Aberrant orbitofrontal cortex reactivity to erotic cues in Compulsive Sexual Behavior Disorder

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FULL-LENGTH REPORT

ABSTRACT

Background and aims: Compulsive Sexual Behavior Disorder (CSBD) is characterized by increased reactivity to erotic reward cues. Cue-encoded reward parameters, such as type (e.g. erotic or monetary) or probability of anticipated reward, shape reward-related motivational processes, increase the attractiveness of cues and therefore might enhance maladaptive behavioral patterns in CSBD. Studies on the neural patterns of cue processing in individuals with CSBD have been limited mainly to ventral striatal responses. Therefore, here we aimed to examine the cue reactivity of multiple key structures in the brain's reward system, taking into account not only the type of predicted reward but also its probability. *Methods:* Twenty Nine men seeking professional help due to CSBD and 24 healthy volunteers took part in an fMRI study with a modified Incentive Delay Task with erotic and monetary rewards preceded by cues indicating a 25%, 50%, or 75% chance of reward. Analyses of functional patterns of activity related to cue type and probability were conducted on the whole-brain and ROI levels. *Results:* Increased anticipatory response to cues predictive of erotic rewards was observed among CSBD participants when compared to controls, in the ventral striatum and anterior orbitofrontal cortex (aOFC). The activity in aOFC was modulated by reward probability. *Discussion and conclusions:* Type of anticipated reward (erotic vs monetary) affects reward-related behavioral motivation in CSBD more strongly than reward probability. We present evidence of abnormal aOFC function in CSBD by demonstrating the recruitment of additional subsections of this region by erotic reward cues.

KEYWORDS

compulsive Sexual Behavior Disorder, fMRI, erotic stimuli, incentive salience

INTRODUCTION

Compulsive Sexual Behavior Disorder (CSBD) has been increasingly studied due to its clinical and societal relevance (Gola & Potenza, 2018; Kowalewska et al., 2018; Kowalewska, Gola, Kraus, & Lew-Starowicz, 2020; Kraus, Voon, & Potenza, 2016a; Kühn & Gallinat, 2016; Lewczuk, Lesniak, Lew-Starowicz, & Gola, 2021; Reid, 2013). Recently, the World Health Organization has included CSBD in the 11th edition of the International Classification of Diseases (ICD-11; World Health Organization, 2018) as an impulse control disorder manifested in a pattern of loss of control over sexual impulses and urges persisting for at least 6 months, causing major distress or malfunctioning in important fields of one's life and

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fulfilling at least one of the following criteria: 1) engaging in repetitive sexual activity at the cost of other interests, commitments, health, and personal care; 2) undertaking numerous but ineffective attempts to control such activity; 3) maintaining this pattern of recurring sexual behavior despite adverse consequences; and 4) engaging in such behavior despite deriving little or no satisfaction from it (Kraus et al., 2018). However, despite the undeniable significance of this inclusion, there is still an ongoing debate regarding the conceptualization of CSBD; in particular, whether CSBD should rather be classified as an addiction (Kraus, Voon, & Potenza, 2016b; Kraus et al., 2018). Hyperreactivity to reward cues related to similar patterns of brain function observed in both CSBD and addictions is one of the issues discussed in this context (Anselme, 2010; Gola & Draps, 2018; Gola, Wordecha, et al., 2017; Kor, Fogel, Reid, & Potenza, 2013; Kowalewska et al., 2018; Potenza, Gola, Voon, Kor, & Kraus, 2017; Stark, Klucken, Potenza, Brand, & Stahler, 2018; Voon et al., 2014).

Stimuli referred to as *reward cues* become a source of predictions about reward through the processes of conditioning and direct attention and motivation towards the anticipated rewards, which is all mediated by the activity of brain structures comprising reward circuitry (Flagel & Robinson, 2017; Schultz, 2015). The cues can signal rewards that differ in respect of some parameters, including type and probability (Haber & Knutson, 2010; Schultz, 2015). Such cue-encoded parameters of anticipated rewards might be worth considering as potential modulators of aberrant cue-reactivity in CSBD and addictions.

Hyperreactivity to cues predicting rewards is usually associated with attentional and motivational biases towards particular types of rewards (e.g. money, sex, or food; Anselme & Robinson, 2020; Starcke, Antons, Trotzke, & Brand, 2018). Previous studies have demonstrated that CSBD patients are particularly reactive to erotic reward cues. As indicated by shorter response times (RTs) and increased blood oxygen level-dependent signal (BOLD signal) following the presentation of cues predictive of erotic rewards, this manifests in greater motivation promoting approach towards anticipated erotic rewards and increased responsiveness of the brain's reward circuitry structures, particularly the ventral striatum (Gola, Wordecha, et al., 2017; Mechelmans et al., 2014; Voon et al., 2014). Such hyperreactivity does not occur for cues associated with other (e.g. monetary) types of rewards (Gola, Wordecha, et al., 2017) or neutral content (Sklenarik et al., 2019; Sklenarik, Potenza, Gola, & Astur, 2020). In contrast, control participants show comparable ventral striatal activations in reaction to erotic and monetary stimuli (Sescousse, Caldú, Segura, & Dreher, 2013). A similar pattern can be observed in the thalamus in healthy subjects (Sescousse, Caldú, et al., 2013). The orbitofrontal cortex (OFC), on the other hand, shows differential activity along the anterior–posterior axis depending on the reward type, with evolutionarily ancient (primary) rewards (e.g. sex) tending to activate more posterior regions of the OFC and evolutionarily recent (secondary) rewards (e.g. money) being processed by more anterior parts of the OFC (Sescousse,

Caldú, et al., 2013; Sescousse, Redoute, & Dreher, 2010). In addition, preference for primary over secondary rewards is also observed in the amygdala and anterior part of the insula (Haber & Knutson, 2010; Sescousse, Caldú, et al., 2013). However, to our knowledge unlike ventral striatal (Brand, Snagowski, Laier, & Maderwald, 2016; Gola, Wordecha, et al., 2017; Kühn & Gallinat, 2014; Voon et al., 2014), the activity of the thalamus, OFC, amygdala and, insula have not yet been extensively studied in CSBD, especially in the cue-evoked anticipatory phase of reward processing, whilst the initial evidence suggests that aberrant patterns of explicit sexual stimuli processing in CSBD may involve these structures (Antons & Brand, 2020; Klein et al., 2020; Sinke et al., 2020; Voon et al., 2014).

It has been demonstrated that cue-reactivity (which triggers *wanting* component of reward processing; see Berridge, 2012) is modulated by the cue-encoded probability of the reward (lower chances = less motivation and reactivity, higher chances = more motivation and reactivity; Schutte, Heitland, & Kannemans, 2019; Tobler, Doherty, Dolan, & Schultz, 2007). In healthy subjects, ventral striatal, thalamic, and insular BOLD responses are modulated by the probability of an expected outcome (Kühn & Gallinat, 2011; Roiser, Stephan, den Ouden, Friston, & Joyce, 2010; Sescousse, Caldú, et al., 2013; Yacubian et al., 2007). Nevertheless, the role of reward probability as a potential modulator of cue-reactivity remains largely understudied in CSBD. Moreover, an increasing body of evidence suggests that the structures of reward circuitry engaged in the dopamine response may be particularly sensitive rather to uncertainty, responding the most strongly for uncertain (50% of probability) cues (Anselme, Robinson, & Berridge, 2013; Fiorillo, Tobler, & Schultz, 2003). Such a pattern seems to correlate with higher susceptibility to substance use and gambling disorders (Anselme & Robinson, 2020; see Hellberg, Russel, & Robinson, 2019 for a review). This association has not been studied in CSBD.

In the face of evidence that reactivity to reward cues is altered in addictions, a broader exploration of the specificity of these processes depending on cue-encoded parameters of anticipated reward (type and probability) seems vital (Haber & Knutson, 2010; Preuschoff, Bossaerts, & Quartz, 2006; Schultz, 2015). We, therefore, decided to reanalyze a dataset that pioneered the use of an Incentive Delay Task in CSBD (published previously in Gola, Wordecha, et al., 2017). As previously we have focused only on ventral striatal reactivity to reward cues, relative to outcomes, here we decided to examine: **(1)** how CSBD group and healthy controls differ at the whole-brain level, broadening the original scope of research from single ventral striatal region-of-interest (ROI), **(2)** whether reward probability (25, 50 and 75%) processing varies between groups, **(3)** how probability and type (erotic vs monetary) of anticipated reward interact in each group at the whole-brain level, and **(4)** in brain regions previously reported as reactive to cue-encoded parameters of reward (ventral striatum, thalamus, anterior and posterior OFC, amygdala, and insula). Finally, we tested **(5)** if BOLD activity in our ROIs is related to sexual arousability, as often discussed in the context of CSBD symptoms.

METHODS

Participants

A total of 29 men seeking treatment in two local clinics because of difficulties controlling their consumption of internet pornography formed the clinical CSBD group (age $M = 30.93$, $SD = 6.45$). Only patients meeting the criteria of a) being exclusively or predominantly heterosexual (measured with Kinsey Scale (Kinsey, Pomeroy, & Martin, 1948; Wierzba et al., 2015), b) having no history of alcohol abuse (scores <7 on the Alcohol Use Disorder Identification Test, Saunders, Aasland, Babor, de la Fuente, & Grant, 1993) or gambling problems (scores <3 on the South Oaks Gambling Screen, Lesieur & Blume, 1987), c) meeting at least 4 out of 5 symptomatic criteria for hypersexual disorder proposed by Kafka (2010) lasting for at least 1 year, d) not meeting the criteria of the other disorders (OCD, ICDs, mood disorders, anxiety disorders, psychotic disorders, substance abuse/dependence according to the results of Structured Clinical Interview for DSM-IV, SCID-I, First & Gibbon, 2004) and e) having no contradictions for MRI examination were invited for the fMRI session.

At the time that the study was conducted, the ICD-11 criteria for CSBD as an Impulse Control Disorder had not been published yet. For recruitment, we have therefore applied the Criteria for Hypersexual Disorder (HD; Kafka, 2010) that had been proposed for the fifth revision of Diagnostic and Statistical Manual (DSM-5; American Psychiatric Association, 2013). For further information on this issue, please see the Supplementary Materials.

A healthy control group was recruited through a web-based survey and consisted of 24 volunteers (age $M = 30.46$, $SD = 7.56$) matched by age (the same year of birth), income (±15%), and handedness to each CSBD subject, having no history of alcohol abuse, pathological gambling or diagnosis of any other psychiatric disorders. All control participants had used pornography at least once in the preceding year but had never experienced pornography use as problematic behavior.

Procedure

All participants completed a modified version of the Incentive Delay Task, which is described thoroughly in previous works (Gola, Wordecha, et al., 2017; Sescousse, Barbalat, Domenet, & Dreher, 2013; Sescousse et al., 2010). The task allows the examination of brain activity during the entire reward processing sequence, therefore each trial consists of a cue-anticipatory phase, a discrimination task, and a reward-outcome phase. However, in the current work, it was used to study the role of cue-encoded predictive parameters (type and probability) of reward only in the cue-anticipatory phase. The trial began with a cue being displayed (2.5 s) in the form of graphic pictograms containing symbols indicating the type (with a woman for erotic reward and a treasure chest for monetary reward), probability (a pie chart indicating 25%, 50%, or 75%) and magnitude (the size

of the pictogram) of reward signaled by the cue. An empty circle was used as the symbol for unrewarded control trials. Next, the cue was replaced by a question mark (1.5–4.5 s). After this cue-anticipatory phase, the participant performed a simple discrimination with a geometric figure as a target: either a square (right button press required) or a triangle (left button press required). Correct and sufficiently fast (<1 s) answers were followed by the presentation of the reward. Erotic rewards consisted of erotic photographs of women randomly drawn without replacement from a broader set in each rewarded erotic trial, while for monetary rewards the amount won was displayed (1–7 PLN). At the end of rewarded trials, participants indicated a hedonic rating for the reward on a 0–9 scale. More details on the study design can be found in our previous paper (Gola, Wordecha, et al., 2017).

We measured the BOLD signal changes accompanying cue presentation and the behavioral measures of performance (accuracy and RTs). The task was performed in four 12-min-long blocks of 57 trials each (24 trials with the monetary reward cue, 24 with the erotic reward cue, and 9 control unrewarded trials). Each probability value was displayed 8 times in each block. The stimuli were presented in a pseudorandom event-related design. Please refer to the Supplementary Materials for the details of MRI acquisition parameters.

Statistical analysis

SPSS Statistics was used for the behavioral data analyses (IBM SPSS Statistics for Windows, Version 25.0, IBM Corp.). A repeated measures mixed-model ANOVA was performed: 2 (type of anticipated reward: erotic, monetary) x 3 (probability: 25%, 50%, 75%) x 2 (group: control, CSBD) with response times as the dependent variable. We did not include a magnitude factor in the analyses of RTs as there was no significant magnitude-by-group interaction in the previous work (Gola, Wordecha, et al., 2017). Bonferroni correction was applied to all posthoc comparisons.

The neural data analysis was conducted in SPM 12 (Welcome Trust Center for Neuroimaging). Functional data were realigned with the field map option, co-registered to T1 images, normalized, and smoothed with an 8 mm isotropic Gaussian kernel.

In the first-level analysis, we used a general linear model for each subject's brain responses during the cue-anticipatory phase, time-locked to the onset of the cue. The cues were modeled separately for each type of reward signaled by the cue depending on the probability value, giving 6 separate cue conditions: 2 (erotic, monetary) x 3 (probability: 25%, 50%, 75%). In the 2nd level analysis, a 2 x 2 x 3 ANOVA (group x type of anticipated reward x probability value) with a full factorial design was conducted to cover **steps 1–3**. The effect of probability in each group was assessed in separate 2 x 3 ANOVA (type of anticipated reward x probability) models. We report the whole-brain results which survived family-wise error correction with cluster extent-based correction (Woo, Krishnan, & Wager, 2014) at

the $P = 0.001$ level of significance. XjView toolbox, with an anatomy mapping database based on MNI coordinates and AAL, was used for automated anatomical labeling of the results (https://www.alivelearn.net/xjview).

Additionally, we used a priori defined Regions of Interest (ROIs) for the key anatomical regions of the reward circuit which have previously been found to be differentially involved in the processing of reward parameters: the ventral striatum, thalamus, anterior OFC, posterior OFC, amygdala, and insula (both left and right ROIs were used for each structure). The thalamus, amygdala, and insula ROIs were taken from the automated anatomical labeling atlas via the Wake Forest University PickAtlas toolbox. The ventral striatal ROIs were 8 mm spheres centered around $x = -12$, $y = 10$, $z = -6$ (left) and $x = 12$, $y = 10$, $z = -4$ (right), defined on the basis of a meta-analysis of functional neuroimaging studies regarding reward anticipation (Liu, Hairston, Schrier, & Fan, 2011). Anterior and posterior OFC ROIs were defined based on previous work on neuronal mechanisms of reward value coding (Sescousse et al., 2010) as 8 mm spheres centered around the following coordinates: $x = -30$, $y = 51$, $z = 0$ (anterior OFC left); $x = 33$, $y = 51$, $z = 0$ (anterior OFC right); $x = -30$, $y = 33$, $z = -15$ (posterior OFC left); and $x = 30$, $y = 33$, $z = -15$ (posterior OFC right). Previously, anteroposterior dissociation has been reported in the OFC in the context of the feedback phase of reward processing (Sescousse et al., 2010). In the current work, we apply this division to study the anticipation phase, as the main goal is to extend the findings reported in our previous paper on cue-related reactivity (Gola, Wordecha, et al., 2017). The percentage of BOLD signal change was calculated using the MarsBaR toolbox (http://marsbar.sourceforge.net). Finally, a mixed model repeated measures ANOVA was performed on the values in IBM SPSS Statistics: 2 (type of anticipated reward) x 3 (probability) x 2 (group). We present only results that passed Bonferroni-Holm correction for the number of ROIs **(Step 4)**.

Finally, Pearson r correlation coefficients were calculated for the relationship between BOLD signal change derived from ROIs and results on the Sexual Arousability Inventory (SAI; Gola, Kowalewska, Wierzba, Wordecha, & Marchewka, 2015; Hoon, Joon, & Wincze, 1976; **Step 5**). In the current study, only the vicarious arousal (induced by erotic visual or verbal stimuli) subscale was used. It has been previously shown to strongly correlate with the frequency of masturbation and pornography use in males, which makes it particularly useful for studying participants for whom problematic pornography use is the dominant symptom of CSBD (Gola et al., 2015). Additionally, the relationship between results on the Sexual Addiction Screening Test (Gola, Skorko et al., 2017) and the reactivity of ROIs was assessed as an indicator of CSBD symptom severity.

Ethics

The experimental procedure was approved by the Ethical Committee of the XXX and was carried out in accordance with the Declaration of Helsinki. All participants received complete information about the study and provided informed consent.

RESULTS

Behavioral results

For response times, we replicated most of the results of previous analyses (Gola, Wordecha, et al., 2017). However, the interaction between group and type of anticipated reward was non-significant and remained at the level of statistical trend, $F(1,51) = 3.68$, $P = 0.061$. In addition to a significant main effect of reward probability consisting of a decrease in RTs with the increase of reward probability, $F(2,50) = 22.30$, $P < 0.001$, $\eta^2 = 0.30$ (Fig. 1A), there was a significant interaction between type and probability of reward signaled by the cues, $F(2,50) = 33.46$, $P < 0.001$, $\eta^2 = 0.40$ (Fig. 1B). RTs preceded by erotic reward cues were similar for 25% and 75% probabilities and were highest for the 50% probability. The interaction between type of anticipated reward, probability, and group was non-significant, $F(2,50) = 0.86$; $P = 0.43$. All results of this analysis are summarized in Supplementary Materials (Table 1).

Neuroimaging results

Step 1. The whole-brain analyses revealed that the only differences in neural reactivity for the monetary rewards cues between CSBD and control groups were observed within the lingual gyrus (Fig. 2A; Table 2, Supplementary Materials). The analysis on the erotic stimuli showed that between-group differences associated with erotic cue processing on the whole-brain level were observed in the frontal and occipito-parietal areas as well as subcortically. In the CSBD group, higher activity was found in the precentral gyrus, postcentral gyrus, supramarginal gyrus, superior parietal gyrus, lingual gyrus, putamen, and pallidum (Fig. 2B; Table 3, Supplementary Materials).

Step 2. The interaction analysis of group and probability factors did not reveal any significant results.

An additional analysis was conducted to examine whether there was a main effect of probability within the groups. In both groups, the effect of reward probability was observed frontally within the supplementary motor area, parietally within the superior parietal gyrus, in the inferior parietal gyrus and angular gyrus, occipitally in the calcarine fissure (sulcus), in the insula, and subcortically within the thalamus. Here we present only the results from CSBD participants, as a similar pattern of response was found in both groups (Fig. 3; Table 4, Supplementary Materials).

Step 3. We observed a significant interaction between type and probability of anticipated reward in the postcentral gyrus, superior occipital gyrus, cuneus, cingulate gyrus, and fusiform gyrus (Fig. 4; Table 5, Supplementary Material). A supplementary within-group analysis of this effect showed
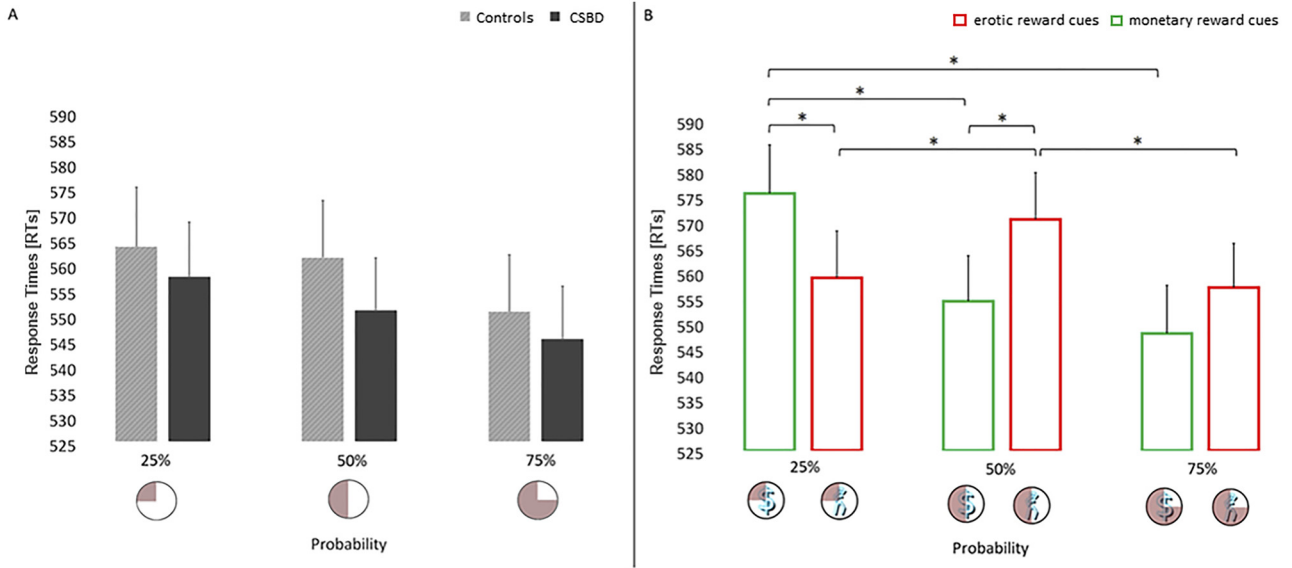
Fig. 1. Behavioral results. (A) Main effect of probability on response times; $P < 0.001$. (B) Interaction of probability and type of anticipated reward with response times; $P < 0.001$. *$P < 0.05$ with Bonferroni correction. Pictograms illustrate which cue-encoded parameters of reward are considered in the analysis (pie chart for probability, woman or $ for reward type, both pie chart and $ or woman for an interaction)
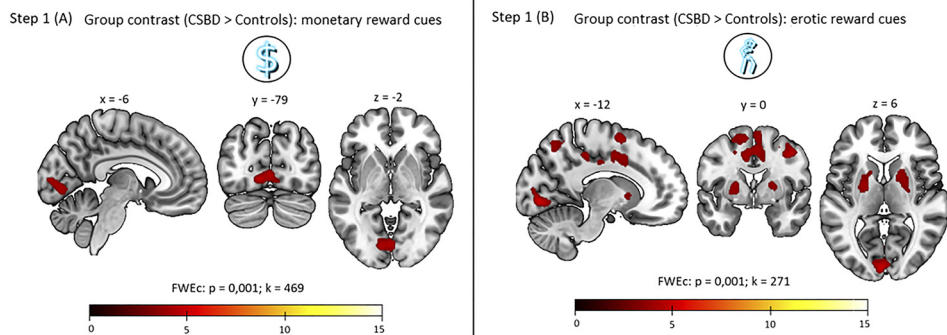

Fig. 2. Step 1: whole-brain results. (A) The effect of group (CSBD > control) on the processing of cues predictive of monetary rewards ($ pictogram). (B) The effect of group (CSBD > control) on the processing of cues predictive of erotic rewards (woman pictogram)
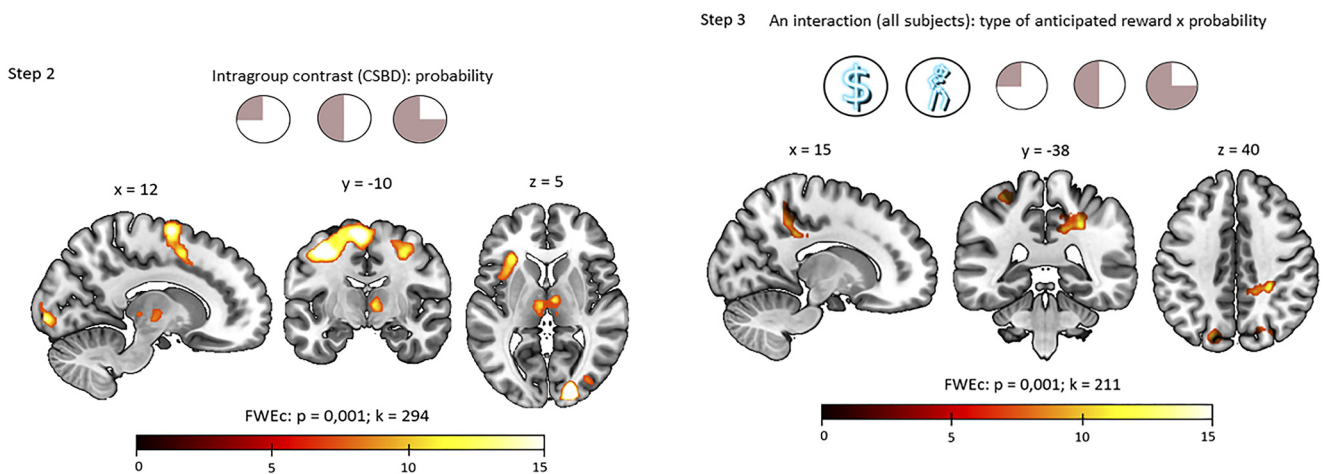

Fig. 3. Step 2: whole-brain results. The effect of probability (pie chart pictogram) in the CSBD group

Fig. 4. Step 3: whole-brain results. The effect of interaction between type (woman pictogram) and probability (pie chart pictogram) of anticipated rewards in all participants

that it was driven mainly by participants from the control group, as no clusters in the CSBD group survived corrections for multiple comparisons for type and probability interaction.

Step 4. We observed a main effect of the type of reward signaled by the cue in the ventral striatum (left: $P = 0.00$; right: $P = 0.001$) and anterior OFC (right: $P = 0.044$). The BOLD response was higher for monetary than erotic reward cues. The main effect of probability was significant for the thalamus (left: $P = 0.001$; right: $P = 0.001$), ventral striatum (left: $P = 0.011$; right: $P = 0.001$), and insula (left: $P = 0.011$). In all of these ROIs, the BOLD signal change values increased in line with the probability of reward. There was a marginally significant interaction between group and type of anticipated reward factors in the thalamus (right: $P = 0.048$). Although the BOLD signal change for cues predictive of monetary rewards was similar in both groups, it was much higher in the CSBD than in the control group for erotic reward cues. We observed such a tendency also in the ventral striatum; however, it only remained at the level of statistical trend after applying corrections for the number of ROIs (right: $P = 0.055$). Additionally, the three-way interaction between anticipated reward type, probability, and the group was significant in the anterior OFC (right: $P = 0.012$). Post-hoc between-group *t*-tests revealed that there were significant differences between CSBD and control participants in the processing of erotic reward cues in the anterior OFC, dependent on reward probability (Fig. 5). The BOLD signal change values were significantly higher in the CSBD group in the right anterior OFC for the 25% probability of receiving a reward, $t(51) = -2.148$; $P = 0.036$. For detailed statistics for all ROIs, see Tables 6–12 in the Supplementary Materials.

Step 5. The results of the SAI (vicarious arousal subscale) in the control group were strongly inversely correlated with the mean BOLD signal change following monetary reward cues in the amygdala (left: $r = -0.52$, $P = 0.012$) and moderately in the insula (left: $r = -0.48$, $P = 0.019$) and thalamus (left: $r = -0.46$, $P = 0.027$). Moreover, there was a strong and significant inverse correlation between SAI results and the response of amygdala to cues predictive of erotic rewards (right: $r = -0.46$, $P = 0.028$; left: $r = -0.51$, $P = 0.013$) in control participants. In the CSBD group, we observed a moderate correlation between results on the same scale and BOLD signal change in the ventral striatal ROI following monetary reward cues (right: $r = 0.42$, $P = 0.039$) and a similar strong correlation for erotic reward cues (right: $r = 0.62$, $P = 0.013$; left: $r = 0.53$, $P = 0.066$, i.e. a stat. trend). For details, see Fig. 6 (A–H). However, the results of these correlation analyses do not pass Bonferroni-Holm correction for the number of ROIs and therefore should be interpreted with caution.

DISCUSSION

This work aimed to deepen the understanding of cue reactivity in CSBD, with a focus on the type (erotic vs monetary) and probability (25, 50, and 75%) of anticipated reward as the potential modulators, at the whole-brain level (expanding previous finding limited only to the ventral striatum; Gola, Wordecha, et al., 2017) and a priori defined ROIs from the reward circuit: the ventral striatum, thalamus, anterior and posterior OFC, insula, and amygdala.

The functional pattern observed in CSBD subjects comprising superior parietal cortices, supramarginal gyrus, pre and postcentral gyrus, and basal ganglia might be indicative of intensified (as compared to healthy controls) attentional, somatosensory, and motor preparation to erotic reward approach and consummation (*wanting*) in CSBD which is evoked by predictive cues (Locke & Braver, 2008; Hirose, Nambu, & Naito, 2018). This is in line with Incentive Sensitization theory of addiction (Robinson & Berridge, 2008) and existing data on cue-reactivity in addictive behaviors (Gola & Draps, 2018; Gola, Wordecha, et al., 2017;
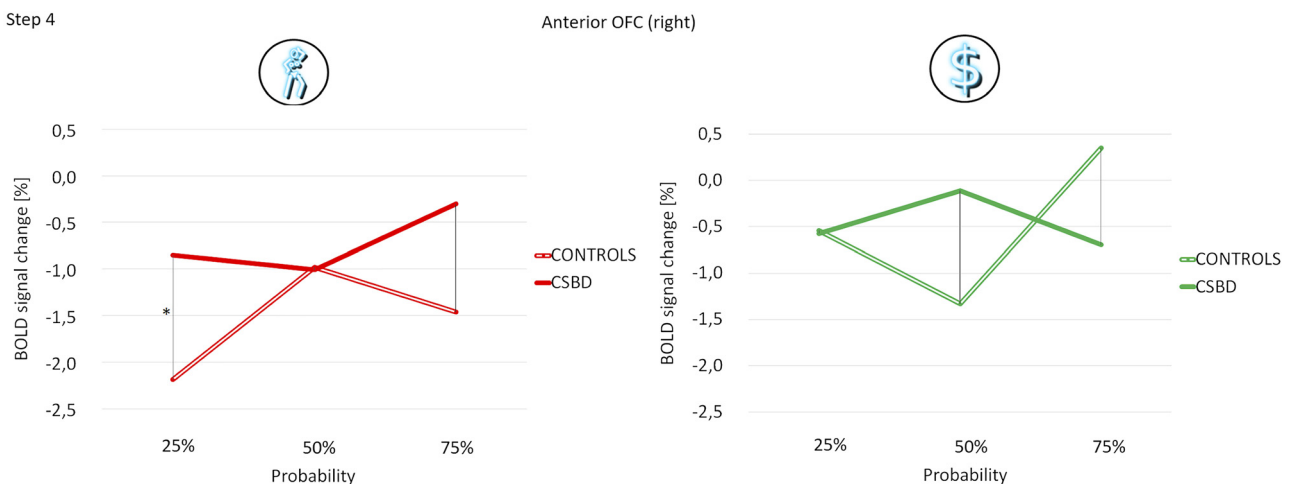

Fig. 5. Step 4: ROI results. Three-way interaction between cue-encoded parameters of reward: type (woman pictogram for cues predictive of erotic rewards, $ pictogram for cues predictive of monetary rewards), probability, and group in the right anterior OFC (aOFC)
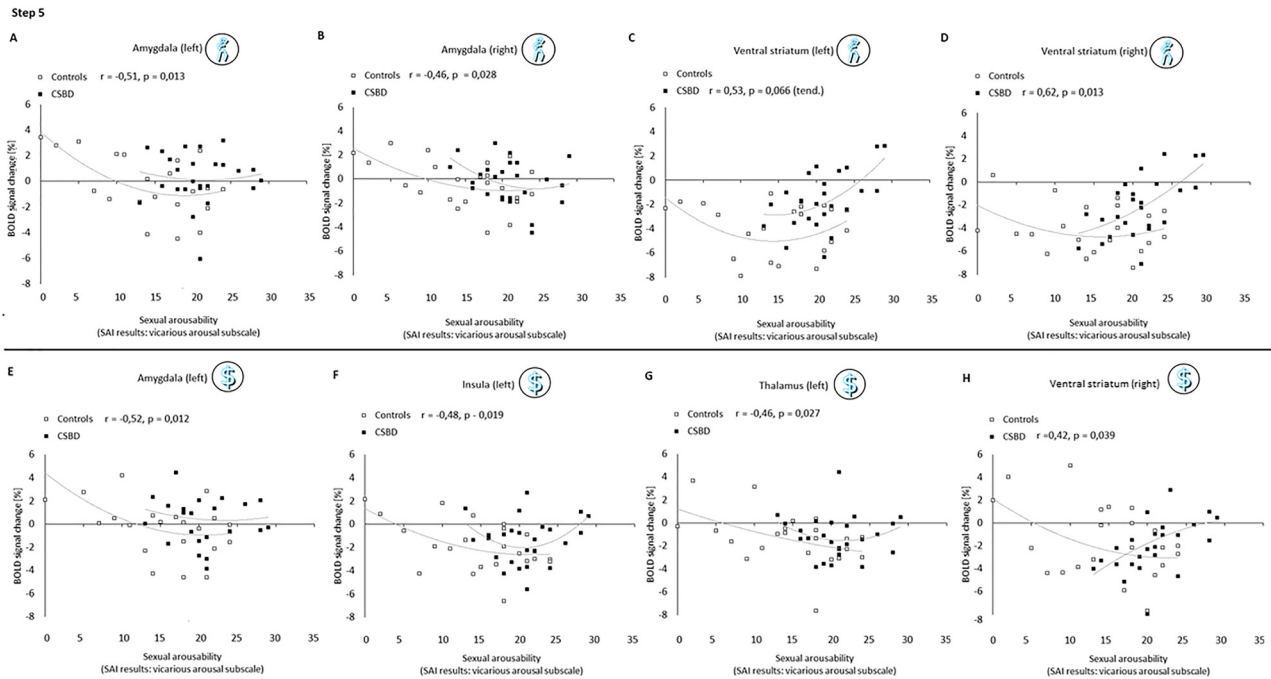
Fig. 6. Step 5: the results of correlation analysis between BOLD signal change derived from the ROIs and the results of the Sexual Arousability Inventory. Pictograms illustrate the type of anticipated reward (woman for erotic cues, $ for monetary cues)

Kowalewska et al., 2018; Kraus et al., 2016b; Potenza et al., 2017; Stark, Klucken, Potenza, Brand, & Strahler, 2018; Voon et al., 2014).

Moreover, we demonstrate the effect of probability as a motivationally salient reward parameter, as illustrated by the whole-brain activity in the supplementary motor area, occipital and parietal cortex, insula, and thalamus which might reflect attentional and motor preparation making up the anticipatory phase of reward processing (Wilson et al., 2018). Additionally, the decrease of RTs with reward probability illustrates that the higher the reward probability, the higher the reward-related motivation. However, as similar patterns of probability-related behavior and neural activity were observed in clinical and control groups, our results do not indicate any exceptional reactivity to reward probability itself in CSBD. Considering the significant between-group differences explained by the type of anticipated reward which are suggestive of increased behavioral motivation related to this parameter in the CSBD group, these results demonstrate that the cue-encoded parameter of reward type (erotic vs monetary) might have a much greater influence on maladaptive patterns of behavior in CSBD.

Most importantly, with the results of ROI analysis, this work broadens the previously-published results (Gola, Wordecha, et al., 2017) by showing that the elevated response of reward circuitry to erotic reward cues in CSBD occurs not only in the ventral striatum in the reward anticipation phase but also in the anterior orbitofrontal cortex (aOFC). Additionally, the activity in this region also seems to be dependent on reward probability. The BOLD signal change was higher in CSBD individuals than in healthy controls, particularly for the lower probability

values, which might indicate that lower chances of obtaining the erotic reward do not decrease the excessive behavioral motivation induced by the presence of the erotic reward cues.

Based on our data, it might be suggested that the aOFC plays an important role in mediating the specific ability of cues of particular reward types to motivate reward-seeking behavior in CSBD participants. In fact, the role of OFC has been implicated in neuroscientific models of addictive behaviors. The Interaction of Person-Affect-Cognition-Execution (I-PACE) model assumes that imbalance between prefrontal and limbic structures of reward circuitry results in decreased situation-specific inhibitory control over reward-oriented desires and, relatedly, impaired control over particular behaviors (Brand et al., 2019). According to Impaired Response Inhibition and Salience Attribution (iRISA) model, the aberrant function of OFC, which takes part in assigning incentive salience to addiction-related cues, may contribute to the development of characteristic symptoms of addiction, like craving and compulsive use, as OFC takes part in the suppression of craving (Goldstein & Volkow, 2011). As CSBD is still an under-investigated phenomenon, in our interpretation we refer to results from studies on different behavioral issues and addictions. In their recent work Gardner and Schoenbaum (2020) have proposed that in general, the role of OFC is to update a cognitive model of causal relationships in the environment which is further used to guide the behavior. This might include latent inhibition: learning to ignore irrelevant cues (Costa, Sengupta, & Schoenenbaum, 2021). In the light of evidence on cue-hyperreactivity in CSBD, an increased orbitofrontal activity could suggest that these

processes might be altered in this condition. In fact, studies on addictions in animals and humans have provided evidence that dopaminergic neurons in the OFC take part in the computation of the expected values of rewards, and abnormal functioning of these neurons is correlated with a bias towards addiction-related reward cues over non-addiction-related cues (Baeg, Jedema, & Bradberry, 2020). Altered metabolism in the OFC and increased neuronal activity in response to drug-associated cues have been also observed in neuroimaging studies in drug users (Schoenbaum & Shaham, 2008). Recently, it has been demonstrated that in the mice model of alcohol addiction the activity of connections between OFC and the striatum is increased in the reward approach phase and decreased in the outcome phase (Renteria et al., 2021). This leads to interrupted value-based decision-making processes on the behavioral level and therefore resembles the pattern of dissociated cue-triggered *wanting* and outcome-related *liking* in CSBD (Olney, Warlow, Naffziger, & Berridge, 2018). Hyperactivity of OFC associated with reward anticipation has been also observed in human subjects with compulsive behavior (Price et al., 2021). The authors hypothesize that the increased transmission from OFC to basal ganglia is related to the occurrence of compulsive behavior. Their results point to the possibility that decreasing the activity of OFC with the use of continuous Theta Burst Stimulation might have a beneficial impact on the effectiveness of training directed at compulsive behavior. In pathological gambling hyperactivity in the OFC related to the processing of expected value of monetary gains has been observed (van Holst, Veltman, Büchel, van den Brink, & Goudriaan, 2012).

Interestingly, our result is surprising with regards to the posteroanterior functional organization of OFC, with the aOFC specializing in secondary rewards processing (Sescousse et al., 2010, 2013a). Instead, in the CSBD group, we do observe the recruitment of the aOFC by erotic reward cues related to primary erotic rewards. In their study on pathological gambling, Sescousse, Barbalat, Domenech, and Dreher (2013) demonstrated that in the reward outcome phase, a posterior OFC region—which responded to erotic rewards in both groups—was recruited by monetary rewards in pathological gamblers but not in control participants. In our study, a similar effect of abnormal posteroanterior organization of the OFC (more robust response to cues predictive of rewards related to the profile of behavioral difficulties) appeared during the cue-elicited reward anticipatory phase. One possible interpretation of these results is that they relate to the recruitment of additional subsections of the OFC by rewards and cues relevant to specific behavioral problems (the posterior OFC in pathological gambling and the anterior OFC in CSBD).

Finally, the relationship between the activity of reward circuitry structures and self-reported sexual arousability (specifically vicarious arousal induced by visual or verbal erotic stimuli) observed in the control group might provide evidence of other abnormal cue-processing mechanisms worth further exploration in CSBD. Whilst in the CSBD group, we found only a positive correlation between sexual arousal and ventral striatal cue-reactivity, which is in line with previous research (Gola & Draps, 2018), we also found that the higher the sexual arousability in healthy participants, the lower the response of the insula, amygdala, and thalamus (reward circuitry structures). The activity of the insula in the context of reward processing has been reported to code awareness of visceral responses related to motivation towards obtaining a reward (Kühn & Gallinat, 2011; Stark et al., 2019). The increase of activity in the amygdala is, in turn, reported to be followed by the enhancement of conditioned anticipatory behaviors (Servonnet, Hernandez, El Hage, Rompré, & Samaha, 2020). The thalamus possibly codes expected reward salience (Sescousse, Caldu, et al., 2013). In future research, it would therefore be interesting to see if such patterns of activity are associated with the level of control over sexual impulses on the behavioral level.

Limitations

Our sample consists only of heterosexual men, as among this is the population in which CSBD is most common (Kraus et al., 2018; Kowalewska et al., 2020; Lewczuk, Szmyd, Skorko, & Gola, 2017). It would be interesting for further research to extend the sample to populations of women and non-heterosexual participants. Moreover, the predominant problematic behavior in the studied population is pathological pornography use, therefore further studies should compare different subgroups of CSBD patients who have other dominant behaviors, such as paid or casual sexual encounters.

CONCLUSIONS

Our study provides new knowledge on the role of cue-encoded predictive value for erotic and non-erotic rewards and its influence on brain reactivity in CSBD. Reward type seems to have a stronger impact on reward-related behavioral motivation in CSBD than does the probability of reward. We provide evidence of abnormal functioning of the anterior OFC in CSBD. The observed anterior OFC responses to cues predictive of erotic rewards in CSBD participants but not control participants suggest the recruitment of additional neural resources in CSBD during reward anticipation. Further studies should assess the clinical symptoms of CSBD associated with the described alteration of anterior OFC reactivity.

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All authors had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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SUPPLEMENTARY MATERIAL

Supplementary data to this article can be found online at https://doi.org/10.1556/2006.2021.00051.

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