants, data from non-pedophilic subjects having conducted child sexual abuse assessed at Hannover Medical School and Essen University Hospital (CSO-P, N = 20) and normal healthy controls (HC, N = 20) matched with respect to age, IQ, handedness, and sexual orientation were included (Table 1). Analyses were restricted to samples from these sites, as both acquired data on a 3T Skyra MRT, and the majority of CSO-P subjects were recruited there. To account for potential confounders, groups were also comparable regarding sexual functioning, sexual characteristics and sexual development **(Supplementary S1, S2 & S3)**. Subjects with a history of CSO were recruited from correctional institutions. A history of CSO was defined as the individual involvement in at least one case of CSO against minors under the age of 14, which includes actions of penetrating the child anally/vaginally with the aim of sexually stimulating themselves. Exclusion criteria were neurological or acute psychiatric disorders assessed within semi-structured interviews (SKID; Wittchen et al., 1997), acute episodes of alcohol or drug abuse/dependence, and current medication related to sexual functioning or the diagnosis of pedophilia. None of the participants took psychotropic medication for a period of at least 3 weeks before assessment. Healthy controls were recruited from the community through advertisements in public institutions. The study was approved by the ethics committee of each research site separately. All participants gave written informed consent to the study protocol before being included and received a monetary recompense for their participation.

2.2. Clinical assessment and psychological questionnaires

In this investigation, we focused on the association of offense-related characteristics with psychopathology and other cognitive processes known to influence sexually deviant behavior. Therefore, for the analyses, we included the following questionnaires and semi-structured clinical interviews: DSM-IV-TR Axis I (SCID I) and Axis II (SCID II; Fydrich et al., 1997; Wittchen et al., 1997; see Table 2); Hamilton

Table 2
Psychiatric axis-I and axis-II Disorders on the basis of SKID I & II interview.

	CSO-P(N = 20)	HC (N = 19)	CSO-P vs HC		
Psychiatric Diagnosis	N (%)	N (%)	p-value	OR	RR
Axis-1-Disorder	17 (85%)	2 (11%)	< 0.0001	48.17	5.97
Affective Disorder	9 (45%)	2 (11%)	.031	6.96	2.08
Anxiety Disorder	7 (35%)	0 (0%)	.008	–	2.46
Addictive Disorder	10 (50%)	0 (0%)	< 0.0001	–	2.90
Axis-2-Disorder	9 (45%)	0 (0%)	.001	–	2.73
Cluster A	2 (10%)	0 (0%)	.487	–	2.06
Cluster B	8 (40%)	0 (0%)	.003	–	2.58
Cluster C	4 (20%)	0 (0%)	.106	–	2.19

Note. CSO-P = non-paedophiles with a history of child sex offending; HC = healthy controls; N = number of subjects in group; OR = odds ratio/RR = relative risk; Differences between groups were assessed using Fishers-Exact-Test.

Depression Rating Scale (HAM-D; Hamilton, 1996b); Hamilton Anxiety Rating Scale (HAM-A; Hamilton, 1996a); Childhood trauma questionnaire (CTQ; Bernstein and Fink, 1998); Barrat impulsiveness scale (BIS; Patton et al., 1995); and The Wender Utah Rating Scale for Attention Deficit Hyperactivity Disorder (ADHD) for adults (Homburger ADHD scales (HASE); Rösler et al., 2008; see Table 3). Correlational analysis of rs-FC and psychological variables were conducted. All assessments were carried out through experienced research associates, trained to use these instruments. In a second session, MRI assessment was performed including structural and functional measurements. CTQ, BIS and ADHD data were not available for two of the twenty control subjects. ADHD data were also not available for one of the CSO subjects. Offense and victim characteristics are shown in detail in Supplementary **S1**.

2.3. Neuroimaging

All images were acquired on two separate 3T Siemens Skyra MRI scanners, one in Hannover and one in Essen, equipped with 32 channel head coils. To preclude signal fluctuations across both sites, standardized MRI Phantom stability measures were conducted (Hellerbach et al., 2013). After a structural T1 image was acquired, participants performed a resting state fMRI scan with a duration of 11 min. Participants were instructed to lie still, keep their eyes closed, and let their mind wander. Structural T1 images were acquired by means of a MPRAGE sequence (slices = 192, FoV = 256 mm, voxel size = 1 × 1 × 1 mm, TR = 2.5 s, TE = 4.37 ms, flip angle = 7°, distance factor = 50%). Functional T2* weighted images were obtained using an echo planar imaging (EPI) sequence (slices = 38, field of view = 240 mm, voxel size = 2.3 × 2.3 × 3 mm, number of volumes = 275, time of repetition = 2.4 s, echo time = 30 ms, flip angle = 80°, distance factor = 10%).

Table 3
Clinical characteristics of the sample.

	CSO-P			HC			CSO-P vs HC	
	N	Mean	SD	N	Mean	SD	t-value	p-value
Hamilton Anxiety Rating Scale	20	4.45	6.013	20	1.00	2.471	2.373	.023
Hamilton Depression Rating Scale	20	5.55	6.832	20	.65	1.089	3.167	.003
Child Trauma Questionnaire								
Emotional Abuse	20	14.00	5.786	18	6.22	1.114	5.892	< .0001
Physical Abuse	20	10.80	4.618	18	5.22	.428	5.376	< .0001
Sexual violence	20	9.95	5.511	18	5.44	1.149	4.946	.002
Emotional Neglect	20	13.90	4.482	18	8.17	2.121	5.118	< .0001
Physical Neglect	20	8.45	3.170	18	6.61	1.975	2.117	.041
Barratt Impulsiveness Scale								
Attentional Impulsiveness	20	16.94	3.101	18	15.56	3.294	1.33	.192
Motor Impulsiveness	20	23.66	4.813	18	20.94	3.351	2.00	.053
Non-Planning Impulsiveness	20	26.35	4.966	18	24.56	3.468	1.27	.210
Homburger ADHD-Scales (HASE)								
Unattention	18	6.50	3.417	18	3.94	5.252	1.730	.093
Impulsivity	18	3.06	2.645	18	1.28	1.809	2.354	.025
Hyperactivity	18	3.61	3.109	18	2.00	2.301	1.767	.086
Wender-Utah-Rating-Scale (WURS-K)								
Impulsivity	18	5.68	3.250	19	8.44	3.417	−2.519	.017
Sum	18	32.94	17.184	19	12.00	15.249	3.913	< .0001

Note. CSO-P = child sexual offender without a pedophilic preference; HC = healthy control; N = number of subjects in group; SD = standard deviation. Differences between groups were assessed using two-sample *t*-test.

2.4. Data processing

Data were analyzed using SPM 8 (Welcome Trust Center for Neuroimaging, London, England) and DPABI 2.3 (Song et al., 2011; Yan et al., 2016). The preprocessing steps followed the standard protocol described by the above-mentioned authors. The first five images were removed to account for instability of the initial signal and the adaptation of the subjects to the scanner. Images were slice time corrected and realigned to a mean image to correct for motion. No subject showed head movement greater than 3 mm in translation or greater than 3° in rotation. Images were spatially normalized to the Neurological Institute (MNI) stereotaxic space (Collins et al., 1998) using unified segmentation on T1 image (Ashburner and Friston, 2005) and resampled to $3 \times 3 \times 3\,mm^3$. Potential sources of undesired signals were regressed out (Weissenbacher et al., 2009), such as nuisance covariates, including voxel-specific 12 motion parameters (Satterthwaite et al., 2013; Yan et al., 2013); white matter signal; and cerebrospinal fluid signal. In addition, global signal was regressed out, as this processing step has been shown to contribute to the improvement of the specificity of functional connectivity (Fox et al., 2009) and can improve the correction of motion artifacts (Yan et al., 2013). The resulting images were then temporally band-pass filtered (0.01–0.08 Hz).

Considering that functional connectivity measures are extremely sensitive to even slight head motions, we conducted a motion scrubbing procedure by removing scans with a frame-wise displacement (FWD) threshold of > 0.4 mm, as described by Jenkinson et al. (2002). After scrubbing, all subjects retained > 50% time points. No significant differences ($p > .05$) in FWD of the remaining time points were found between CSO and HC in both datasets. Before statistical analysis, images were smoothed with a Gaussian kernel of $6 \times 6 \times 6\,mm^3$ (full width at half maximum).

2.5. Statistical analysis

Data analysis and ROI selection: In order to assess between-group differences in amygdala network functional connectivity, the left and right amygdala were selected as ROIs for a seed-based analysis. In particular, the centromedial part (CMA) of the left and right amygdala were a priori defined as seeds (Fig. 1) and extracted from the Anatomy toolbox (Eickhoff et al., 2007; 2006, 2005; Qin et al., 2014), due to their critical role in emotion regulation deficits (Moul et al., 2012), directing behavioral responses (Davis, 1997; Roy et al., 2009), and organizing sexual behavior (Gillespie et al., 2012). In order to access functional connectivity, Pearson's correlation coefficients were computed between the time series of the amygdala seeds and the time series of all other voxels in the brain. To account for statistical normality, correlation coefficients were then normalized by the Fisher's *Z*-transformation. These transformed values were used for a 1st level model in SPM 8. On a 2nd level analysis, age, site, and IQ were included as covariates into the model estimation. A random effect two-sample *t*-tests between groups was performed on the individual *Z*-values in a voxel-wise manner to determine the brain regions showing significant FC group differences between the amygdala and other voxels within the amygdala network. To avoid circular analysis (Kriegeskorte et al., 2009) also called “double dipping” the amygdala network was extracted from an independent sample of 30 healthy controls not used in this analysis but measured with exactly the same MRI protocols. We defined the amygdala network during rest as voxels showing significant correlations with the amygdala, $p < 0.05$ (uncorrected), in the whole sample. For every subject, the amygdala network was used as a mask for region-of-interest (ROI) analysis ($p < 0.05$, small volume corrected for multiple comparisons within the entire amygdala network, see Fig. 1) between groups (Poldrack, 2007; Worsley et al., 1996).

Results were considered significant using $p < 0.05$ family wise error (FWE), corrected for multiple comparisons on a cluster level.

2.6. Behavioral analysis

Post-hoc correlation analyses were performed in SPSS v 24 (IBM Inc.) using single subject contrast estimates (CEs) of the individual FC values (mean Z-scores). These values were extracted from the location, indicating significant between-group differences in FC (peak voxel from the MNI coordinates at −24, 18, −51 (dlPFC; seed ROI: right CMA)) using the SPM8 plot function. The CEs were correlated with psychometric and clinical measurements (ADHD, HAM-A, CTQ, and BIS). A Pearson correlation of $p < 0.05$ was considered significant.

3. Results

3.1. Demographics and clinical parameters

The child sexual offender group (CSO-P) had significantly higher

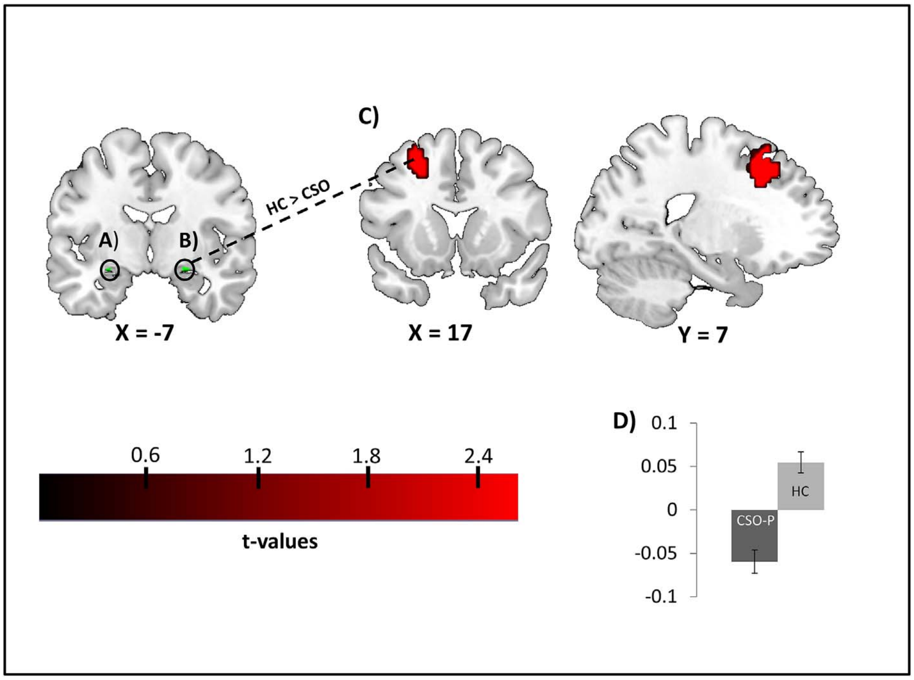

Fig. 1. Between-group differences in resting state functional connectivity (rs-FC) of the left (A) and right (B) CMA ($p < 0.05$, FWE correction at the cluster level): No significant differences in rs-FC between the groups were detected using the left amygdala as a seed region (A). CSO-P showed significantly lower functional connectivity between the right CMA and the dlPFC (C). rs-fc differences are overlaid on the MNI standard space template. Bar graphs depict mean Z scores in each group for dlPFC (D). *Abbr.:* MNI Montreal Neurological Institute FWE family wise error right CMA = right centromedial amygdala. CSO-P = non-paedophiles with a history of child sex offending. HC = healthy controls. rs-FC: resting state functional connectivity.

scores on all five childhood trauma questionnaire (CTQ) subscales (Table 3). There was an elevated rate of anxiety ($p < 0.05$) and depression-related symptoms ($p < 0.01$) according to HAM-A and HAM-D, as well as higher rates of personality disorders (Mann-Whitney-U. = .015), and past psychiatric axis-one disorders (p = < .001) (Table 2). There was no significant difference of current ADHD symptoms between CSO-P and healthy controls (HC). However, group comparison revealed a significant difference in WURS-K scores, implicating ADHD symptoms in childhood in child sexual offenders (11 individuals with a cut-off-score higher than 30 indicating ADHD in childhood; 2 among healthy controls and 9 among CSO-P). There were no differences in impulsivity according to the Barratt-impulsiveness scale (BIS).

3.2. Functional connectivity

Group comparisons revealed significantly diminished resting state functional connectivity (rs-FC) within the amygdala network in CSO-P between the right centromedial amygdala (CMA) and the left dorsolateral prefrontal cortex (dlPFC) (Table 4 & Fig. 1). The major part of the cluster was localized in the middle PFC while 24 voxels extended into the superior PFC based on automated anatomical labeling (AAL; Tzourio-Mazoyer et al., 2002). No significant differences of fc between the left CMA and other brain structures were found in CSO-P compared to HC. There were no significant associations between rs-FC and psychometric measures including the CTQ, HAM-A, HAM-D, ADHS, or BIS.

Table 4
Significant differences in RS-FC between non-pedophilic child sexual offenders and healthy controls.

Seed: right CMA		HC > CSO-P					
Structure	Laterality	MNI			t-value	Cluster size	p-value
		x	y	z			
dlPFC	l	-12	27	60	5.18	126	0.001

Note. CMA = centro medial amygdala; MNI = Montreal Neurological Institute; dlPFC = dorsolateral prefrontal cortex; L = left. r = right. Differences between groups were assessed using two-sample t-tests. Results were corrected for multiple comparisons using family-wise error rates and were restricted to the amygdala network.

Additionally, the influence of axis-I disorders as a categorical variable (affective yes/no, anxiety yes/no, addictive yes/no) was tested in correlating the extracted parameter estimates of the dlPFC cluster in the whole sample and in the different groups separately using a non-parametric test. No significant correlations were found.

4. Discussion

To our knowledge, this is the first study to investigate alterations in brain functional connectivity at rest in an exclusive sample of non-pedophilic child sexual offenders compared to carefully matched healthy controls. The results revealed evidence for diminished functional connectivity between the right CMA and the left dlPFC, in child sex offenders as compared to non-offending healthy controls. The results were not attributable to age, IQ, handedness, or sexual orientation and did not relate to depression, anxiety, aversive childhood experiences, impulsivity, symptoms of ADHD parameters, or sexual development factors, such as the onset of masturbation, ejaculation, coitus, or the number of TSO or sexual partners. The reported diminished fronto-limbic connectivity is supported by a broad literature showing that aberrant functioning of prefrontal and subcortical structures contributes to different forms of deviant behavior (e.g. Birbaumer et al., 2005; Contreras-Rodríguez et al., 2015; Joyal et al., 2007; Kiehl et al., 2001; Raine et al., 1997; Yang and Raine, 2009). Even if there is doubt that general alterations in limbic and/or prefrontal structures might be specific for sexual offending (e.g. (Joyal et al., 2007), there is empirical data indicating a specific involvement of the dorsolateral part of the prefrontal cortex and the amygdala in regulating emotion (Lee et al., 2012) and sexual behavior (Schmidt et al., 2017). These areas are assumed to participate in child sexual offending (Kärgel et al., 2015; Mohnke et al., 2014; Poeppl et al., 2013) and deviant sexual behavior probably because of strong interconnections to the OFC (Gillespie et al., 2012) but further research is needed. Diminished functional connectivity between limbic structures and prefrontal cortex, including the amygdala and the orbitofrontal cortex extending into dorsolateral parts, was previously shown in a sample of offending pedophiles in comparison to non-offending pedophiles and healthy controls (Kärgel et al., 2015). Our findings support the previous study's assumption that this effect could be driven by child sexual offending rather than by the presence of a mere pedophilic preference. In contrast to Kärgel and colleagues (Kärgel et al., 2015), Poeppl and colleagues argued that structural alterations of the left dlPFC and the right amygdala are pedophilia-specific, and affect neural networks that are important for sexual processing by disturbing the emotional evaluation and subsequent miscategorization of children as sexually interesting (Poeppl et al., 2015). However, when considering studies that carefully control for and distinguish the effects of CSO and pedophilic preference, one might suggest that aberrant coupling between the dlPFC and the amygdala as a functional entity is specific for offending behavior, rather than for sexual preference (Kärgel et al., 2015). In this case, the sexual preference would simply be relevant when selecting potential victims.

Current and previous findings emphasize the importance of the interplay between prefrontal and limbic structures—i.e., functional connectivity—for cognitive, motivational, and emotional functioning during the processing of sexual and/or emotional incentives in child sexual offenders (Cunningham and Brosch, 2012; Janak and Tye, 2015; Kärgel et al., 2015; Poeppl et al., 2013). Appropriate sexual behavior depends on the processing of relevant emotional information together with adequate moral judgment (Massau et al., 2017), and needs to be regulated through inhibitory processes guided by prefrontal structures. Only recently, Kärgel et al. (2016) even demonstrated superior inhibitory control in pedophiles without CSO when compared to pedophiles with CSO and healthy controls, as reflected by significantly lower rates of commission errors and increased recruitment of the left posterior cingulate and left superior frontal cortex in a GoNogo paradigm. Thus, recent findings, together with the current study, may further corroborate the theory of disturbed fronto-limbic functioning (Cohen et al., 2002; Kärgel et al., 2015; Poeppl and Nitschke, 2013; Walter et al., 2007; Ward, 2014) as a possible causal factor for child sexual offending independent of the occurrence of a pedophilic preference. While the OFC, lateral PFC and the dorsomedial PFC are strongly interconnected with the amygdala – the way how the dlPFC exerts his influence on regulation of emotional and sexual behavior is not well understood (Mohnke et al., 2014; Phillips et al., 2008). Regarding insights on the structural and functional connectivity of the Amygdala, it is surprising, that we did not find altered functional connectivity to the OFC and ventromedial PFC. While recent studies revealed also direct anatomical connections between the amygdala and the dlPFC (Bracht et al., 2009) others argue that the reciprocal connection to the OFC are most relevant for the inhibitory control over limbic structures (Delgado et al., 2008; Phillips et al., 2008; Rolls, 2004) The behavioral relevance of this finding is rather speculative. While the found PFC cluster comprises not only the middle PFC but also the superior PFC cortex which is known to be an important structure for inhibitory behavioral control (Kärgel et al., 2016) the FC was not significantly correlated to impulsivity measurements extracted from BIS, ADHS-SB and WURS-K. As we did not observe a correlation with impulsivity, one can speculate that the diminished functional connectivity is related to higher order executive functioning (planning, working memory, set shifting), which is closely related with dorsolateral prefrontal cortex integrity. Some methodological issues should be discussed at this point. When it comes to investigations of correctional samples in general, and of sensitive topics such as sexual behavior in particular, social demand effects have to be taken into consideration. Resting state functional connectivity is a parameter which is relatively easy to assess and not deliberately manipulable and could, therefore, provide a promising approach for future diagnosis and risk-assessment in CSO. The vast majority of studies investigating brain alterations in child sexual offenders were carried out using samples of incarcerated child sexual offenders, making it difficult to disentangle paraphilia and offense-specific effects (Mohnke et al., 2014). Therefore, we focused on non-pedophilic child sexual offenders to validate the occurrence of offense specific effects, as hypothesized in earlier research (e.g. Kärgel et al., 2015). Further research should take this issue into account and carefully control their effects for sexual preference and behavior. Despite immense difficulties during recruitment and clinical assessment of imprisoned subjects, we finally succeeded in comparing a highly burdened and socially relevant criminal population, who, besides imprisonment, received high levels of attention, such as psychiatric and/or psychotherapeutic treatment. To control for potential confounders as best as possible, we limited our investigation to a group of child sexual offenders without pedophilia and without current severe co-morbid mental illness or psychopharmacological medication. However, the CSO-P sample still had elevated levels of lifetime psychiatric comorbidity (e.g. personality disorders), which could also be one part in the complex etiology of offending behavior. It could be argued that our findings are not specific for child sexual offending in particular, but for sexual offending or antisocial behavior in general. Finally, the mere fact of living in a correctional institution could have had an influence on functional connectivity and mental wellbeing (Kim, 2015). To account for incarceration as a potential confounder, it would be useful to compare child sexual offenders from the dark field to incarcerated child sexual offenders. To ascertain the found effects to be offense or pedophilia specific, the ideal design would be a 2×2 factorial design (CSO + P, P-CSO) to account for each phenomenon separately. Further research should take this into consideration. Finally, we would like to emphasize the implications of our findings for future research, as well as for improvement of therapeutic approaches and prevention of CSO. There is no doubt that effective treatment strategies for sexual offending are urgently needed. A Cochrane review on the drug (Khan et al., 2015) and psychological treatment in sexual offenders (Dennis et al., 2012) concluded that there is no evidence that actual treatment strategies are capable of reducing the long-term risk of reoffending, hence, new treatment approaches and their proper evaluation are necessary. Our findings provide insights into the pervasive relationship in regard to the relevance of resting state functional connectivity, prefrontal regulation of limbic structures, and child sexual offending. An effective approach to treating sexual offenders should address these diminished fronto-limbic FC, either through specific therapeutic approaches known to enhance these structures, such as mindfulness-based cognitive therapy (MBCT; Frewen et al., 2010) and transference-focused psychotherapy (Perez et al., 2016), or by means of specific techniques to stimulate these areas through transcranial stimulation techniques (tDCS; Gbadeyan et al., 2016; Padberg et al., 2017) or indirect real-time fMRI (Paret et al., 2016).

5. Conclusion

In summary, our findings suggest that diminished functional connectivity between the right CMA and the left dlPFC, might be a part of the neurobiological mechanisms underlying child sexual offending. Deficits in functional connectivity of these structures might lead to impaired behavioral control. Thus, therapeutic interventions should be examined regarding whether they are able to strengthen functional connectivity between these structures. Surprisingly we did not find altered functional connectivity to OFC and ventrolateral or ventromedial PFC. Further research is necessary to shed light on the interplay between emotional and behavioral control, and may contribute to a better understanding of the occurrence of deviant sexual behavior in general, and sexual offending in particular, as well as more differentiated and effective interventions.

Declaration of interest

The authors declare no competing 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.jpsychires.2018.01.012.

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