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FULL-LENGTH REPORT

Alterations in voxel based morphometry and resting state functional connectivity in men with compulsive sexual behavior disorder in the Sex@Brain study

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ABSTRACT

Aim: Compulsive Sexual Behavior Disorder (CSBD) is a new category in ICD-11. Research examining underlying brain mechanisms is sparse. Research into neurobiological differences can be helpful in advancing the possibilities of new diagnostic approaches and therapeutic methods. The present study aimed to examine brain matter volume and resting state functional connectivity (rs-FC) in CSBD. *Methods:* Structural and rs-FC magnetic resonance imaging and data from questionnaires were collected in 30 men with CSBD and 32 age- and education-matched controls. Whole brain voxel based morphometry (VBM) and seed based rs-FC in a-priori defined seeds were analyzed. *Results:* Structural analyses showed that men with CSBD had significantly increased gray matter volume in the right cerebellum, middle occipital and superior frontal lobe. No differences in rs-FC could be detected when using these brain structures as seed regions in rs-FC. In contrast, literature based rs-FC analysis revealed decreased rs-FC between the right orbital middle frontal cortex (mOFC) and the right gyrus rectus, as well as between left pallidum and right post/precentral gyrus in men with CSBD. In the left amygdala we observed increased rs-FC with precuneus in this group. In addition, most of these measures correlated with symptom severity. *Conclusion:* Structural findings may underscore the idea that the cerebellum plays an important role in sexual arousal and CSBD. Perhaps, a simultaneous activation of the left amygdala and the precuneus reflects a constant sexual occupation of men with CSBD. Furthermore, lower connectivity between mOFC and gyrus rectus in CSBD may support the assumption that sexual stimuli are evaluated more positively because inhibition is decreased.

KEYWORDS

compulsive sexual behavior disorder, brain imaging, voxel-based morphometry, resting-state functional connectivity, hypersexual disorder, sexual addiction

INTRODUCTION

In 2019, the World Health Organization included compulsive sexual behavior disorder (CSBD) in the ICD-11 (WHO, 2019). CSBD is defined as persistent patterns of uncontrollable sexual urges and behaviors, resulting in clinically significant distress and functional impairment (Reed et al., 2022) with excessive masturbation in combination with the online use of sexual content as its most common manifestation (Kafka, 2010). CSBD refers to the same clinical condition as the term of Hypersexual Disorder (HD) which Kafka proposed as an atheoretical umbrella term (Kafka, 2010) to include the concepts of sexual compulsivity,

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sexual impulsivity or sexual addiction. Recent evidence supports the notion that CSBD shares some similarities, in terms of conceptualization, therapeutic intervention and neuronal mechanisms, with behavioral addictions (Brand et al., 2019). Determining whether CSBD shares neurobiological similarities with any of these disorders will help in understanding the underlying mechanisms and by that developing better tailored treatment approaches.

Most evidence that links CSBD to brain differences is derived from MRI studies that were either studies of brain structure (e.g. gray matter volumes), task-related (fMRI) or resting-state functional connectivity, measured when the brain was at rest without a specific task (for an overview see Stark, Klucken, Potenza, Brand, & Strahler, 2018). The earliest study investigating structural differences in CSBD (Schmidt et al., 2017) compared 23 men with CSBD to 69 men without the condition and demonstrated a left amygdala GM volume increase in participants with CSBD using VBM, an area that plays a role in motivational salience. In addition, men with CSBD displayed reduced rs-FC between left amygdala and bilateral dlPFC, suggesting an alteration of prefrontal-mediated regulation on emotional and motivational networks. The authors conclude, that a reduced rs-FC could explain dysfunctional behavioral patterns resulting in an increased reactivity towards relevant erotic cues (Schmidt et al., 2017).

Contrasting this finding, Seok and Sohn (2018) also used VBM and rs-FC analysis and demonstrated a significant GM volume reduction in the left superior and the right middle temporal gyrus in seventeen men with CSBD, compared to nineteen men without. The authors stated that temporal areas may be part of a functional circuit associated with CSBD, as these are known to play an inhibitory control in sexual arousal and that a local reduction in GM results in increased sexuality (Seok & Sohn, 2018). Further, the rs-FC between the left superior temporal gyrus (STG) with both the left precuneus and the right caudate was found to be lower in CSBD. They reasoned that a reduced rs-FC between temporal areas and the precuneus and nucleus caudatus could reflect a reduced inhibition of sexual arousal in CSBD (Seok & Sohn, 2018).

Further contributing to the mixed findings in the literature, Draps et al. (2020) compared GM differences using VBM in CSBD (n = 26), Gambling Disorder (n = 26), Alcohold Use Disorder (n = 21), and healthy controls (n = 25). Their findings point to a reduction of GM in the orbitofrontal cortex. However, only differences in Gambling Disorder were significant after FWE correction. In a second study, Draps, Adamus, Wierzba, and Gola (2022) compared rs-FC from 52 men with CSBD and 29 men without the condition. They showed decreased FC in CSBD between left middle temporal gyrus and bilateral insula and right parietal operculum. Moreover, rs-FC was increased in many areas in men with CSBD, namely left inferior frontal gyrus and right planum polare and temporale, left and right insula, right supplementary motor area (SMA), right parietal operculum, as well as between right planum polare and left supramarginal gyrus, and between left OFC and left insula (Draps et al., 2022). They conclude that their results are in favor of the incentive sensitization process, meaning a changed motivation for rewards that are driven by both physiological state and previously learned associations about sexual cues. In the incentive sensitization theory the essence of dependencies are conceptualized as excessive amplification specifically of psychological 'wanting', which are triggered by cues, without the obligatory amplification of 'liking' (Berridge, 2012).

The fourth study investigating structural brain differences in CSBDconducted by Görts et al. (2023) compared 22 men with CSBD to 20 healthy controls. Results indicated that the men with CSBD showed a lower cortical surface area in right posterior cingulate cortex (PCC) which was negatively correlated to symptoms of CSBD (Görts et al., 2023). Due to the PCC's involvement in the reward system they concluded that reward-related processes are impacted in CSBD.

In summary, it is still unclear which structural changes may be present in CSBD, as the findings on this differ between studies. Structural abnormalities have been found in limbic regions (Schmidt et al., 2017), but also in the temporal lobe and cerebellum (Seok & Sohn, 2018), as well as in in subcortical areas (Görts et al., 2023). Similar divergent findings are evident in the findings on rs-FC. For example, findings of reduced rs-FC between the dlPFC and amygdala (Schmidt et al., 2017) were not replicated; rather, connectivity differences between temporal regions with the precuneus and caudate nucleus emerged (Seok & Sohn, 2018). In another study many connectivity differences were shown, but not the previously known ones just named (Draps et al., 2022). From this, it can be concluded that further studies are needed to get an overview of which areas differ structurally and in rs-FC in CSBD and to collect more data to make comparisons with the studies already done.

Perhaps, further evidence for areas altered in CSBD can be inferred from studies that have measured task-related brain activity. Gola et al. (2017) and Golec, Draps, Stark, Pluta, and Gola (2021) conducted studies on cue reactivity using an incentive delay task with erotic and monetary cues in men with CSBD and healthy controls. The main findings were that men with CSBD showed greater neural responses to the erotic cues in the reward anticipation phase in the ventral striatum and in the anterior orbitofrontal cortex, which was modulated by reward probability (Gola et al., 2017; Golec et al., 2021). Gola et al. (2017) concluded that their results show higher "wanting" for erotic cues in men with CSBD, Golec et al. (2021) added that the type of reward (e.g. erotic cues in CSBD) seems to be more important than the expected probability of reward.

In addition, Liberg et al. (2022) used an incentive delay task with erotic and control images of bodies. The activity of the ventral striatum corresponded with reaction time differences and on how much men with CSBD were anticipating erotic stimuli, which was measured prior to the experiment (Liberg et al., 2022).

Concerning GM and rs-FC alterations in CSBD, it remains open if previous findings can be replicated and whether new, potentially relevant brain regions for CSBD

can be identified: Therefore, based on the literature review and previous findings we aimed to examine 1) volumetric differences between men with CSBD and without. Furthermore, as it is likely that structural changes may be accompanied by changes of brain function and changes in VBM imply a different usage of the areas in question we investigated 2) whether GM alterations are linked to altered rs-FC. To examine possible alterations in the rs-FC that occur independent of structural changes, we additionally performed a seed-based rs-FC analysis in a priori defined regions of interest (ROI). We hypothesized that men with CSBD are more likely to show changes in addiction-related networks, such as higher cognition areas (prefrontal cortex, PFC) and subcortical limbic and salience structures (amygdala, striatum), as well as reward and sexual desire-related circuits (orbitofrontal cortex).

METHODS

Participants

The sample constitutes a subsample of the Sex@brain study (Engel et al., 2019), socio-demographic characteristics can be found in Table 1. Participants were screened for CSBD in a semi-structured interview including the proposed diagnostic criteria for HD (Kafka, 2010) and had to exceed the proposed cut-off score of 53 for the Hypersexual Behavior Interview (HBI-19, Reid et al., 2012). HD shares largely overlapping characteristics with the newly published ICD-11 criteria for CSBD (Kraus et al., 2018). Of the 50 included men with CSBD in the Sex@brain study, 5 were not eligible for the MRI investigation due to MRI exclusion criteria and 1 due to medication affecting his sexual drive (salvacyl). In addition, 12 subjects were excluded due to an acute depression, anxiety or obsessive compulsive disorder based on the SCID interview. Thirty right-handed male participants formed the CSBD group (Fig. 1). Thirty-two men without CSBD (HC) were recruited using advertisements on the intranet of the Hanover Medical School and were matched in regard to age and education.

Table 1. Socio-demographic characteristics of the analyzed participants

Socio-demographic Variables	Men with CSBD %	Men with CSBD M (SD)	Men without the condition %	Men without the condition M (SD)	*p*-value
Age		35.8 (10.79)		37.5 (11.65)	0.554†
Highest Educational Qualification‡					0.299‡
Secondary school leaving certificate of secondary education (4 years)	6.6		3.1		
Secondary school leaving certificate (5 years)	16		3.1		
Completed apprenticeship	20		31.2		
Secondary school leaving certificate (8 years)	20		31.2		
University degree	36		34		
Employment status¶					0.512‡
Unemployed	3.3		9.3		
In training	23.3		31.2		
Retired	3.3		3.1		
Employed	77		50		
Family status [6]					0.208‡
Single	42.6		34.2		
In a relationship	17.0		36.8		
Married	25.5		23.7		
Divorced	12.8		5.3		
Widowed	2.1		–		
Duration current/last relationship (in months)		75.14 (112.69)		68 (74.03)	0.817†
Number of children		0.71 (1)		0.77 (1.04)	0.75¶

Note. † Statistical analysis: *t*-test. ‡ Statistical analysis: Fisher's exact test. ¶ Statistical analysis: Wilcoxon-Mann-Whitney test.

Clinical assessment and questionnaires

Sexual characteristics. The German versions of HBI-19 (Reid et al., 2012) and the SAST-R (Carnes, Green, & Carnes, 2010) were used. Cybersex addiction was measured using the Internet Addiction Test for online sexual activities - short version, sIATsex (Pawlikowski, Altstötter-Gleich, & Brand, 2013). Since problematic pornography use is viewed by many as the main behavioral symptom of CSBD (Gola et al., 2020) we asked participants to report their average pornography consumption (average minutes per day during the last week & time consumed most) to assess severity of the disorder. Furthermore, we asked participants for average number of orgasms per week, to estimate their total sexual outlet. Additionally, sexual excitation and inhibition were assessed using the Sexual Inhibition Scale/Sexual Excitation Scale/(SIS/SES; Janssen, Vorst, Finn, & Bancroft, 2002). Lastly, a semi-structured interview was conducted by trained personnel for further assessment of sexual characteristics.

Psychological characteristics and comorbidities. To identify the presence of psychiatric comorbidities among subjects with CSBD, the German version of the Statistical Clinical Interview for DSM-IV (Wittchen, Wunderlich, Gruschwitz, & Zaudig, 1997) was used. Impulsivity was assessed using Barrat Impulsiveness Scale-11 (BIS-11; Patton, Stanford, & Barratt, 1995).

Depending on the distribution of the data, assessed using the Shapiro-Wilk test, between group differences were either tested using independent samples *t*-test or Mann-Whitney U test.

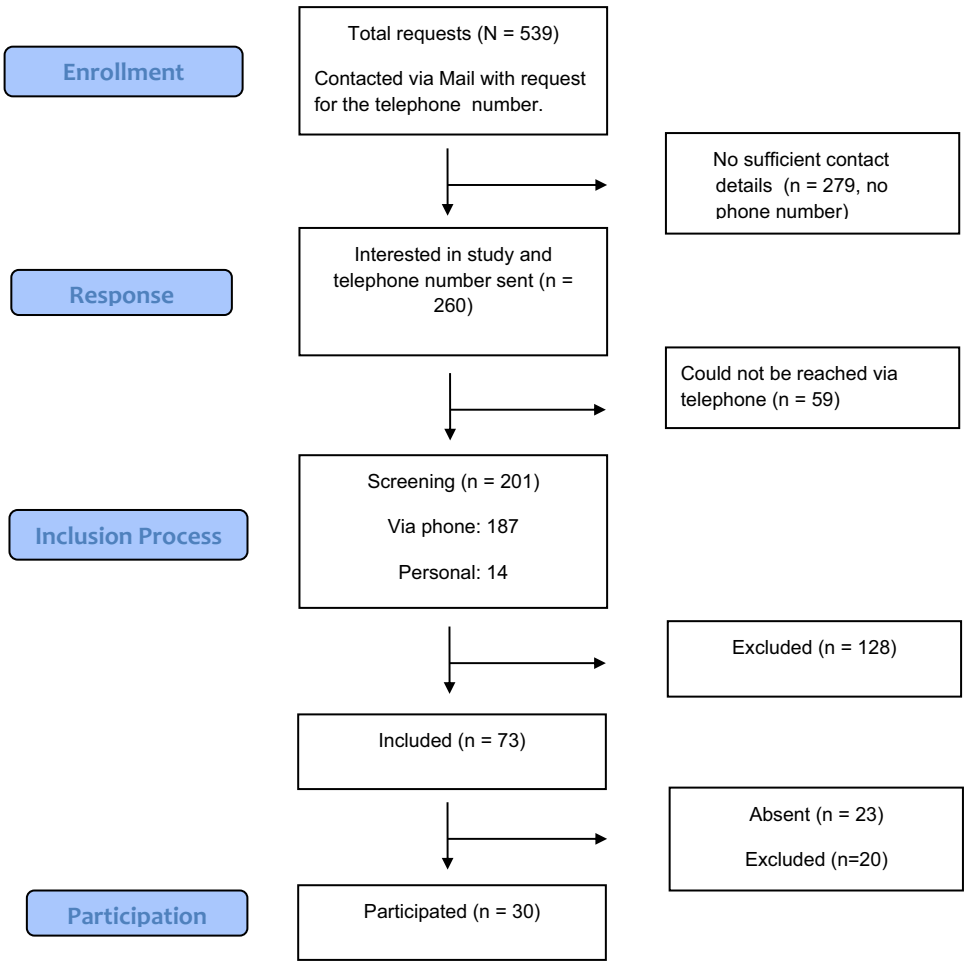

Fig. 1. Recruitment process of patients suffering from CSBD

Neuroimaging

Data acquisition. A 3.0 T MRI scanner (Siemens Skyra) equipped with 64-channel head coil was used for image acquisition. A total of 400 volumes with 84 axial slices (resolution $2 \times 2 \times 2$ mm) per volume were acquired in interleaved order using a gradient simultaneous multislice EPI T2* sensitive sequences with the following parameters: repetition time (TR) = 1.55s, echo time (TE) = 32 ms, flip angle = 90°, field of view = 256×256 mm, acceleration factor = 4, total time = 10min 20sec). The resting state data was acquired at the beginning of the MRI session. An individual high-resolution anatomical image was acquired for each participant using a T1 weighted magnetization prepared rapid acquisition gradient-echo sequence (resolution $0.9 \times 0.9 \times 0.9$ mm, TR = 2.3s, TE = 3 ms, flip angle = 9°, 255×270 mm). Participants were instructed to look at a fixation cross and stay awake.

VBM analysis. VBM analysis was performed using the Computational Anatomy Toolbox (CAT12, http://dbm.neuro.uni-jena.de/cat/), based on the Statistical Parametric Mapping software (SPM12, http://www.fil.ion.ucl.ac.uk/spm/software/spm12). The default settings were used for the pre-processing of the data (http://dbm.neuro.uni-jena.de/cat12/CAT12-Manual.pdf). First, all T1 images underwent bias, noise and intensity correction. Then the images were spatially normalized using an affine registration to the Montreal Neurological Institute (MNI) template after the whole brain structural data were segmented into white matter, GM and cerebrospinal fluid. The total intracranial volume (TIV) of each subject was calculated and the normalized GM images were smoothed using a Gaussian filter ($8 \times 8 \times 8$ mm^3 full width at half maximum).

After pre-processing, GM volume was compared between groups. The GM tissue maps differences were assessed by voxel-wise two-sample *t*-tests within the brain mask with age as a covariate. Due to the lack of orthogonality between TIV and the other parameters of interest, the mean TIV of the sample was used as the grand mean scaled value. The statistical significance of group differences was set at a cluster-level threshold of $p < 0.05$ corrected for multiple comparisons, using family wise error (FWE) corrections.

Resting state functional connectivity analysis. Functional MRI data pre-processing and statistical analyses were performed using SPM12 and DPABI 2.3 (Song et al., 2011; Yan, Wang, Zuo, & Zang, 2016). The pre-processing steps followed the standard protocol. In order to correct for the

instability of the initial signal and the subjects' adaptation to the scanner, the first five images were removed. Next, images were realigned, spatially normalized to the standardized template brain space (MNI) using stereotaxic space and unified segmentation on T1 image and resampled to $2 \times 2 \times 2\,mm^3$. Potential sources of undesired signals were regressed out, such as nuisance covariates, including voxel-specific motion parameters, white matter signal, and cerebrospinal fluid signal. Also global signal was regressed out, since it has been shown to contribute to the improvement of the specificity of rs-FC and can also contribute to the correction of motion artefacts (Almgren, Van de Steen, Razi, Friston, & Marinazzo, 2020; Birn, 2012). Then the images underwent a motion scrubbing procedure where scans with a frame-wise displacement (FWD) threshold of >0.4 mm were discarded. To increase the signal to noise ratio, the images were smoothed using a Gaussian kernel of $6 \times 6 \times 6\,mm^3$ (full width at half maximum). To extract the specific frequency area related to nerve cell activity, a band-pass filter (0.01–0.08 Hz) was applied.

To assess rs-FC properties in the regions indicated by the VBM analysis, we conducted a seed-based rs-FC analysis, by choosing the right cerebellum cluster peak (27, −54, −36) and the left precuneus (−12, −65, 56) as the relevant regions of interest (ROIs).

In addition, to investigate further possible alterations in rs-FC, independent of structural alterations, we performed a second, literature-based seed-based rs-FC analysis.

Therefore, the following 5 brain regions were defined as ROIs: The orbitofrontal cortex (OFC (Dolan, 2007; Probst & van Eimeren, 2013) is chosen due to its role in motivation drive, salience evaluation (Volkow & Fowler, 2000) and its implication in several addictions (Draps et al., 2020; Hong et al., 2013). The amygdala is used as it is implicated in emotion regulation and salience (Biundo et al., 2015; Chan et al., 2009; Schmidt et al., 2017) and is generally associated with several addictions, including CSBD (Kühn & Gallinat, 2014; Schmidt et al., 2017). The striatum, due to its involved in the brain's reward system (Béreau, 2017) with indications for rs-FC alterations in CSBD as well (Kühn & Gallinat, 2014) and the pallidum as part of the basal ganglia due to its prominent role in addiction and its function in motivation and reward processing (Farrell et al., 2021; Nall, Heinsbroek, Nentwig, Kalivas, & Bobadilla, 2021). Finally the ACC was chosen, as it has been found to play a role in habituation in CSBD (Banca et al., 2016), a process related to both substance use disorders (SUD) and behavioral addictions (Kraus, Voon, & Potenza, 2016). See also Fig. 2.

The ROI masks were created using automatic anatomical labelling (AAL; Tzourio-Mazoyer et al., 2002). As the striatum is not defined in the AAL atlas, the putamen and caudate nucleus were used instead. In the AAL atlas the nucleus accumbens as crucial part of the reward system is part of the caudate nucleus mask.

The temporal correlation between the average BOLD signal time course of these ROI voxels and other voxels in the whole brain was calculated using Pearson's correlation coefficients. The resulting values were then normalized using the Fisher r-to-Z transformation.

On a 2nd level between-groups analysis, random effect two-sample *t*-tests were performed to compare groups. The statistical significance of group differences was set at a cluster-level threshold of $p < 0.05$ FWE corrected for multiple comparisons.

Correlation analysis. To investigate the relationship between GM volume, rs-FC and sexual/clinical characteristics, a post-hoc correlation analysis using the extracted parameter estimates from significant clusters and the relevant behavioral data (total sexual outlet, SIS/SES, BIS-11, HBI, average pornography consumption, SAST-R) in all subjects was conducted. Two-tailed Pearson's correlations were calculated and results were considered significant after correction for multiple comparisons for $p < 0.00625$ (0.05/8).

Ethics

The study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics committee of Hanover Medical School (Nr.7122). Subjects gave written informed consent to participate, were free to withdraw from the study at any time and received reimbursement for their participation.

RESULTS

Participants' sexual and clinical characteristics

Regarding problematic online sexual behavior, men with CSBD were found to show more symptoms of cybersex addiction (i.e., sIATsex, t (59) = 10.41, $d = 2.62$, $p < 0.001$, Table 2). Men with CSBD reported more sexual excitation (i.e., SES, t (60) = 4.26, $d = 1.12$, $p < 0.001$) and lower sexual inhibition due to threat of performance consequences (i.e., SIS2, t (60) = 3.236, $d = 0.84$, $p < 0.001$). Counterintuitively, the men with CSBD did not score higher regarding the perceived threat of performance failure (i.e., SIS1, t (60) = 1.238, $p = 0.22$). Lastly, the average duration of pornography consumption per day during last week was found to be almost four-times greater for the CSBD group (t (57) = 4.404, $d = 0.67$, $p < 0.001$) as well as the time of pornography consumption per day during the time they consumed most (t (57) = 4.721, $d = 1.26$, $p < 0.001$). Also men with CSBD showed higher impulsivity levels (BIS-11, t (58) = 4.601, $d = 0.96$, $p < 0.001$).

Voxel-based morphometry analysis

VBM analysis showed that the CSBD group had significantly increased GM volume in the right cerebellum, middle occipital and superior frontal lobe (see Table 3).

A significant positive correlation were found between the GM volume in the right cerebellum and sexual excitation (SES, $r = 0.346$, $p = 0.006$), Significant positive correlations were found between the GM volume in the middle occipital

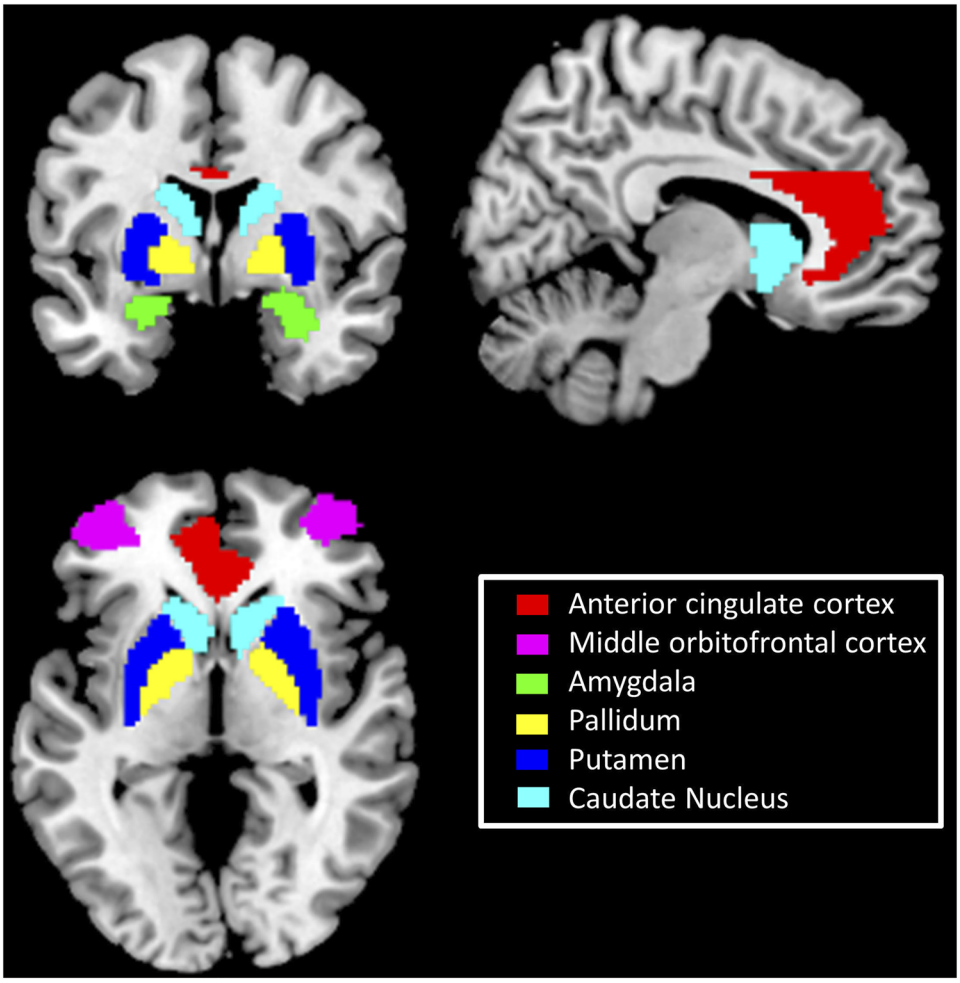

Fig. 2. ROIs used for the seed-based functional connectivity analysis extracted from the AAL toolbox

Table 2. Sexual characteristics

	Men with CSBD $n = 39$			Men without the condition $n = 34$				
	N	Mean	SD	*N*	Mean	SD	*t*-value	*p*-value
Hypersexual Behavior Inventory (Sum of HBI-19)	30	71.33	10.33	32	28.16	8.86	17.7	<0.001***
Sexual Addiction Screening Test (Sum of SAST-R)	29	12.34	2.94	32	2.29	2.38	14.89	<0.001***
Short Internet Addiction Test (Sum of sIATsex)	29	38.41	9.19	32	16.56	7.18	10.42	<0.001***
Sexual Excitation (SES)	30	59.68	10.34	32	49.27	8.87	4.26	<0.001***
Sexual Inhibition (SIS1)	30	34.23	7.8	32	32.18	5.74	1.23	<0.226
Sexual Inhibition (SIS2)	30	25.8	5.46	32	29.84	4.36	−3.43	= 0.002*
Av. Porn. consumption per day (min) last week	30	58	47.22	32	16.63	16.34	4.4	<0.001***
Porn. Consumption per day (min) period of max. consumption	28	155.71	129.15	31	37.45	31.44	4.72	<0.001***
Average number of orgasms (per week)	28	13	11.68	31	3.74	2.6	4.1	<0.001***
Impulsivity levels (sum of BIS-11)	29	68.93	9.14	31	59.19	9.67	4	<0.001***

Note. Av. Porn. Consumption = average duration of pornography consumption during last week; min = minutes; *n* = number of subjects in group; *N* = number of participants; SD = standard deviation; * for $p < 0.05$, and *** for $p < 0.001$ *; Higher score values indicate greater problems.

Table 3. VBM analysis: Regional gray matter (GM) volume differences between men with CSBD and men without the condition

Condition	Brain region	MNI coordinates			t_{max}	*p*-value FWE cluster	Cluster size
		x	y	z			
Men with CSBD > Men without the condition	R Cerebellum	27	−50	−38	5.26	<0.001	1889
	R Middle Occipital	38	−66	27	4.76	<0.001	658
	L Superior Frontal	−15	−5	53	4.14	0.005	390
Men without the condition > Men with CSBD	R Post Central	54	0	27	3.94	0.021	300

Note. Differences between the groups were assessed using two-sample *t*-tests. Results were corrected for multiple comparisons using family-wise error correction on cluster level and are reported for $p_{FWE} < 0.05$; MNI coordinates of maximum t-score are shown for each cluster; VBM = Voxel Based Morphometry; MNI = Montreal Neurological Institute; CSBD group = Compulsive sexual behavior disorder group; L = Left; R = Right.

lobe correlated with impulsivity scores (BIS-11, $r = 0.405$, $p = 0.001$), and sexual excitation (SES, $r = 0.340$, $p = 0.001$).

VBM-based rs-FC analysis

No differences in rs-FC between groups could be detected using a 5 mm sphere around the peaks of the clusters detected in the cerebellum, the middle occipital gyrus and superior frontal gyrus as seeds.

Seed-based rs-FC analysis

Group comparisons revealed significant differences in the rs-FC of various areas between the two groups. Men with CSBD had decreased rs-FC between the middle part of the right orbital frontal gyrus (mOFC) and the right gyrus rectus as well as the inferior parietal sulcus. See Table 4 for details of the significant results.

The rs-FC to the inferior parietal sulcus correlates with impulsivity (BIS-11, $r = -0.367$, $p = 0.003$). See also Fig. 3.

In the left amygdala we observed increased rs-FC in men with CSBD with precuneus/superior parietal lobule. The rs-FC correlates with average pornography consumption per day during the last week ($r = 0.445$, $p = 0.0004$), as visualized in Fig. 4.

In addition, the rs-FC was decreased in men with CSBD between left pallidum and two clusters in right post/pre-central gyrus.

DISCUSSION

Main findings

The present study combined structural and rs-FC magnetic resonance data to investigate brain alterations in individuals with CSBD and their relation to sexual and clinical characteristics. VBM analysis revealed significant GM enlargement of the right cerebellum, middle occipital/angular and superior frontal/SMA in men with CSBD. No rs-FC differences between groups of these areas could be found. However, decreased rs-FC between the right middle orbital frontal cortex and gyrus rectus, as well as the inferior parietal lobule in CSBD was detected. Furthermore, CSBD showed lower rs-FC between the left pallidum and the right pre- and postcentral gyrus.

Comparison to previous findings on structural differences

When putting our results in the context of preexisting findings of structural MRI in men with CSBD (Görts et al., 2023; Schmidt et al., 2017; Seok & Sohn, 2018), results remain inconsistent. Findings regarding structural differences in CSBD, namely an increased volume of the left amygdala (Schmidt et al., 2017), left superior and right middle temporal gyrus temporal gyrus (Seok & Sohn, 2018) could not be replicated in the current study. Moreover, we

Table 4. rs-fMRI: functional connectivity differences between men with CSBD and HC

Seed	Condition	Brain region	MNI coordinates			t_{max}	*p*-value FWE cluster	Cluster size
			x	y	z			
R mOFC	HC > CSBD	R Rectus	12	32	−14	5.64	0.034	154
	HC > CSBD	L inferior Parietal	−44	−54	44	4.26	0.045	144
Amygdala	CSBD > HC	R Precuneus	−6	−64	62	4.37	0.042	146
L Pallidum	HC > CSBD	R Precentral	10	−24	80	5.37	0.018	182
	HC > CSBD	R Postcentral	36	−28	44	4.46	0.019	179

Note. Differences between the groups were assessed using two-sample *t*-tests. Results were corrected for multiple comparisons using family-wise error correction on cluster level and are reported for $p_{FWE} < 0.05$; MNI coordinates of maximum t-score are shown for each cluster; VBM = Voxel Based Morphometry; MNI = Montreal Neurological Institute; CSBD group = Compulsive sexual behavior disorder group; L = Left; R = Right.

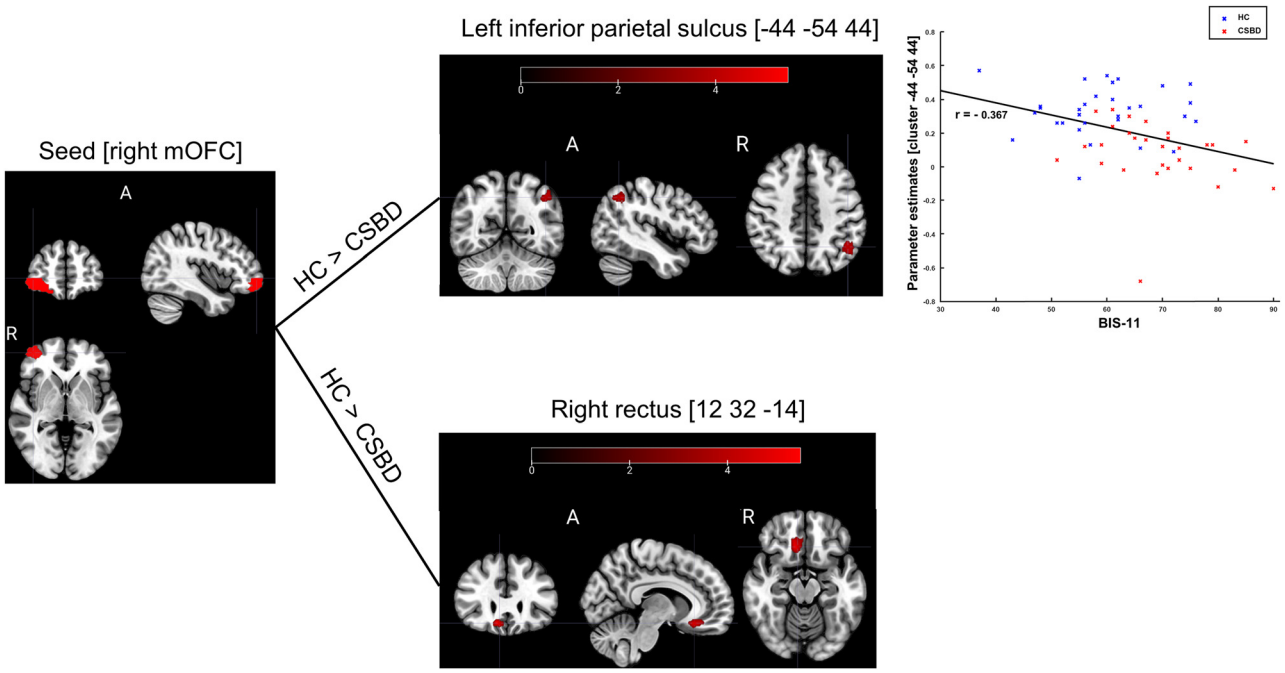

Fig. 3. Functional Connectivity differences using the mOFC as seed region. Depicted is the mask of the seed region, the areas showing significant differences using FWE correction on a cluster level, as well as the significant correlation between BIS-11 scores and parameter estimates of the cluster in the left inferior parietal sulcus

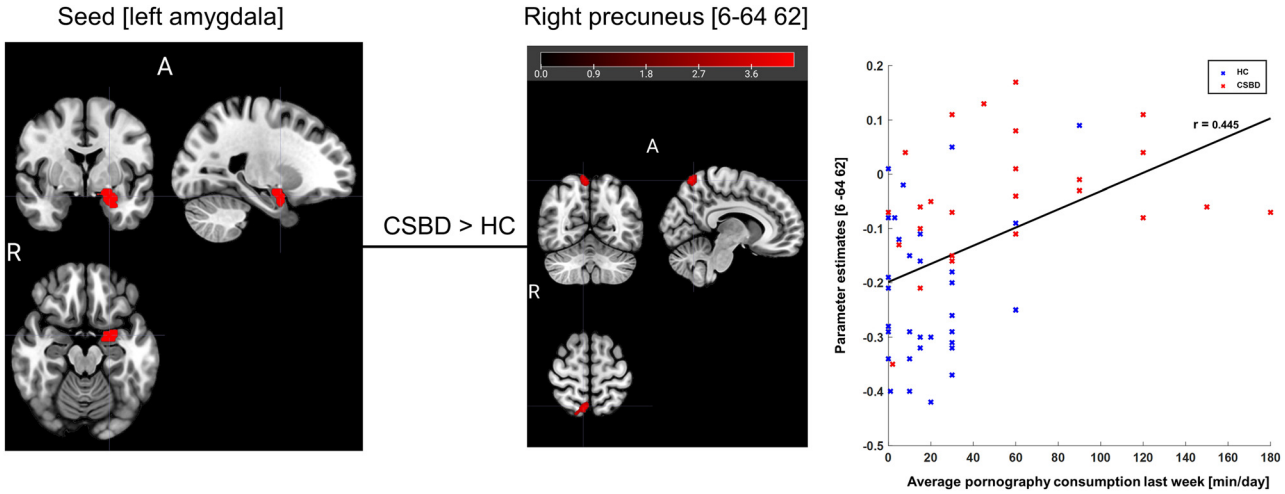

Fig. 4. Functional Connectivity differences using the amygdala as seed region. Depicted is the mask of the seed region, the area showing significant differences using FEW correction on a cluster level as well as the significant correlation between average pornography consumption per day and parameter estimates of the cluster in the precuneus

did not observe any alterations in the right posterior cingulate cortex in CSBD, which could have been expected based on the results of Görts et al. (2023), as they found a lower cortical surface in men with CSBD. As CSBD is discussed in relation to behavioral addictions in elaborated theoretical models (Brand, 2019), one could expect similar findings among behavior addiction and impulse control disorders. This may be true to a lesser extent when comparing our findings to GM alterations in SUD, especially GM reductions in the left superior temporal gyrus (Zhang et al., 2021). Furthermore, one must take into account the potential effects neurotoxic effects of drugs that are potentially seen (Zhang et al., 2021). Rather atrophies of GM in the left ACC, right putamen, and right supplementary motor area seem to be of relevance in behavioral addictions (Qin et al., 2020). We could neither observe changes of GM in the left ACC nor in the OFC, as could have been expected from a comparative study on GM alterations that included CSBD, gambling and alcohol use disorder (Draps et al., 2020). Perhaps, this can be best explained by a lack of statistical power as the decrease in GM volume in the OFC were most pronounced in Gambling and Alcohol Use Disorder and

least in CSBD (Draps et al., 2020). In fact, the only finding on structural differences we could replicate from findings on structural alterations in CSBD was an increase of GM in the cerebellum (discussed in detail further below). However, as Görts et al. (2023) point out further similarities may not have been detected, as the previous studies used different methodological approaches, including using different ROI and/or VBM vs. cortical thickness and surface area.

Structural differences in the cerebellum

As mentioned above, increase in the GM of the right cerebellum in individuals with CSBD replicates an aforementioned structural study in CSBD (Seok & Sohn, 2018). Generally, the cerebellum is thought to be closely connected to functional loops which sustain compulsive and impulsive behaviors (Bostan & Strick, 2018; Ding et al., 2013; Herrera-Meza et al., 2014), possibly due to connections to cortico-striatal-thalamic circuits (de Wit et al., 2014) and a regulatory role over dopamine release (Fong, 2006). Seok & Sohn (2018) speculated a link between cerebellar alterations and CSBD's compulsive behavior-related traits. Interestingly, the increase in the GM of the right cerebellum in CSBD group was positively associated with levels of sexual excitation. This is in agreement with the recent findings reporting an association between sexual excitation (SES scores) and cerebellar activation, underlining the role of the cerebellum in sexual arousal (Unterhorst et al., 2020). Other studies showed that the cerebellum activates in response to visual sexual stimuli (Beauregard, Lévesque, & Bourgouin, 2001; Garavan et al., 2000). Markers of sexual arousal were also directly linked to cerebellar activation (Stoléru, Fonteille, Cornélis, Joyal, & Moulier, 2012). Stoléru et al. (2012) proposed a neurobehavioral model of brain processes involved in SA (based on the work of Redouté et al., 2000) and identified the cerebellum as part of the model's cognitive components. Later, Hu et al., 2008 suggested that the cerebellum might not only be related to emotional but also to motivational and motor imagery processes induced by sexual stimuli.

Comparison to previous findings on rs-FC

Similar to the findings on structural alterations in CSBD, the previous findings on rs-FC (Draps et al., 2022; Schmidt et al., 2017; Seok & Sohn, 2018) diverge. In the present study, we did not detect any differences in rs-FC based on our VBM-based analysis, investigating rs-FC from cerebellum, the middle occipital gyrus and superior frontal gyrus. This could mean that the differences in size is not driven by widespread changes in addiction related networks but is possibly induced through different frequency of activation of these areas within an otherwise intact network. Moreover, based on our seed regions we derived from the literature, we would have expected an altered rs-FC in the striatum, pallidum, and ACC. We did, however, observe alterations in rs-FC in the amygdala, and OFC (discussed in detail further below). The absence of altered rs-FC of the striatum is particularly puzzling, as it is part of the mesolimbic dopamine pathway, in which altered rs-FC is known to play a crucial role in SUD (Tolomeo & Yu, 2022). Furthermore, in CSBD the ventral part of the striatum has been shown to be involved in reward-anticipation (Gola et al., 2017; Golec et al., 2021; Liberg et al., 2022) and in an appetitive-conditioning task (Klucken et al., 2016). Possibly, rs-FC does not detect alterations of the striatum in CSBD, like in experiment-based studies, because the hyperconnectivity of the striatum is stronger in SUD, when compared to behavioral addictions (Tolomeo & Yu, 2022). To enable comparisons of rs-FC of CSBD with behavioral addictions, it would be useful to examine further brain areas as ROIs that show hyperconnectivity in behavioral addictions, e.g. the medio-temporal lobe (Tolomeo & Yu, 2022).

Altered rs-FC between amygdala and precuneus

In the context of behavioral addictions, an imbalance between the ventral striatum, amygdala, and dorsolateral PFC is discussed, especially in the early stages of addiction (Brand et al., 2019). However, the amygdala did not show divergent FC to the implied structures, but to precuneus and parts of the superior parietal cortex. This finding correlates positively with the average pornography consumption per day during the last week. In an overview about brain imaging studies, Salu (2013) found that amygdala activation shows a positive correlation with sexual arousal.

The precuneus is an important component of the default mode network and plays a role in mental imagery (Cavanna & Trimble, 2006; Dong et al., 2020). Furthermore, the precuneus is involved in behavioral addictions, as the addiction severity modulates the precuneus involvement in internet gaming disorder (Dong et al., 2020). Addiction-related functional and structural alterations of the precuneus are usually linked to (subjective) craving levels, cue-induced craving responses, duration and severity in both SUD and behavioral addictions (Courtney, Ghahremani, London, & Ray, 2014; Ko et al., 2013; Park et al., 2007; Yuan et al., 2013). So far, no reliable method to assess craving in CSBD has been developed; hence, further examination are needed to clarify whether this increase in rs-FC could be related to craving.

In addition, the precuneus is involved in attention shifting, a process found to be affected in several addiction studies (Courtney et al., 2014; DeWitt, Ketcherside, McQueeny, Dunlop, & Filbey, 2015; Dong, Lin, Zhou, & Lu, 2014; Zhang et al., 2016). Previous studies on the involvement of the precuneus in CSBD showed a significantly lower rs-FC between left STG and left precuneus (Seok & Sohn, 2018). During early stages of behavioral addictions, triggering stimuli might attract increased attention and urges whereas conditioning might promote the development of cue-reactivity and craving, causing addicted individuals to experience hypersensitivity towards addiction-related stimuli or triggers and exhibit attentional bias or seemingly automatic attention towards them (Brand et al., 2019). An increased attentional bias towards sexually explicit cues (Mechelmans et al., 2014) and sexual rewards (Banca et al., 2016) has been reported. Activation in the amygdala, as well

as in the reward system (ventral striatum, dACC) seems to play a role in cue-reactivity to explicit sexual cues (Voon et al., 2014). Moreover, Klucken et al. (2016) found a significant difference in the conditioned BOLD responses in the amygdala between men with and without CSBD. Possibly, a simultaneous activation of the left amygdala and the precuneus reflects a constant sexual occupation of men with CSBD.

Altered rs-FC between OFC and gyrus rectus

In our rs-analysis we found a decreased FC between the right middle OFC and the gyrus rectus. Draps et al. (2022) found increased rs-FC between left OFC and left insula. The OFC has strong projections to the dorsal striatum, is involved in salience attribution, and motivation and plays an important role in SUD (Koob & Volkow, 2010). The gyrus rectus has been discussed as an inhibitory component in sexual arousal (Basson, 2015; Stoléru et al., 2012), lesions in the gyrus rectus can lead to desire for sexual and other pleasurable activities (Basson, 2015; Miller, Cummings, McIntyre, Ebers, & Grode, 1986). Collectively, a diminished rs-FC between middle OFC and the gyrus rectus perhaps supports the idea of sex-specific impulsivity deficiency. In the context of behavioral addictions Brand et al. (2019) propose that a diminished level of general inhibitory control seen in the early stages of addiction can only poorly mediate the relationship between cognitive and affective responses to certain trigger stimuli and decisions to engage in certain behaviors and therefore constitutes a vulnerability factor for the addictive behavior. As the addiction develops, the authors suggest that stimuli-specific inhibitory mechanisms may take control and act as additional mediators. They argue that, although general inhibitory control mechanisms may also be affected in addiction, the development of decreased specific stimulus-related inhibitory control may be involved in habitual and automatic behaviors in the late stages of the addiction (Brand et al., 2019). Hereby, we propose that the decreased connectivity between the mOFC and the gyrus rectus reported in the CSBD group suggests the existence of a diminished stimulus-specific inhibitory control.

Possible explanations for diverging findings

There are several reasons that potentially lead to different results between the studies conducted on rs-FC. One of them is the different conceptualizations of the disorder concept, as the measurement of CSBD was operationalized differently in the studies. Kafka's (2010) proposed criteria for HD in DSM-5 were used in four studies (Görts et al., 2023; Schmidt et al., 2017; Seok & Sohn, 2018, and the present study). Two studies additionally used criteria for sexual addiction as were proposed by Carnes et al. (2010), namely Schmidt et al. (2017), and Seok & Sohn (2018). However, Draps et al. (2022), used the newly released criteria of CSBD in ICD-11 (WHO, 2019), and Görts et al. (2023) combined approaches and additionally used Kafka's (2010) criteria.

Some differences between the concepts of HD and CSBD should be noted. Moral incongruence was explicitly named and exclusion criterion in Kafka's criteria, but not in the CSBD diagnosis of ICD-11 (Gola et al., 2020). We would argue, however, that moral incongruence is implicity included in the HD criteria, as they state that the symptoms must be "recurrent and intense" (Kafka, 2010). In contrast to CSBD in the ICD-11 (WHO, 2019), criteria for HD name maladaptive emotion regulation strategy as a symptom, and the incorporation of bipolar and SUD as exclusion criteria (Gola et al., 2022). In sum, it can be argued, that criteria of CSBD and HD describe the same underlying condition, as they share crucial criteria, such as the impaired control over sexual impulses, resulting in negative consequences, accompanied by unsuccessful efforts to control behavior (Böthe, Koos, & Demetrovics, 2022). Nevertheless, it cannot be ruled out that differences in the definition may lead to variations in the different data sets, resulting in different results.

What may be even more important than different conceptualizations is the fact that three studies excluded participants with other psychiatric diagnoses (Draps et al., 2022; Görts et al., 2023, the present one), while two others did not (Schmidt et al., 2017; Seok & Sohn, 2018), as CSBD comes with a higher rate of comorbid affective disorders (Engel et al., 2019). Thus, on the one hand, effects of other disorders cannot be excluded, and on the other hand, adjusted studies may not show a picture of the actual clinical conditions that make comorbidities appear common (Engel et al., 2019; Wéry et al., 2016).

However, it also cannot be ruled out that the previous findings are statistical artifacts and that actual brain-organic differences cannot be detected by means of structural examinations and rs-FC with the previous limited sample sizes.

LIMITATIONS

This study has been the second study conducted with a substantial ($N > = 30$) sample of men with CSBD and comes with some limitations. It is correlational in nature and does not allow for causal explanations of the altered brain areas (i.e. it is not clear if the observed structural and functional alterations could be associated with pre-existing characteristics or be a consequence of CSBD or are even due to other reason). The current study involved only heterosexual white men of the German population. Inclusion of various genders, sexual orientations and ethnic backgrounds could be helpful in understanding CSBD. Also the present sample consisted of individuals who voluntarily took part in the study and agreed to report intimate information. Neurotoxic effects, especially of alcohol consumption, cannot be excluded as a confounding variable in our analyses, since alcohol consumption is widespread in Western societies and the participants in our study have all experienced alcohol consumption, even though we listed alcohol dependence as an exclusion criterion. We cannot control for this because we did not record the amount of a participant's life history and/or current consumption but diagnosed according to the criteria for dependencies.

CONCLUSIONS

Despite the aforementioned limitations, the present study provides useful insight into the characteristics and relevant neural mechanisms of CSBD. Structural alterations in the cerebellum can possibly be linked to CSBD features associated with sexual arousal and compulsive behavior, while functional and structural alterations in the precuneus were found to be associated with addiction-related attention deficits. Aberrancies in the rs-FC between OFC and gyrus rectus indicate alterations in brain networks responsible for (sexual) reward processing, motivational salience and impulse control. In conclusion, the findings give further insights on similarities and differences between behavioral additions and CSBD. Atrophies of GM in the left ACC, right putamen, and right supplementary motor area as are often seen in behavioral addictions could not be observed. However, we could observed altered rs-FC involving amygdala and precuneus, as well as mOFC and gyrus recuts. Future studies should use additional ROI to compare CSBD with behavioral addictions, i.e. putamen and medio-temporal lobe.

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