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Neural mechanisms of appetitive learning impairment in compulsive sexual behaviors

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Abstract

Despite the growing body of research and the inclusion of Compulsive Sexual Behavior Disorder (CSB, code 6C72) in the International Classification of Diseases (ICD-11), published in the 11th edition in recent years, many of the neural mechanisms underlying the development and persistence of symptoms of compulsive sexual behaviors (CSB) are poorly understood. The Incentive Sensitization Theory of addiction suggests that maladaptive attentional and motivational processes directed toward reward-associated cues, coupled with impaired extinction of these previously learned associations, may drive addictive behaviors through alterations of the brain reward system.

The aim of this dissertation was to investigate whether individuals with CSB exhibit altered appetitive associative learning, including both appetitive conditioning and extinction of cue–reward relationships and its underlying neuronal underpinnings. Additionally, it was examined whether these alterations are specific to erotic rewards or extend to other appetitive stimuli (e.g. monetary), whether neurofunctional differences also manifest outside of any task (at rest), and whether structural changes in prefrontal regions accompany these functional abnormalities. To this end, men struggling with CSB (n=33) and healthy control subjects (n=33) underwent neuroimaging examinations whilst performing behavioral tasks, allowing to probe their self-assessed, behavioral and neuronal effects of associative learning.

Obtained results show that men struggling with CSB are prone to short-term general conditioning and extinction alterations towards cues of both erotic and monetary rewards. These alterations were present in self-assessment, reaction times, and reactivity of the ventral striatum, anterior orbitofrontal cortex, and dorsal anterior cingulate cortex. Intriguingly, the notion of generalized aberrant associative learning, however, was not supported by task-based functional connectivity analyses, which provided an account of erotic-biased processing of appetitive cues in both conditioning and extinction. No group differences were observed in actual reward processing, in default brain reward system functional connectivity, nor in morphological alterations in the CSB group, suggesting CSB brain reward system alterations are functional and more context-specific.

In line with Incentive Sensitization Theory, these findings contribute to the growing evidence that CSB may share certain neurobiological characteristics with addictive disorders, particularly regarding enhanced conditioning, cue-reactivity and disrupted extinction of conditioned responses. As demonstrated in the study presented in this dissertation, analytical approach towards neurobiological underpinnings of CSB drawing on functional connectivity complementing the classically used task-based activity analysis, in tandem with self-reported and behavioral indices, provide a richer view of this complex disorder.

Streszczenie

Pomimo rosnącej liczby badań i włączenia Zaburzenia związanego z Kompulsywnymi Zachowaniami Seksualnymi (ang. Compulsive Sexual Behaviour Disorder, kod 6C72) do opublikowanej w ostatnich latach 11 edycji Międzynarodowej Klasyfikacji Chorób (ICD-11), wiele mechanizmów neuronalnych leżących u podstaw rozwoju i utrzymywania się objawów kompulsywnych zachowań seksualnych (CSB) jest słabo poznanych. Model postulowany przez *Incentive Sensitization Theory* sugeruje, że nieprawidłowe procesy uwagowe i motywacyjne ukierunkowane na sygnały związane z przetwarzaniem nagród, w połączeniu z zaburzonym wygaszaniem wcześniej wyuczonych skojarzeń, mogą zwiększać szansę na rozwój objawów uzależnienia poprzez wtórne zmiany neuronalne w obrębie układu nagrody.

Celem niniejszej rozprawy było zbadanie, czy osoby z CSB wykazują odmienne wzorce uczenia się asocjacyjnego w zakresie zarówno warunkowania jak i wzorce wygaszania wcześniej występującego skojarzenia nagroda-wskazówka, oraz stojące za nimi neurobiologiczne mechanizmy. Dodatkowo zbadano, czy zmiany te są specyficzne dla nagród erotycznych, czy też mają charakter uogólniony na inne bodźce apetytywne (np. pieniężne), czy różnice neurofunkcjonalne przejawiają się również poza kontekstem zadań poznawczych (w stanie spoczynkowym), oraz czy zmiany strukturalne w obszarach przedczołowych towarzyszą tym nieprawidłowościom funkcjonalnym. W tym celu mężczyźni cierpiący na objawy CSB (n=33) i osoby kontrolne (n=33), wzięli udział udział w procedurze badań neuroobrazowania podczas wykonywania zadań behawioralnych, co pozwoliło zbadać ich samoopisowe, behawioralne i neuronalne efekty uczenia się asocjacyjnego.

Uzyskane wyniki pokazują, że mężczyźni cierpiący na objawy CSB są podatni na krótkoterminowe uogólnione zmiany w procesach warunkowania i wygaszania w względem wskazówek dotyczących zarówno nagród erotycznych, jak i pieniężnych. Zmiany te były obecne w miarach samoopisowych, czasach reakcji i aktywności neuronalnej brzusznego prążkowia, przedniej kory oczodołowo-czołowej i grzbietowo-przedniej kory zakrętu obręczy. Co ciekawe, hipoteza uogólnionego nieprawidłowego uczenia się asocjacyjnego nie została jednak poparta analizami połączeń funkcjonalnych podczas zadania, które wykazały

silniejsze połączenia specyficznie podczas przetwarzania wskazówek erotycznych, zarówno w warunkowaniu, jak i wygaszaniu. Potwierdzono brak różnic grupowych w przetwarzaniu nagród, oraz wbrew założeniom, brak różnic w sile połączeń funkcjonalnych układu nagrody mózgu w aktywności spoczynkowej. Nie zaobserwowano także zmian morfometrycznych w zakresie grubości podstawno-brzusznej kory przedczołowej w grupie CSB, co sugeruje, że zmiany w układzie nagrody mózgu u osób z CSB są ograniczone do zmian funkcjonalnych zaangażowanych w procesy przetwarzania kontekstowego, tj. w sytuacjach zawierających kontekst erotyczny, a więc związany z specyficznymi zachowaniami nałogowymi.

Zgodnie z Incentive Sensitization Theory, wyniki otrzymane w badaniu przedstawionym w niniejszej dysertacji przyczyniają się do rosnącej liczby dowodów za tym, że CSB może mieć pewne cechy neurobiologiczne wspólne z zachowaniami nałogowymi, szczególnie w odniesieniu do wzmocnionego warunkowania, reaktywności na bodźce i zaburzonego wygaszania reakcji warunkowych. Ponadto zastosowanie narzędzi analitycznych opartych na połączeniach funkcjonalnych układu nagrody w tandemie z klasycznymi analizami aktywności mózgu oraz miarami samoopisowymi i behawioralnymi dostarczyło pełniejszego obrazu złożonego zjawiska CSB.

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Abbreviations

Amy	Amygdala
ANOVA	Analysis of Variance
aOFC	Anterior orbitofrontal cortex
APA	American Psychological Association
AUDIT	Alcohol Use Disorders Identification Test
BF	Bayes factors
BOLD	Blood-Oxygenation-Level-Depended
BPS	Brief pornography screener
CBT	Cognitive Behavioral Therapy
CS	Conditional stimulus
CSB	Compulsive sexual behaviors
CSBD	Compulsive sexual behavior disorder
dACC	Dorsal anterior cingulate cortex
dlPFC	Dorsolateral prefrontal cortex
DPFC	Dorsal prefrontal cortex
DSM-5	Diagnostic and statistical manual of mental disorders
EPI	Echo-planar imaging
fMRI	Functional magnetic resonance imaging
FOV	Field of view
GLM	General linear model
HADS	Hospital Anxiety and Depression Scale
HBI	Hypersexual Behavior Inventory
HD	Hypersexuality Disorder
Hipp	Hippocampus
Hypo	Hypothalamus
ICD-11	11th edition of the International Classification of Diseases for Mortality and Morbidity Statistics
IS-12	Impulsiveness Scale
LHb	Lateral habenula
MNI	Montreal Institute of Neurology
MRI	Magnetic resonance imaging
NAPS-ERO	Nencki Affective Picture System Erotic Subset
OCD	Obsessive-compulsive disorder
OCI-R	Obsessive compulsive inventory revised
OFC	Orbitofrontal cortex
pOFC	Posterior orbitofrontal cortex
PPT	Pedunculopontine nucleus
PPU	Problematic pornography use
ROI	Region of interest
s-IATsex	Sexual Internet Addiction Test
SAST-R	Sexual addiction screening test revised
SN	Substantia nigra
SOGS	South-Oak gambling screen
STN	Subthalamic nucleus
TE	Echo time
THAL	Thalamus
TI	Inversion time
TR	Repetition time
UCS	Unconditional stimulus
vmPFC	Ventromedial prefrontal cortex
VP	Ventral pallidum
VTA	Ventral tegmental area
WHO	World Health Organization

1. Introduction

1.1. Compulsive Sexual Behaviors

The significant technological advancements witnessed in recent years have fundamentally transformed daily life, offering unprecedented conveniences such as easy access to information via the internet. However, this technological advancement is not without potential harm. Easy and unlimited access to high quality pornographic content is one of the consequences of this transformation (Kohut et al., 2020). In a recent study, Lewczuk, Wójcik and Gola (2019) demonstrated that the use of pornography between 2004 and 2016 increased over threefold in Poland, from estimated 2.76 million to 8.54 million active users, which corresponds to 7.7% to 25.1% of Polish population. While such access can fulfill some of the usual sexual needs of certain humans, increased *accessibility, affordability,* and *anonymity* to high quality pornographic content leads to a higher number of individuals consuming pornography regularly and extensively (Cooper, 1998). This "*Triple-A Engine*" (term introduced by Cooper) has been implicated in the escalation of ***Compulsive Sexual Behaviors (CSB*)** (Griffiths, 2012). For some individuals, the quantity and intensity of pornography consumption can gradually increase over time, leading to misuse or engagement in uncontrolled use of pornography, leading to negative consequences and becoming difficult to cease. This phenomenon is referred to as ***Problematic Pornography Use (PPU)*** and is understood as a common manifestation of ***CSB*** (Kafka, 2010; Antons & Brand, 2021). Indeed, up to 81% of treatment-seeking males in relation to loss of control over their sexual behaviors report problematic pornography use, 78% report compulsive masturbation and 45% risky and anonymous sexual contacts (Reid et al., 2012). The prevalence of ***CSB*** is ambiguously reported and it is estimated to range between 1-6% of the population (Sutton et al., 2014; Wéry & Billieux, 2017). This ambiguity in reported prevalence is in large part the result of varying terminology, definitions and methodology used in the research, and it highlights the urgent call for more comprehensive research.

The ***Compulsive Sexual Behaviors*** group of phenomena is characterized by repetitive, intrusive and disturbing sexual thoughts, urges and behaviors that negatively affect many aspects of the life of a person struggling with CSB. For years, researchers and clinicians used various terms, e.g. *sex addiction* (Schneider, 1991; Goodman, 1998), *hypersexuality disorder* (Kafka, 2010), *problematic pornography*

use (Kor et al., 2014; Gola et al., 2017), *pornography addiction* (D'Orlando, 2011), *cybersex addiction* (Brand et al., 2011), *internet sex addiction* (Griffiths, 2001); *excessive sexual desire disorder* (Carnes & Schneider, 2000) or CSB (Fong, 2006) somewhat interchangeably, sometimes differentiating between nuanced definitions. It was not until 2022 that the World Health Organization officially introduced the unit ***Compulsive Sexual Behavior Disorder*** **(*CSBD***) into the 11th edition of the International Classification of Diseases for Mortality and Morbidity Statistics Eleventh Revision (ICD-11, code 6C72, WHO, 2022). This entity is described as:

"*Compulsive sexual behaviour disorder is characterised by a persistent pattern of failure to control intense, repetitive sexual impulses or urges resulting in repetitive sexual behaviour. Symptoms may include repetitive sexual activities becoming a central focus of the person's life to the point of neglecting health and personal care or other interests, activities and responsibilities; numerous unsuccessful efforts to significantly reduce repetitive sexual behaviour; and continued repetitive sexual behaviour despite adverse consequences or deriving little or no satisfaction from it. The pattern of failure to control intense, sexual impulses or urges and resulting repetitive sexual behaviour is manifested over an extended period of time (e.g., 6 months or more), and causes marked distress or significant impairment in personal, family, social, educational, occupational, or other important areas of functioning. Distress that is entirely related to moral judgments and disapproval about sexual impulses, urges, or behaviours is not sufficient to meet this requirement.*" (WHO, 2022).

One of the current problems in psychiatry is understanding the mechanisms behind CSB. The occurrence of CSB is associated with a range of severe and persistent consequences, such as depressive symptoms, deterioration of personal and family relationships, difficulties in functioning in the workplace, and an overall reduction in quality of life (Duffy, Dawson & das Nair, 2016; Wéry & Billieux, 2017). Moreover, people struggling with CSB are increasingly seeking help from specialists (Gola, Lewczuk & Skorko, 2016; Kraus et al., 2016; Kühn and Gallinat, 2016).

The social relevance of this research is particularly high in light of the dramatic increase in the availability of the internet and pornography among children which co-occurs with an increased chance of developing problematic sexual behaviors in adolescents, interfering with their development (Efrati & Amichai-Hamburger, 2020). Indeed, in the United Kingdom, the average age of first

pornography use is 10, and that 12% of boys and girls before 12 years of age are using pornography regularly, i.e. at least one a week (Opinium Research, 2015). In Poland, in the 2006 to 2016 period, estimated 26% of girls and 24% of boys between 7-12 years of age viewed pornography at least once (Lewczuk, Wójcik & Gold, 2019). These phenomena have potentially broader implications in the near future, as the technology progresses, i.e. more stimulating pornographic materials, artificially generated content, more engaging interfaces and augmented online sexual interactions and sexual sponsoring.

Research indicates that CSBD predominantly affects men, who constitute the majority of individuals seeking treatment and participating in studies (Kafka, 2010; Gola, Lewczuk & Skorko, 2016). For instance, Gola, Lewczuk & Skorko (2016) found that men are more likely to report symptoms of CSBD, particularly those related to compulsive use of pornography and excessive masturbation. This male predominance may be influenced by sociocultural factors, including societal norms that make it more acceptable for men to express sexual concerns and seek help (Kraus et al., 2016; Gola & Potenza, 2018).

Most data on CSBD come from individuals exhibiting compulsive use of pornography and related behaviors, creating a bias in the understanding of the disorder (Reid et al., 2012; Gola et al., 2017; Wordecha et al., 2018). In a study involving a Polish sample of 3200 respondents seeking treatment for CSBD symptoms, the most common behavior was compulsive pornography use accompanied by excessive masturbation (Gola et al., in preparation). Other forms of compulsive sexual behaviors, such as engaging in risky or paid sexual activities, are less frequently reported or studied (Kraus et al., 2016; Kühn & Gallinat, 2016). Nevertheless, based on these data and insights, the ICD-11 CSBD has been proclaimed. However, this is not the only reason for fiery discussion among psychologists, psychiatrists and scientists on the controversial definition of the CSB.

1.2. Compulsive Sexual Behavior Disorder - controversy around diagnostic entity in ICD-11

The classification of CSB has been a subject of ongoing debate within the scientific community. While the recent ICD-11 officially recognizes CSBD, it categorizes it as an *Impulse Control Disorder* rather than an addictive disorder. This categorization has sparked controversy, as researchers are arguing that the accumulating evidence pointing to similarities between CSB and addiction warrants more targeted research and consideration about its reclassification as an addictive behavior (e.g. Gola et al., 2022; Rumpf & Montag, 2022; Liberg et al., 2022; Sinke et al., 2020; Draps et al., 2020; Bőthe et al., 2019; Gola & Draps, 2018; Kowalewska et al., 2018; Chatzittofis et al., 2016; Mechelmans et al., 2014; Kor et al., 2013). The discussion focuses on whether CSB symptoms stem from impulsivity, compulsivity, or are a form of behavioral addiction (Kingston & Firestone, 2008).

The idea of compulsivity in CSBD, as is reflected in the current name of the disorder in ICD-11, relates to CSB symptoms as similar to those in obsessive-compulsive disorder (OCD) (Bostwick & Bucci, 2008; Coleman et al., 2003; Fuss et al., 2019; Mick and Hollander, 2006). In OCD, the pathological cycle of obsession and compulsion is that intrusive thoughts trigger anxiety, while compulsions are undertaken to reduce it, despite causing significant distress (Schwartz & Abramowitz, 2005; Fineberg et al., 2014; Stein et al., 2019). From this perspective, patients with CSBD experience involuntary, intrusive thoughts with sexual content that lead to compulsive behavior to reduce tension. This interpretation was included in the diagnostic criteria of *Hypersexuality* proposed by Martin Kafka (Kafka, 2010). However, subsequent research has not confirmed that sexual behavior only serves the function of regulating negative emotions resulting from obsessive thoughts in CSB, resulting in the absence of such a criterion in the ICD-11 (Spenhoff et al., 2013; Reid et al., 2012; WHO, 2022). In fact, even the description of CSBD diagnostic criteria boundary with Obsessive-Compulsive Disorder in ICD-11 points out that despite the inclusion of “compulsive” in CSBD, “sexual behaviors in CSBD it not considered to be a true compulsion” (WHO, 2022).

On the other hand, impulse control disorders, to which CSBD is assigned in the ICD-11, are characterized by the inability to resist strong impulses to perform activities that are harmful to oneself or others (WHO, 2022). Examples include pyromania and kleptomania. In these disorders, there is a build-up of tension before

the behavior, temporary relief during, and guilt after the behavior (Garcia & Thibaut, 2010). The placement of CSBD in this category stems from the observation of patients' repeated inability to refrain from sexual behavior despite awareness of its long-term negative consequences (Grant et al., 2014; Kraus et al., 2018; Stein et al., 2016). However, the lack of clear evidence of high levels of impulsivity among patients with CSBD and impaired control of sexual behavior raises doubts about this classification (Draps et al., 2021, Antons & Brand, 2018; Bőthe et al., 2019; Potenza et al., 2017).

The phenomenological similarity between CSB and behavioral addictions has been studied for many years. The introduction of the category of “substance-related disorders and addictions” in the DSM-5 and therein inclusion of gambling disorder (APA, 2013) opened the door to a broader understanding of addiction. Researchers point to symptoms such as compulsive craving (craving), focus on compulsive behavior, emotional changes, and difficulty maintaining abstinence as common to substance addiction and CSB (Griffiths, 2005; Miner et al., 2019; Reid et al., 2012; Wordecha et al, 2018). Additionally, neurobiological similarities and the appetitive nature of sexual behavior support this analogy (Sassover & Weinstein; 2020; Kowalewska et al., 2018; Gola et al., 2017; Kühn & Gallinat, 2016; Young, 2008). Some researchers even suggest the existence of a withdrawal syndrome in CSB, manifested by negative emotional states (Karila et al., 2014; Lewczuk et al., 2022; Fernandez, Kuss & Griffiths, 2021; Garcia and Thibaut, 2010). This debate is not an isolated case, though, as gambling disorder has gone through a similar classification path, initially being categorized as an impulse control disorder and then, after accumulating scientific evidence, being classified as a behavioral addiction (Potenza, 2006, 2015). Researchers wonder whether a similar reclassification will occur for CSBD (Kraus, Voon, & Potenza, 2016). For this to be possible, however, additional scientific evidence needs to be gathered to better describe the mechanisms of how this disorder is created and maintained (Bőthe et al., 2019; Gola & Potenza, 2018). This shift in classification reflects a growing understanding of the role of reward system dysfunction and loss of control in these conditions, leading to behavioral symptoms comparable to those observed in substance use disorders.

1.3. Theoretical model of addictive behaviors

One of the most widely discussed conceptions of CSB symptoms emergence within behavioral addiction (Antons & Brand 2020; Golec et al., 2021; Gola et al., 2017; Draps et al., 2022; Seok & Sohn 2020; Sinke et al. 2020; Starcke et al., 2018; Liberg et al. 2022; Voon et al., 2014; Wang et al., 2024; Wang & Dai 2020; Wang & Li, 2023; Wang, Chen & Zhang, 2021; for review see: Klein et al., 2021) is the Incentive Sensitization Theory of Addiction model (Robinson & Berridge, 1993, 2001, 2008). Although this model was created to explain the mechanisms behind the emergence and maintenance of chemical addictions, it has been extended to behavioral addictions as well (Berridge & Robinson, 2016). Its usefulness has been appreciated in understanding behavioral addictions like gambling disorder or gaming disorder (Brewer & Potenza, 2006; Grant & Chamberlain, 2016; Thomsen et al., 2014; Linnet et al. 2012, Limbrick-Oldfield et al. 2017, Anselme & Robinson 2020; Diers et al., 2023).

The Incentive Sensitization Theory aims to explain the mechanisms of emergence of persistent craving and seeking behavior observed in addiction. It distinguishes between the hedonic experience of a reward ("liking") and the motivational drive to obtain it ("wanting"), and posits that addiction is primarily driven by an excessive "wanting" or craving (albeit not necessarily with cognitive component of desire), even if the "liking" or pleasure derived from the behavior diminishes over time (sometimes to experiencing no pleasure at all). This heightened "wanting" is attributed to the process of incentive sensitization, a neurobiological adaptation in the brain's reward system that occurs with repeated exposure to rewarding stimuli (Figure 1). Repeated exposure to rewarding stimuli leads to an amplified attribution of incentive salience to the cues that predict their availability via process of associative learning - both classical and instrumental conditioning. Cues associated with the reward, such as drug paraphernalia, gambling environments, or sexual images, become increasingly attention-grabbing and trigger strong motivational urges to engage in the associated behavior e.g. binge drinking, gambling or CSB (Anderson & Yantis, 2013). To illustrate this process, we can imagine a person who starts smoking cigarettes. At first, the urge to smoke is not compelling, and is usually triggered in social situations. The pleasure from smoking a cigarette is rewarding, but as the time goes on, pleasure is transformed to mere relief, but the urge itself is becoming stronger. Additionally, a

sight of another person smoking a cigarette, or associated with smoking stimuli like a smell of coffee, will ignite arousal directed to fulfilling the compulsive urge to smoke.

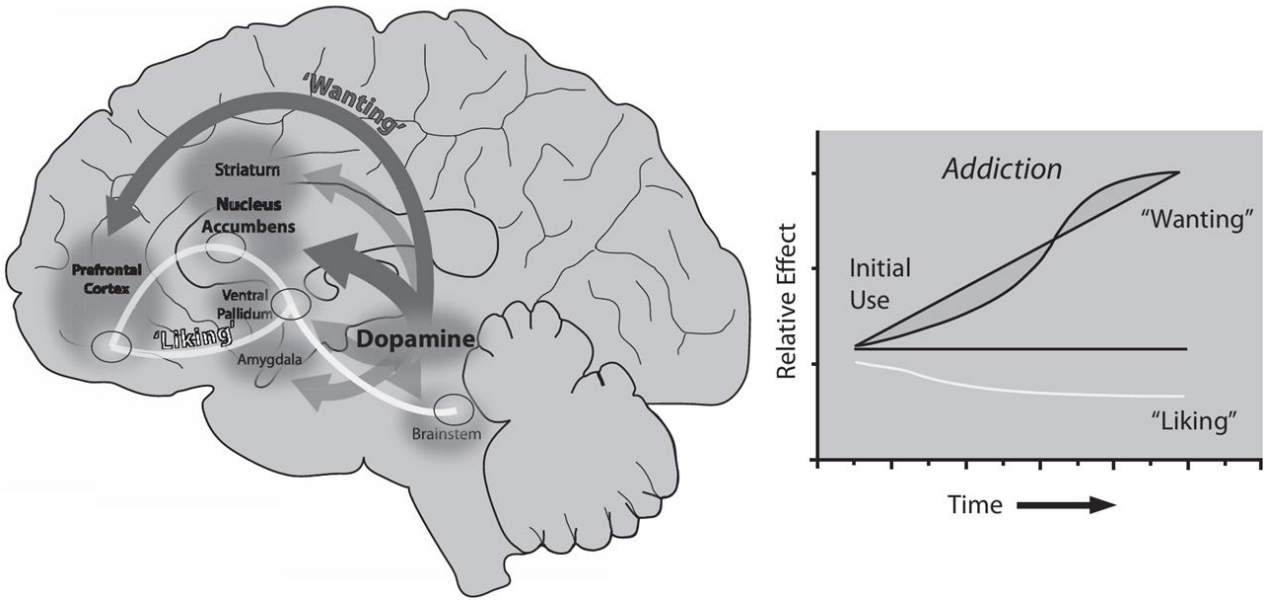

Figure 1. The Incentive Sensitization Theory of addiction progression with “wanting” and “liking” components emphasized and their neuronal pathways. Dopaminergic pathways support the “wanting” - the salient stimuli or behavior sensitize mesolimbic pathways, increasing the motivation and goal-directed behaviors towards repeated pleasant experience. Mesocortical pathways drive the subjective pleasantness of the experience itself - the “liking”, which may diminish over time. Importantly, the discrepancy of motivation and positive experience grows over time. Reproduced with permission from: Berridge & Robinson (2016). Liking, wanting, and the incentive-sensitization theory of addiction. *The American psychologist*, *71*(8), 670–679. Copyright © 2016 by American Psychological Association.

The sensitization process involves neurobiological changes within the mesolimbic dopamine system. This pathway originates in the ventral tegmental area (VTA) and projects to several brain regions, including the ventral striatum (with its nucleus accumbens), dorsal striatum, amygdala, ventromedial prefrontal and orbitofrontal cortices (described in more details in subsection 1.7). The "liking", on the other hand, can be traced to the hedonic “hotspots” sharing some of the regional overlap, i.e. ventral striatum, ventromedial prefrontal and medial orbitofrontal cortices. (Berridge & Kringelbach, 2015). From neuromodulatory point of view, dopamine plays a central role in neurotransmitting process of "wanting" and the

experience of "liking" is more (but not exclusively) connected to the opioid and endocannabinoid systems within mesocorticolimbic pathways (Berridge & Kringelbach, 2015). In addiction, incentive sensitization is related to amplification of "wanting", without necessarily affecting "liking". It means that patients can experience compulsive urges to pursue addictive substances/behaviors, yet the satisfaction or pleasure from actual outcome is on a minimal level. Dysregulation of dopamine in the reward system may lead to various other psychiatric symptoms and disorders, like consummatory and motivational anhedonia in major depressive disorder, and motivational anhedonia and psychosis in schizophrenia. Indeed, the motivational anhedonia is directly related to the deficit of “wanting” (Szczypiński & Gola, 2017). Importantly, the addicted brain’s reward system is not hyperactive at all times, but rather is hyper-reactive (sensitive) towards the addiction-related cues of rewarding outcomes, triggering short-term arousal and a state of motivation. This increased reactivity is further influenced by the process of associative learning, which is vital in the shift from perceiving stimuli as neutral to viewing them as addictive. This shift enhances attention and goal-oriented behavior toward these context-dependent stimuli, further perpetuating the cycle. From the perspective of Incentive Sensitization Theory, this constellation of phenomena is important not only in development of addiction but is critical for persistence of addictive compulsions and propensity to relapses (Berridge & Robinson, 2016).

1.4. Incentive Sensitization in CSB

A question of great importance concerns the causes of increased sensitivity to erotic stimuli cues in CSB subjects. Some researchers (Kühn and Gallinat, 2016; 2014; Kor et al., 2014, Hoffman et al, 2014) state that it results from sensitization caused by frequent pornography consumption, others suppose it to be an individual trait related to increased sexual needs (see for review: Ley et al., 2014; Prause et al., 2015, cf. review by Gola, 2016c). Regardless of the position in that discussion, scientists agree upon insufficient evidence for any explicit conclusions and therefore point at the need for further studies.

One of the predictions of pathological incentive sensitization is for the desired stimuli, or cues associated with them, to produce strong, conditioned automatic approach behaviors (Berridge, 2012; Flagel & Robinson, 2017), influencing cognitive resources, i.e. attention to be biased towards those cues (Franken, 2003).

This is one of the reasons for relapse propensity among addicted individuals (Field & Cox, 2008; Field, Munafo & Franken, 2009; Marissen et al., 2006; Tibboel, Houwer & Field, 2010). Indeed, attentional bias towards visual sexual stimuli (or related to them) among either individuals with CSB or correlational analysis with symptoms on general population, has been demonstrated using various experimental cognitive tasks (Albery et al., 2017; Draps et al., 2021; Mechelmans et al, 2014; Pekal et al, 2018; Wang, Chen, & Zhang, 2021), supporting the sensitization view.

The experiment conducted by Flagel et al. (2011), based on an animal model and Incentive Sensitization Theory framework, demonstrated that rats can be divided into two groups with respect to their high or low novelty response trait, which is related to impulse control and the amount of dopamine released in nucleus accumbens. Rats with high novelty response were learning the cue-reward relationship faster, had increasing dopamine releases for subsequent cue exposition (related to *wanting*), which was decreasing for food rewards (related to *liking*). The low novelty response group exhibited a stable pattern of nucleus accumbens activity for both stimuli throughout the training sessions (see Figure 2).

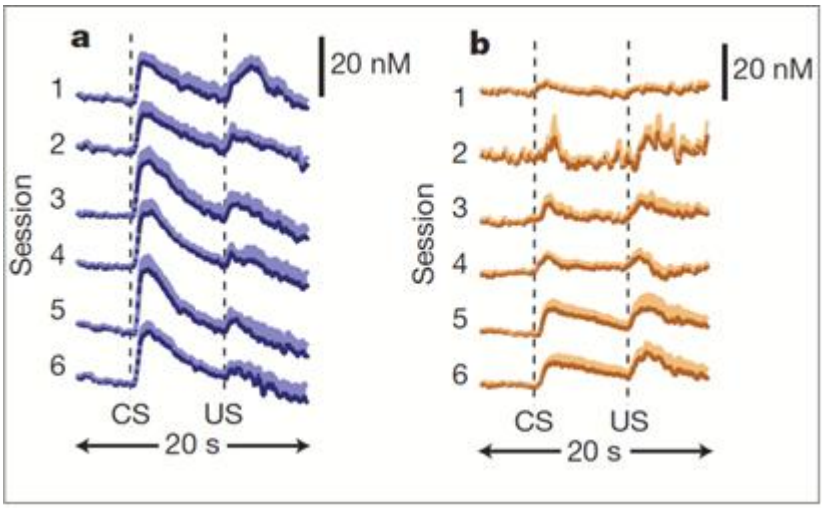

Figure 2. Activity of dopaminergic neurons in nucleus accumbens in response to conditioned stimuli (CS; cues) and unconditioned stimuli (US, rewards) throughout 6 classical conditioning sessions. Illustration of: a) high *novelty-response* rats; b) low *novelty-response* rats. Reproduced with permission from: Flagel et al. (2011). A selective role for dopamine in stimulus-reward learning. *Nature*, 469(7328), 53–57. Springer Nature. Copyright © 2011, Springer Nature Limited.

Two important conclusions emerge from the Flagel et al. (2011) study: 1) increased reward-circuit sensitivity (especially within ventral striatum) is related to

learning rate of the reward cues and development of specific addictive behaviors; 2) it appears to be an individual trait stable in time. The second conclusion finds partial confirmation in a couple of human studies, showing that high novelty-seeking co-occurs with chemical addictions and pathological gambling (e.g. Banca et al., 2015; Redolat et al., 2009, Belin et al., 2011). On the other hand, studies of subjects successfully withdrawing from addictions, fighting the urge for reaction triggered by stimuli previously associated with addiction-related stimuli, are rather pointing to the conclusion that these cues may be extinct or re-learned. A behavioral study by Negash et al. (2016) could address these two conclusions in relation to CSB – they observed a negative relationship between delay discounting and frequency of pornography consumption in a sample of general population (both males and females). These subjects then refrained from pornography consumption for 3 weeks, which improved their delay discounting, whereas the control group who refrained from consuming their favorite food/snacks did not improve. Delay discounting is related to impulse control (Winstanley, 2010) and it is diminished in substance and behavioral addictions (e.g. Dixon et al., 2006). These results indirectly point at the feasibility of attenuating the addictive pattern of CSB, although in another study on CSB patients no group differences were reported in Sexual Discounting Task (Draps et al., 2021). Nevertheless, to better characterize and understand the development of propensity for sensitization towards sexual stimuli and behaviors, and the resulting compulsive behaviors among individuals with CSB, an associative learning framework can be used.

1.5. Association learning through conditioning and extinction processes

The process of conditioning is fundamental for learning and adapting to the environment (Pavlov, 1927). It is based on the association of two initially independent stimuli (or events), through their co-occurrence in time, leading to the transfer of the subjective value of the following stimulus to the preceding one. The preceding stimulus (cue) is called a conditioned stimulus (CS), while the following stimulus paired with it, is called an unconditioned stimulus (US or UCS). The US has to have intrinsic value in order to be a successful reinforcer (Holland, 1990). There are two basic types of conditioning: classical (Pavlovian) and instrumental (operant; Skinner, 1937). In classical conditioning, the co-occurrence of stimuli is a sufficient condition for the value transfer process to occur. In instrumental

conditioning, the appearance of the second stimulus occurs only after an adequate action is carried out by the actor, thus reinforcing the action in context of the CS that led to receiving the reward or avoidance of punishment (see Figure 3). Appetitive form of conditioning has rewarding stimuli as its US, and US are usually of sufficient value to the actor for there to be motivation to obtain them. Successful appetitive conditioning results in an emotional/motivational response to the appearance of the CS, which gives rise to the cue-reactivity phenomenon posited in Incentive Sensitization Theory (Starcke et al., 2018; Robinson & Berridge, 1993, 2001). Conditioning processes are crucial in the development and maintenance of addictive behaviors (Everitt & Robbins, 2005; Robinson & Berridge, 1993, 2001; Torregrossa, Corlett, & Taylor, 2011). Conditioning and reinforcement learning are also linked to cue-reactivity and craving (Carter & Tiffany, 1999; Drummond, 2001; Scott & Hiroi, 2011; Skinner & Aubin, 2010; Weiss, 2005).

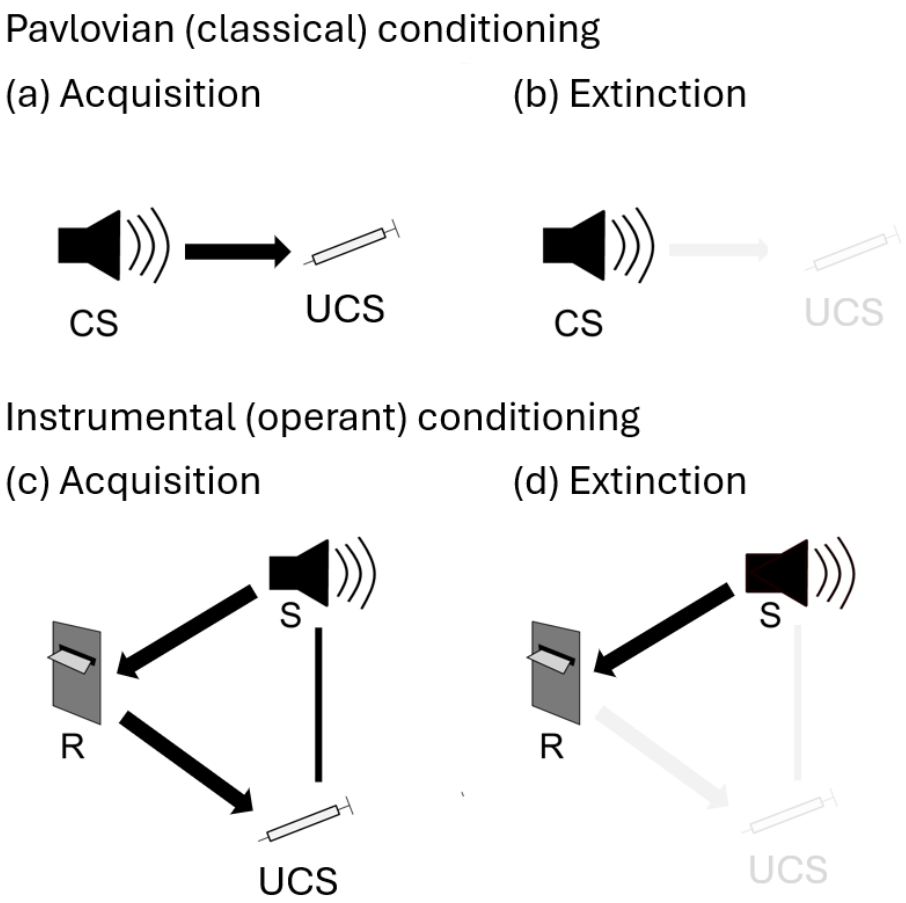

Figure 3. Basic conditioning and extinction designs. In classical conditioning, (a) acquisition of association between neutral stimulus (S) and rewarding/aversive unconditioned stimulus (US) is produced by temporally coherent occurrences of neutral stimulus and outcome US.

Once the association is acquired, the previously neutral stimulus becomes a conditioned stimulus (CS), and (b) extinction is then possible. In extinction, the US is no longer delivered after the presentation of CS, which drives new (lack of) association between CS and USC. In instrumental (c) conditioning, association is reinforced between US and action/choice performed by the subject in context of presented S. In instrumental extinction then, the new (lack of) association is between the action and UCS. Reproduced and modified under CC-BY 4.0 license from: Lay & Khoo (2021). Associative processes in addiction relapse models: A review of their Pavlovian and instrumental mechanisms, history, and terminology. *Neuroanatomy and Behaviour*, 3, e18.

Extinction is another important form of associative learning, in which the previous association between CS and (CS-UCS) or between action connected to CS and UCS (action-UCS) relationship is discontinued, leading to eventual inhibition of the motivational response. This inhibition is the result of learning a new (lack of) CS-UCS relationship, which masks previously developed association (Konorski, 1967; Quirk & Mueller, 2008). Extinction is a fundamental process aiding reduction in unadaptive reactions and behaviors, and it is an essential mechanism in psychotherapy (Millan, Marchant, & McNally, 2011). Indeed, therapies based on extinction, such as virtual exposure or cue exposure, were demonstrated to be effective in substance use disorder and behavioral addictions (Segawa et al., 2020; Byrne et al., 2019; Waters et al., 2004; Conklin & Tiffany, 2002), although mounting evidence shows that this effectiveness is nuanced and not applicable to every clinical population (Torregrossa & Taylor, 2013).

1.6 Conditioning and CSB

As described in Incentive Sensitization Theory, the emergence of cue-reactivity through associative learning may play an important role in the development and persistence of addictive behavior, including the formation of CSB symptoms. Interestingly, previous neuroimaging studies of cue-reactivity in CSB sample (more precisely subjects suffering mainly with symptoms connected to the problematic pornography use) have shown similarities between this disorder and other behavioral addictions, reporting increased reactivity of the subcortical area, i.e. bilateral (Gola et al., 2017) or right (Golec et al., 2021) ventral striatum and the right orbitofrontal cortex (Golec et al., 2021) during stimulation with cues of erotic

rewards, but in study on general male (non-clinical) sample researchers found no correlation of reactivity of the both (right and left) ventral striata with indicators of problematic pornography use, time spent on pornography use, or with trait sexual motivation (Markert et al. 2021). However, adding to the complexity of comparing the results, a study by Markert et al. (2021) used neutral cue preluding rewards, unlike the two former studies (Gola et al., 2017; Golec et al., 2021), which used pictograms of naked women.

The associative learning process itself has so far been examined in only two neuroimaging studies (Klucken et al., 2016; Banca et al., 2016) and three behavioral studies (Snagowski et al. 2016; Wells et al. 2022; Hoffmann et al. 2014), in either diagnosed CSB patients or among general male population of pornography users. In their 2022 study, Wells et al. used Pavlovian and instrumental conditioning to probe alterations in associative learning related to CSB symptoms severity. To this end, the general male pornography user's population was divided into high and low-severity by median split based on Internet Sex Screening Test—Online Sexual Behaviours (ISST-OSB, Delmonico & Miller, 2003). They found no significant differences between such defined groups in either self-report or behavioral effects of conditioning. Importantly, though, only monetary rewards were included in this procedure, aiming to evaluate general propensity to altered conditioning, and not specifically towards erotic stimuli. It is worth noting that therefore no sexual context was present in this study. Sagnowski and colleagues (2016), also on a sample of general male pornography using subjects, studied relationship between cybersex addiction tendencies (measured with Sexual Internet Addiction Test, s-IATsex; Laier et al., 2013) and associative learning with erotic-only stimuli. Authors found that cybersex addiction tendencies were positively related to conditioning effects, i.e. the higher the tendencies the stronger self-reported sexual arousal and erotic CS valence change between pre- and post-conditioning. This was not the case for control CS, i.e. cue signaling no reward. Importantly, there were no other types of rewarding stimuli to test the specificity of these effects. Hoffman and colleagues (2014) used a different approach to conditioning, as well as studied sample in their pilot study. They recruited "men who have sex with men", who also think they might be "sex addicts". Then, based on the Sexual Compulsivity Scale (Kalichman et al., 1994), they were divided into high- and low-severity of experienced symptoms groups. The experimental procedure involved classical conditioning with odors as

cues and sexuality explicit short video material (or no reward for control group). The measures used to probe the conditioning effects were genital response, implicit and explicit affective response, sexual risk-taking task and CS-UCC contingency, i.e. association between cue and outcome stimulus. While only physiological and implicit measures captured increased conditioning effects in high-severity experimental groups, these conditioning effects were not discriminative between erotic and neural cues, i.e. any odor cue elicited arousal, unlike the results of Sagnowski and colleagues (2016). Similarly, only erotic vs. control stimuli were used. As demonstrated, these behavioral studies used conditioning tasks that included both classical and instrumental aspects to investigate the phenomenon of altered associative learning in the contexts of CSB, but varying methodology used therein obscures conclusions.

To investigate on a neuronal level, in a study conducted by Banca and colleagues (2016), researchers used two conditioning tasks: one outside the magnetic resonance imaging (MRI) scanner, which had classical conditioning followed by instrumental conditioning phases, and a second classical conditioning task inside the MRI scanner. In the behavioral part, researchers found an increased behavioral non-reward-dependent (towards both monetary and erotic cues) instrumental conditioning effect among CSB subjects. However, they found no differences in brain activity related to cue processing. The second study by Klucken et al. (2016), also used classical conditioning, but with erotic rewards only. Researchers demonstrated no self-reported nor psychophysiological effects of altered conditioning in the CSB group. On neuronal level they found increased amygdala responses towards rewarding (erotic) cues in the CSB group. Results of functional connectivity during conditioning task revealed decreased connectivity between bilateral ventral striatum and right ventromedial prefrontal cortex in the CSB group compared to healthy subjects (see Figure 4).

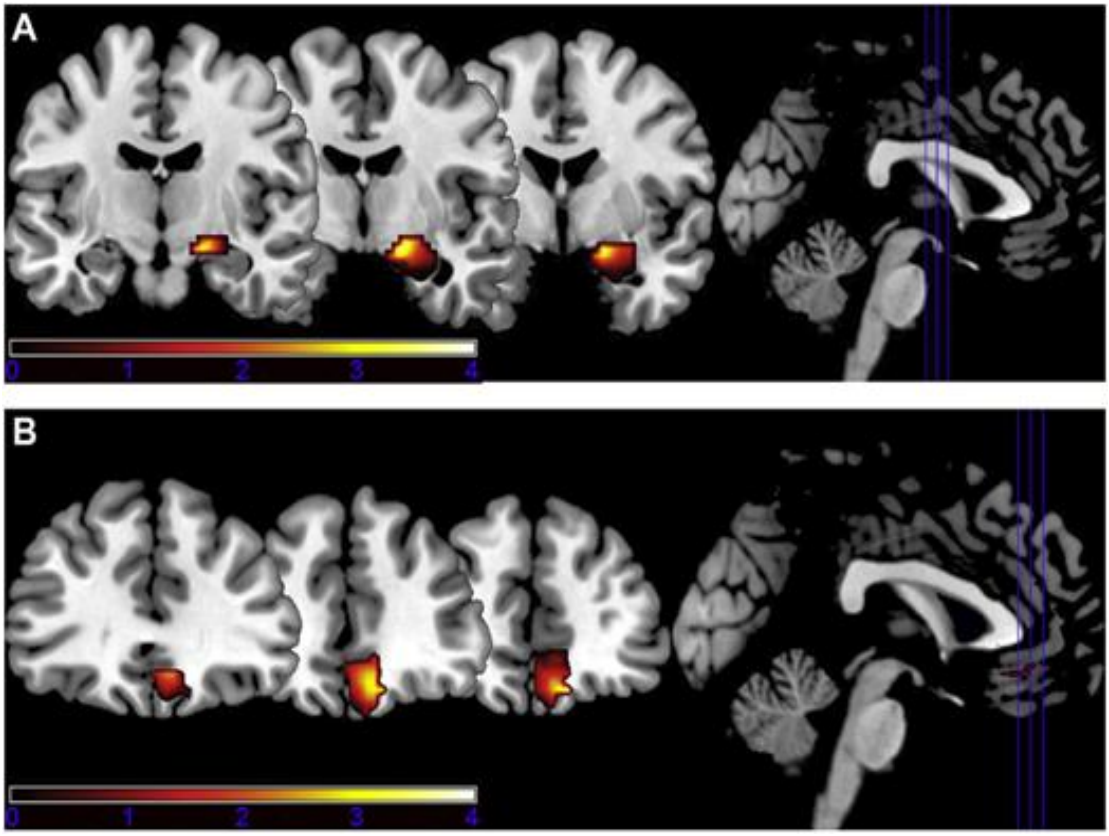

Figure 4. The neuroimaging results of conditioning in CSB vs. healthy control subjects from a study by Klucken et al., (2016). Only erotic or no reward outcomes were presented to the participants. (a) The right amygdala in CSB group had higher activation for erotic vs. control cue; (b) the functional connectivity between bilateral ventral striatum and ventromedial prefrontal cortex was lower in CSB group in similar to (a) erotic vs. control conditions contrast. No altered functional connectivity was found between amygdala and ventromedial prefrontal cortex. Reproduced with permission from: Klucken et al. (2016). Altered Appetitive Conditioning and Neural Connectivity in Subjects With Compulsive Sexual Behavior. *The journal of sexual medicine*, 13(4), 627–636. by permission of Oxford University Press. Copyright © 2016, International Society for Sexual Medicine. Published by Elsevier Inc. All rights reserved.

As for the appetitive extinction process, to date there have been no direct studies specifically on behavioral level. However, in a neuroimaging study, an extinction procedure was conducted as part of a larger battery of experimental tasks (Banca et al., 2016). In this study, participants underwent the classical extinction task, i.e. after previously associated CS-UCS (erotic pictures) through classical conditioning, individuals were presented with CS but without the expected rewarding outcome. While no significant group differences (CSB vs. healthy control) were

found in neither self-reported valence post-extinction nor brain activations towards the cues, it is important to note that the statistical thresholds used for the neuroimaging part was relatively restrictive compared to the sample size - no hypothesis-driven a priori region-of-interest analysis was performed to alleviate this matter. Such an approach is one of the most commonly used in neuroimaging studies to increase the power of statistical testing of otherwise restrictive thresholding regimes (Poldrack, 2007).

As demonstrated, the current understanding of this area of research is severely limited, with a significant gap in empirical evidence on behavioral and most importantly neurobiological level of understanding. Given the parallels between CSB and addictive behaviors (Brand et al., 2020), the Incentive Sensitization Theory with conditioning and extinction processes at its core, emerges as a potential framework for explaining the mechanisms underlying CSB symptoms. The persistence of these symptoms might be interpreted as an abnormal extinction process with noticeable neglect of negative consequences in patients' personal and professional life. As previously demonstrated, central to this theory is the brain's reward system, particularly the mesolimbic dopamine pathway, which is implicated in the attribution of incentive salience to rewarding stimuli. Studying the brain reward system within this theoretical context is therefore crucial to advancing the understanding of mechanisms driving CSB.

1.7. Brain reward system and its role in associative learning

The human reward system is a sophisticated network of neural circuits that underlie the processes of motivation, pleasure, and reinforcement learning. Central to this system, especially in reinforcement learning and motivation, are the mesolimbic and mesocortical dopamine pathways, which play critical roles in evaluating rewarding stimuli and guiding goal-directed behaviors such as behaviors related to gaining human needs and goals (Olds & Milner, 1954; Berridge, 2001; Wise, 2004), although reward system is a complex network of afferent and efferent connections using various neurotransmitter communication pathways, including glutaminergic, GABAminergic, serotonergic, noradrenergic, opioid and endocannabinoid systems, showcasing myriad of self-regulating properties (Bayassi-Jakowicka et al., 2021; Berridge & Kringelbach, 2015). In the context of addiction, reward circuitry becomes dysregulated, leading to compulsive seeking of

substances or behaviors despite adverse consequences, e.g. continuing to gamble, seeking the sensation of excitement, despite losses resulting in not having enough resources to sustain oneself, or even going into debt (Koob & Volkov, 2010). Mirroring many of the mechanisms observed in substance use disorders, the reward system in the human brain plays a crucial role in the development and maintenance of behavioral addictions e.g. pathological gambling or gaming (Grant et al., 2010; Potenza, 2006). The role of altered dopamine signaling within the striatum in gaming disorder and gambling disorder has also started to be explored by scientists (Weinstein et al., 2017; Grant et al., 2016).

The ventral striatum serves as a critical hub in the reward circuitry (see Figure 5). While there is no clear cytoarchitectonic boundary between ventral and dorsal parts of the striatum, the afferent projections from reward/punishment processing parts of prefrontal, orbitofrontal and limbic structures are more prominent to the former one, especially from amygdala and hippocampus (Haber, 2009). Central and most studied part of ventral striatum is the nucleus accumbens, but it also comprises ventromedial parts of putamen and caudate and posterior parts of olfactory tubercle (Fudge and Haber, 2002). It is connected via extensive pathways with the prefrontal, orbitofrontal and dorsal anterior cingulate cortices (Haber & Knutson, 2010). The ventral striatum also integrates signals from limbic structures such as the amygdala and hippocampus, allowing it to assess the motivational significance of stimuli and influence decision-making processes (Heimer et al., 1982; Kelley & Berridge, 2002). Dopamine release in the ventral striatum is associated with the reward expectation and reinforcement of behaviors through conditioning that lead to rewards (Schultz, 2000; Wise, 2004). In addiction, this system is hijacked by causing exaggerated dopamine release, reinforcing drug-taking or problematic behavior and contributing to the development of more compulsive use (Volkow et al., 2016; Koob & Volkow, 2010). The identified core similarities between substance use disorder and behavioral addictions in regards to the altered neuronal characteristics are the hypersensitive ventral striatum, hypoactive inhibitory functions of dorsolateral and ventrolateral prefrontal cortices and altered amygdala responses towards both negative (threatening/stressful) and rewarding stimuli (Zeng et al., 2023), all of which are crucial for cognitive functions subserving adaptive behaviors, like learning and memory processes (Ngetich et al., 2024).

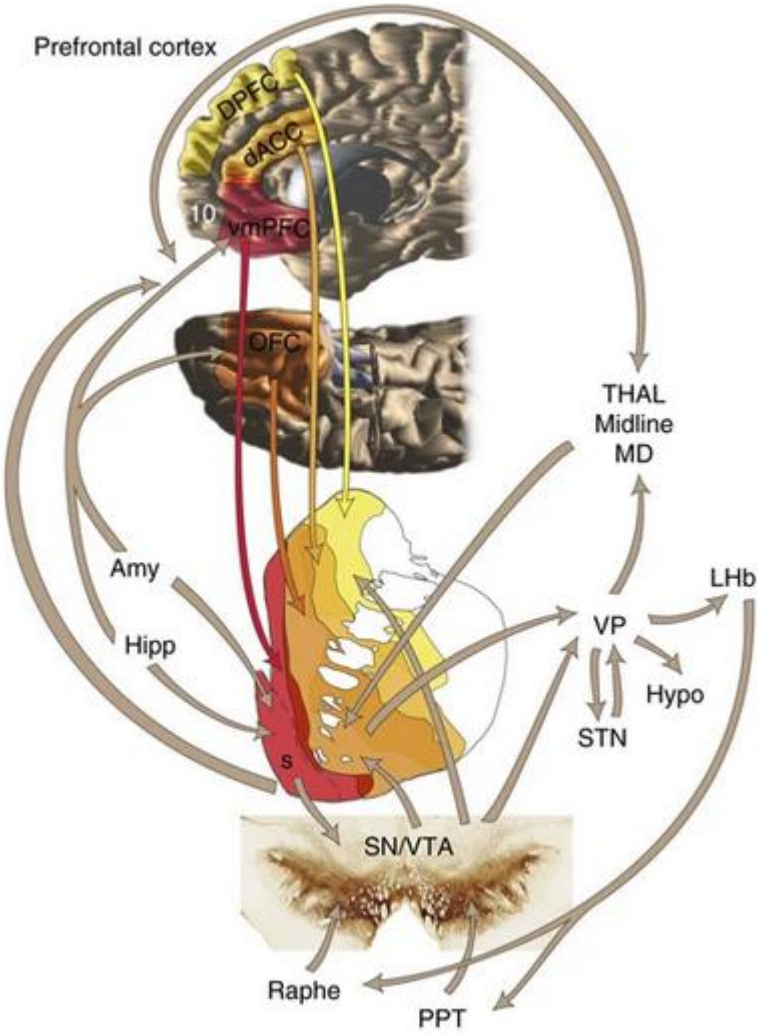

Figure 5. Reward system's key regions and their pathways. At the heart is the striatum, and the gradient from ventral to dorsal is depicted from red to white, accordingly. Similarly, the colors of the arrows reflect connectivity between each cortical area and the part of the striatum. Other subcortical pathways between each other, to striatal and to the cortical areas are depicted in gray. LHb-lateral habenula; STN-subthalamic nucleus; Hypo-hypothalamus; THAL-thalamus; VP-ventral pallidum; Hipp-hippocampus; Amy-amygdala; SN/VTA-substantia nigra/ventral tegmental area; PPT-pedunculopontine nucleus, S-shell; OFC-orbitofrontal cortex; vmPFC-ventromedial prefrontal cortex; dlPFC-dorsolateral prefrontal cortex; DPFC-dorsal prefrontal cortex. Reproduced with permission from: Haber, S. N., & Knutson, B. (2010). The reward circuit: linking primate anatomy and human imaging. *Neuropsychopharmacology: official publication of the American College of Neuropsychopharmacology*, 35(1), 4–26. Springer Nature. Copyright © 2009, American College of Neuropsychopharmacology.

The orbitofrontal cortex, especially its medial subregions, constitute a crucial region for value encoding, including its probability and magnitude, as well as updating the stimulus-outcome contingencies (Rudebeck & Murray, 2014; Rudebeck et al., 2013). In fact, based on studies on animal models, lesions in this region impedes re-evaluation of change in stimulus-outcome from rewarding to lack of reward (Izquierdo et al., 2004; Pickens et al., 2003; Gallagher, McMahan & Schoenbaum, 1999). It maps both primary (like food or sex) and secondary (like social or monetary) rewards, and with its dense projections to ventral striatum and amygdala, it regulates the motivational “approach” reactions and emotional salience of stimuli (Rudebeck et al., 2013). Medial orbitofrontal cortex has been demonstrated to play an important role in addition and other behavioral dysregulations (Volkow & Fowler, 2000). Interestingly, while the value of rewarding stimuli is mostly encoded in medial orbitofrontal cortex, lateral orbitofrontal cortex responds to negative stimuli (O'Doherty et al., 2001).

Closely related to medial parts of orbitofrontal cortex and ventral striatum, both spatially and in neuronal processing stream, ventromedial prefrontal cortex is thought to compute decision-costs and other external contingencies in addition to subjective value forwarded by orbitofrontal cortex. The ventromedial prefrontal cortex then informs reaction choice via connections to the dorsal anterior cingulate cortex and to the supplementary motor area (Barta, McGuire & Kable, 2013; Diekhof et al., 2012; Grabenhorst & Rolls, 2011). Interestingly, ventromedial prefrontal cortex is a critical component of extinction and reversal learning, which was extensively demonstrated in fear extinction, but also in appetitive extinction (Konova et al., 2017; Konova & Goldstein, 2019; Kruse et al., 2020). Indeed, ventromedial prefrontal cortex thickness as well as activity has been documented to be associated with extinction success, implicating its role in adaptive inhibition of mismatched or negative associations (Ebrahimi et al., 2019; Milad and Quirk, 2012; Phelps et al., 2004). Insufficient context updating in face of increasingly adverse consequences of actions is a hallmark in addiction, and aberrant ventromedial prefrontal cortex is emerging as one of the culprits of that phenomena (Konova & Goldstein, 2019).

The dorsal anterior cingulate cortex is a part of salience brain network, and it serves as a hub for diverse signals computation due to its unique neuronal projections with limbic, prefrontal and motor areas. As dorsal anterior cingulate is a versatile area, critically involved in cognitive, emotional/motivational and motor

functions, it has been a focus of vast amounts of neuroimaging studies. Its role has been proposed to be monitoring, controlling and outcome evaluation, especially in goal-directed behaviors (Heilbronner & Hayden, 2016), although its exact computational functions remain controversial (Shenhav, Cohen & Botvinick, 2016). The complex nature of the role of dorsal anterior cingulate in reward processing is proposed to be related in all three of the latter functions, as it continuously analyzes any conflict or competition between internal model (motivational and cognitive) and external contingency of stimuli or associations, indicating a required modulation of cognitive resources and motor actions to adjust arisen discrepancy (Yee et al., 2021; Shenhav et al. 2013). It is therefore an important part of associative learning. Unlike the orbitofrontal cortex areas, the dorsal anterior cingulate cortex seems to be activated regardless of type of reward (Kennerley, Behrens & Wallis, 2011).

The amygdala resides in the mesial temporal lobe, and it is a key structure of the limbic system. It was traditionally known for its role in processing emotions such as fear and anxiety (Ehrlich et al., 2009). However, extensive scientific research has documented its critical involvement in the brain's reward system, influencing reward processing, motivation, and reinforcement learning (Malvaez, Greenfield & Wassum, 2019; Sah et al., 2003). Its crucial role in both appetitive and fear conditioning, and more generally in associative learning, is related to encoding emotional valence elicited by the outcome stimuli, which is then transferred to the preceding stimuli or undertaken action (Martin-Soelch, Linthicum & Ernst, 2007; Everitt et al., 2003). It interacts with key regions involved in reward circuitry, including the ventral striatum, orbitofrontal and ventromedial prefrontal cortices, hippocampus, ventral tegmental area, as well as thalamus (Janak & Tye, 2015). The amygdala’s complex involvement in emotional, learning and memory processing is in part related to its anatomy - while many anatomical and functional parcelations of amygdala have been proposed, its basic components are basolateral, central and medial (Sah et al., 2003; Avecillas-Chasin et al., 2023), although in human neuroimaging it is rarely considered in its subsections due to relatively small volume and physiological noise impacts (Boubela et al., 2015).

1.8. Reward system in CSB

The ventral striatum is central to the Incentive Sensitization Theory of Addiction, which suggests that over time, cues (both understood as environmental

cues in the form of visual, auditory stimuli, etc., but also internal cues such as given emotional states) associated with rewards (such as sexual stimuli) become hyper-salient, leading to compulsive behaviors even in the reduction or in the absence of pleasure (Robinson & Berridge, 2008). Indeed, heightened ventral striatum activity, along with behaviorally measured motivation in response to explicit sexual cues was demonstrated in individuals with CSB, suggesting an overactivation of this reward system in the presence of conditioned stimuli specific for CSB (Gola et al., 2017).

The relationship between reward system's functions and the formation and inhibition of CS-UCS or action-US relationships in humans is complex and far from well understood, but several key brain regions were identified in studies in both general and clinical populations, including patients with lesions. These regions involve the ventral striatum, orbitofrontal cortex, amygdala, ventromedial prefrontal cortex, and dorsal anterior cingulate cortex, although the complete list of those regions and their role in appetitive conditioning processes in human literature remains debated, as experimental tasks used to study these complex phenomena vary (Corlett, Mollick & Kober, 2022; Klein et al., 2022; Kurse et al. 2020; Chase et al, 2015; Martin-Soelch, Linthicum, & Ernst, 2007). These regions has been previously described as altered in CSB, in more broad experimental context of cue-reactivity (Engel et al., 2023; Voon et al., 2014; Klucken et al., 2016; Banca et al., 2016; Gola et al., 2017; Golec et al., 2021), suggesting that similarly to other behavioral addictions, functional alterations in these key reward system regions could be related to the development and persistence of CSB symptoms. Indeed, in a functional MRI study during which subjects were exposed to 9 second videos of either sexually explicit, mildly erotic, non-sexual exciting, monetary and control, individuals with CSB displayed increased activity of ventral striatum, dorsal anterior cingulate cortex, amygdala and substantia nigra (Voon et al., 2014). This between-group difference was only significant in sexually explicit vs. non-sexual exciting conditions contrast. Additionally, functional connectivity between dorsal anterior cingulate as a seed region, and the other three regions were positively correlated with self-reported sexual desire in CSB individuals to a larger extent than in healthy control group. These results along with increased self-reported desire towards sexually explicit clips by the CSB group were interpreted by the authors as akin to craving phenomena. While authors conceptualized these 9 second clips as *cues*, by comparing it to other cue-reactivity studies in the framework of incentive delay task

or conditioning, there were no cues but only rewarding stimuli. Therefore, it is conceptually hard to directly compare these results to other cue-reactivity studies, nevertheless key brain reward system areas were visibly altered in its processing of stimuli related to the CSB problems (for review, see Gola et al., 2016). Also in the behavioral addiction framework, study by Gola et al. (2017) demonstrated that bilateral ventral striatum was hyperactive specifically towards explicit cues preluding erotic rewards (and not monetary), arguing for pathological sensitization of this key brain reward system region in individuals with CSB (see Figure 6). This was further grounded in behavioral and brain-behavior results, i.e. reaction times were specifically faster in erotic than monetary trials in CSB group, unlike healthy group with no difference between them. Additionally, mimicking the increased reaction time difference toward explicit erotic cues in CSB, ventral striatal activity during cue period was subtracted between conditions (erotic vs. monetary) and then correlated with severity of various CSB symptoms, i.e. sexual addiction measured with sexual addiction screening test (SAST-R, Carnes, Green & Carnes, 2010), and number of times and hours spent watching pornography during a week preceding the study. The positive relationship between such striatal activity index and these symptoms was interpreted by the authors as further reflecting erotic-specific reward system sensitization in CSB. What is more, authors demonstrated lack of group differences in brain reactivity towards outcome stimuli, both erotic and monetary, in line with the Incentive Sensitization Theory and the postulated altered motivational “wanting”, but not the consummatory “liking”. As a follow-up study on the same dataset, Golec et al. (2021) interrogated the anterior orbitofrontal cortex’s role in cue-outcome probability and magnitude mapping in CSB. They found that indeed the right anterior orbitofrontal cortex has increased anticipatory activation during explicit erotic cue presentation in a manner modulated by probability of the outcome related to cue, suggesting increased evaluation along with motivation during outcome expectation.

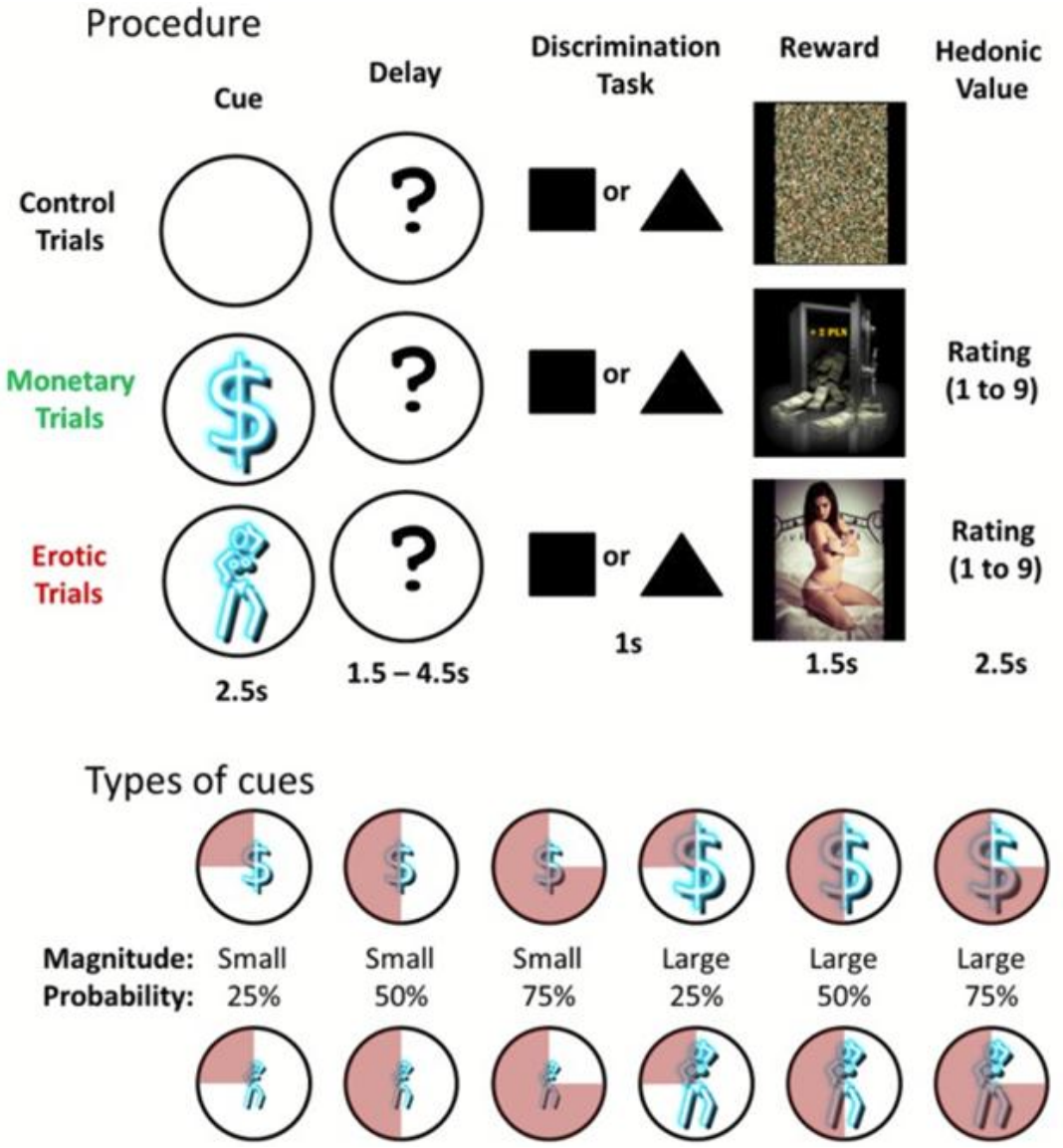

Figure 6. The experimental design of cue-reactivity task implemented in Gola et al., (2017) and Golec et al., (2021) studies. The cues were explicitly signaling the type of upcoming reward type - either monetary, erotic or no reward. Only in trials with the correct discrimination reaction the reward was obtainable (left of right button press depending on the shape displayed). Additionally, trials were divided into probability of obtaining a reward after correct response (25%, 50% or 75%), and into magnitude of the reward (small or large). In monetary trials that meant the amount of monetary gain accumulated and paid to the subjects, whereas in erotic trials it indicated whether the outcome image will be mildly erotic or explicitly sexual. After each outcome presentation, a scale to indicate the hedonic score of the stimulus was displayed. Reproduced with permission from: Gola et al., (2017). Can Pornography Be Addictive? An fMRI Study of Men Seeking Treatment for Problematic Pornography Use'. *Neuropsychopharmacology: official publication of the American College of Neuropsychopharmacology, 42*(10), 2021–2031, Springer Nature. Copyright © 2017, American College of Neuropsychopharmacology.

Although the body of neuroimaging research of CSB is relatively slim, several studies demonstrated alterations within reward circuitry beyond cue-reactivity and conditioning, in both the structural morphology (Engel et al., 2023; Draps et al., 2020; Schmidt et al., 2017), and functional connectivity in its default state (Engel et al., 2023). Importantly, the reward system itself was not always the focus of the study, and sample sizes were not always satisfactory. Without the hypothesis-driven focus on selected brain regions, brain metrics and measures of symptoms, the harsh multiple-comparison nature of neuroimaging hinders the probability of uncovering alterations of medium or small effect sizes, especially in task-free or structural neuroimaging (Marek et al., 2022; Poldrack, 2007). This might be one of the reasons behind inconsistent reports of observed alterations in the reward system in the CSB. Nevertheless, the following studies will be described only from the perspective of reward system alterations.

In study by Engel et al. (2023), no structural alterations within the reward system were observed, and increased in CSB group functional connectivity within subregions of the orbitofrontal cortex. Authors interpret this result as diminished arousal inhibition ability among individuals diagnosed with CSB. Probing also structural and functional alterations, Schmidt et al., (2017) demonstrated increased left amygdala gray matter volume, as well as decreased functional connectivity between left amygdala and bilateral dorsolateral prefrontal cortex, implicating less effective emotional and sexual regulation exerted by prefrontal cortex on the limbic system. Mapping structural characteristics, Draps et al. (2020) found reduced gray matter volume in frontal pole/anterior orbitofrontal cortex, similar between CSB, gambling disorder and substance use disorder vs. control group. In their follow-up study of functional connectivity among individuals with CSB, Draps et al. (2022) demonstrated increased functional connectivity of the left orbitofrontal cortex and left insula, interpreting these results in light of maladaptive reward system. Finally, Görts et al. (2023) performed cortical surface analysis in CSB vs. control group and found reduction in cortical surface area in posterior cingulate cortex. This brain area has indeed been implicated in reward processing (Oldham et al., 2018), although it is speculative, and more results are needed to better understand its role in the reward system. Nevertheless, authors discuss this result in light of altered reward processing.

2. Aims of the dissertation

The purpose of this dissertation is to examine the role of associative learning (active conditioning and extinction process) at behavioral and neural level among individuals with CSB and relating it to the Incentive Sensitization Theory model of developing addictive behaviors.

In line with Incentive Sensitization Theory, the sensitized brain's reward pathways to conditioned stimuli play a pivotal role in maintaining addictive behaviors, in the category of which CSBs may be considered, taking the data presented in the introduction. Among addicted individuals, there is an observed increase in the activity of the mesocorticolimbic system, which is central to reward processing and most importantly the reinforcement of behaviors. Heightened activity within the reward system strengthens the association between specific actions and the experienced reward, leading to more robust reinforcement of these behaviors. This sensitization of the reward system then hampers the efforts to ignore salient cues or actions, which leads to persistent addictive behaviors. In line with these assumptions, this dissertation is an attempt to verify the hypotheses described in detail in the following sections.

2.1. Conceptualization of the study

The following research questions and hypotheses were posed to address the main aims of this study on different levels of description of the phenomenon meaning different sources of data:

(a) *questionnaires* - self-report instruments in the form of questionnaires on a variety of symptoms and traits, allowing better characterization of the participants' psychological functioning,

(b) *behavioral* - two behavioral tasks: appetitive active conditioning task and extinction task; the former included rewarding stimuli both specifically related to CSB (erotic photos) and non-specific ones in the form of monetary rewards; self-assessed (arousal and valence ratings) and behavioral (reaction times) measures of conditioning and extinction effects were derived from these tasks, in both early and late phase of in both to better characterize the dynamics of associative learning,

(c) *task-based brain activity* - neuroimaging using functional magnetic resonance, during the above behavioral tasks, which by comparing a range of task's conditions allowed for the functional characterization of reward system,

(d) *default brain connectivity* - investigation of functional connectivity within the reward system during resting-state, thus enabling the assessment of neuronal functioning in a context that does not contain potentially disturbed cognitive functions,
(e) *morphometric* - examination of brain structure within the reward system, relating changes therein to impaired associative learning.

2.2. Research questions with corresponding hypotheses:

1) The first research question posed in the dissertation concerns the underlying mechanisms of CSB, of which associative learning is argued to be an important component. It is established that individuals with CSB show increased neural reactivity within ventral striatum and anterior orbitofrontal cortex to explicit cues of erotic stimuli (Gola et al., 2017; Golec et al., 2021), and within amygdala during conditioning to cues of erotic reward system stimuli (Klucken et al., 2016). However, no systematic study of the role of reward system in associative learning in CSB has been conducted so far. It is crucial to understand whether the acquisition of associations between conditioned stimuli and erotic outcome stimuli during the course of active conditioning is sensitized in individuals with CSB, and whether this sensitization applies specifically to conditioned stimuli associated with erotic outcome stimuli, or whether it is a manifestation of a more generalized dysfunction of the reward system, that causes increased sensitivity to conditioned stimuli associated with other types of reward during associative learning. Importantly, since conditioning and extinction are processes that were demonstrated to be changing over the course of the procedure (cf. Kruse et al., 2020), early and late phases of both conditioning and extinction will be defined. This will allow it to capture both the early stage of acquisition of the associations, and the late stage showcasing cue-reactivity when the cue-outcome contingencies are established.
Corresponding to this research question hypotheses 1-3 could be stated:

- *Hypothesis 1 (neuronal (c) data source)*

CSB group will be characterized by stronger conditioning effects for erotic cues (than monetary cues and with comparison to control group), reflected by altered activation of selected region of reward system: ventral striatum, amygdale, orbitofrontal and ventromedial prefrontal cortices and dorsal anterior cingulate

cortex. Specifically, in the early phase of conditioning, when the relationship between cues and outcomes is not yet formed, the dorsal anterior cingulate cortex, amygdala and ventral striatum will be hyperactive in the CSB group for both the erotic and monetary cues. In the late conditioning however, ventral striatum, orbitofrontal cortex and amygdala will be hyperactive specifically towards erotic cues in the CSB group.

- *Hypothesis 2 (behavioral and neuronal (b) (c) data source)*

Stronger conditioning effects in the reward system for erotic cues in the CSB group will also be reflected by increased connectivity between orbitofrontal cortex with ventral striatum and amygdale during the task. This increased connectivity will be correlated with the self-assessed conditioning and extinction effects in CSB, reflecting interplay between incentive salience attribution and common information processing patterns within the reward system.

- *Hypothesis 3 (questionnaires and behavioral (a) (b) data source)*

The stronger conditioning effects for erotic cues in the CSB group will also be evident in increased arousal and motivation. This will be reflected by self-assessment (arousal and valence towards cues after conditioning) and reaction times during the conditioning task. Specifically, reaction times will be faster for erotic cues in the CSB group in late conditioning, after the cue-outcome contingencies are learned. Moreover, the self-reported effects of conditioning will be correlated with CSB symptoms in the CSB group.

2) The second important research question pertains to whether altered reactivity of the reward system in individuals with CSB also manifested during reward processing. This is crucial to understanding the neurobiological basis of the clinical problem in the context of the Incentive Sensitization Theory (Robinson & Berridge, 2008; Berridge & Robinson, 2016). According to this model, hyper-sensitization of the reward system occurs mainly in response to cues (conditioned stimuli), which manifests as an increase in motivation to obtain a reward (“wanting”). In contrast, the actual receipt of the reward itself and its processing (“liking”) does not play a key role in the development and maintenance of addictive behaviors.

Corresponding to this research question hypothesis 4 could be stated:

- *Hypothesis 4 (neuronal (c) data source)*

There will be no differences in brain reactivity during either erotic or monetary reward processing in the CSB group compared to the control group in any of the selected reward system regions: ventral striatum, amygdale, orbitofrontal, dorsal anterior cingulate and ventromedial prefrontal cortices.

3) The third research question concerns impaired extinction in individuals with CSB symptoms, which is crucial to understanding the mechanisms of persistent problematic pornography use despite repetitive experience of its negative consequences in someone's life Effective extinction is crucial for adaptive learning and behavioral flexibility. Research into whether this process is impaired in individuals with CSB, and if so, whether it is specific to sexual stimuli or more general in nature, will provide valuable insights into the neurobiological underpinnings of CSB, the similarity of CSB to addiction, and potential targets for therapeutic intervention. Research shows that people with CSB show difficulty controlling sexual behavior despite negative consequences (Stark et al., 2018; Kraus, Voon & Potenza, 2016). One potential explanation for this phenomenon is the extinction dysfunction. If individuals with CSB have difficulty extinguishing responses to sex-related conditioned stimuli, then even when they do not have access to sexual reward, these stimuli can still trigger strong desire and automatic behavioral responses. During extinction, activity in the ventral striatum, orbitofrontal cortex and amygdala, should gradually decrease as the conditioned stimulus loses its motivational significance. However, among individuals with CSB, it is possible to observe other patterns of neuronal activity, i.e. sustained or even increased activity in these brain regions in response to conditioned stimuli despite the absence of reward, which could indicate difficulty in extinguishing. During the process of conditioned responses extinction, a key role is played by the ventromedial prefrontal cortex, which facilitates extinction by updating the subjective value and effort cost of obtaining the conditioned stimuli.

Corresponding to this research question hypotheses 5-7 could be stated:

- *Hypothesis 5 (neuronal (c) data source)*

CSB group will be characterized by weaker extinction effects for erotic cues (than monetary cues and then control group), reflected by altered activation of selected region of reward system: ventral striatum, amygdale, ventromedial prefrontal cortex and dorsal anterior cingulate cortex. Specifically, in the early phase of extinction, when the new rule of lack of reward following the cues is not yet formed, the dorsal anterior cingulate cortex, ventral striatum and orbitofrontal cortex will be hyperactive in CSB group for the erotic cue. In the late extinction, ventral striatum, orbitofrontal cortex and amygdale will remain hyperactive for the erotic cues, and ventromedial prefrontal cortex hypoactive only for erotic cues in the CSB group.

- *Hypothesis 6 (behavioral and neuronal (b) (c) data source)*

Weaker extinction effects within the reward system for erotic cues in CSB group will also be reflected by decreased connectivity between ventromedial prefrontal cortex with ventral striatum and amygdala during the task. This decreased connectivity will be correlated with the self-assessed extinction effects in CSB.

- *Hypothesis 7 (questionnaires and behavioral (a) (b) data source)*

The weaker extinction effects for erotic cues in the CSB group will also be evident in persisting higher arousal and motivation. This will be reflected by self-assessment (arousal and valence towards cues after the extinction) and reaction times during the extinction task. Specifically, reaction times will be shorter for erotic cues in the CSB group in both early and late extinction phases, reflecting lasting disrupted extinction of motivational responses to sensitized erotic cues. Moreover, the effects of extinction will be correlated with CSB symptoms in the CSB group.

4) Is the reward system functionally altered among individuals with CSB in its default state, i.e. without a context of any task at hand? Previous research (Engel et al., 2023; Voon et al., 2014; Klucken et al., 2016; Banca et al., 2016; Gola et al., 2017; Golec et al., 2021) on CSB has mainly focused on neuronal reactivity to visual stimuli associated with sexual activity. Analyzing the activity of the brain's reward system during resting-state (Biswal et al., 1995) will provide information about the tonic, baseline activity of this system and its relationship to CSB, independent of direct

exposure to desire-inducing stimuli or other cognitive contexts. More importantly, examining the correlation between resting reward system activity and the effects of active conditioning and extinction will provide a better understanding of the interplay between neurobiological alterations and CSB propensity.

a) Do individuals with CSB display altered baseline functional connectivity between areas of the reward system, particularly between the ventral striatum, orbitofrontal cortex, amygdala and ventromedial prefrontal cortex? Such changes could reflect the hypothesis that CSB is associated with more fundamental alterations in reward system functioning that are not dependent on direct stimulation by sexual stimuli or other types of rewards or cues associated with them. Studies of resting brain functional connectivity in substance use disorders have shown the existence of such alterations (cf. Canario, Chen & Biswal, 2021), suggesting the possibility of similar mechanisms in CSB.

b) Is the baseline functional connectivity within the reward system related to the altered effects of active conditioning and extinction in individuals with CSB? It can be hypothesized that individuals with CSB who exhibit stronger conditioning effects and difficulties with extinction will also show altered patterns of resting functional connectivity, e.g. that higher resting functional connectivity between ventral striatum and orbitofrontal cortex and amygdala will be associated with greater sensitivity to conditioned stimuli (sensitization), while reduced functional connectivity between ventromedial prefrontal cortex and amygdala and ventral striatum will reflect impaired updating and inhibition of conditioned responses even after extinction procedure.

Corresponding to this research question hypothesis 8 could be stated:

- *Hypothesis 8 (behavioral and default connectivity (b) (d) data source)*

During resting state, the neuronal functional connectivity within the reward system will be altered in the CSB group, reflecting abnormal patterns of information processing within regions related to self-reported arousal. Specifically, functional connectivity between ventromedial prefrontal cortex with amygdale and ventral striatum will be lower in the CSB group, reflecting weakened inhibition of the limbic and motivational system, and increased between orbitofrontal cortex and ventral striatum, indicating stronger propensity for reward-seeking behaviors. The

alterations in resting state functional connectivity pattern will be correlated with self-reported effects of the conditioning and extinction.

5) Are there structural changes in the cortical regions of the reward system in CSB that could explain the observed alterations in associate learning? It has been demonstrated in one study that the ventromedial prefrontal cortex is functionally altered during conditioning acquisition in CSB (Klucken et al., 2016), and more broadly in addictions (Konova et al., 2019) - the region that is involved in successful extinction of conditioned responses. The thickness of the ventromedial prefrontal cortex has also been related to less efficient extinction (Hartley, Fischl & Phelps, 2011; Milad et al., 2005) and reported to be thinner among individuals with diagnosed addictions (Mackey et al., 2019). Therefore, echoing research question number three, reduced neuronal population in the ventromedial prefrontal cortex may impair the ability to update and suppress conditioned responses during extinction, leading to continued salience of sexual cues. This failure of inhibition may explain why individuals with CSB experience difficulty disengaging from sexual thoughts or behaviors, even when they recognize the negative consequences.
Corresponding to this research question hypothesis 9 could be stated:

- *Hypothesis 9 (behavioral and morphometric (b) (e) data source)*

The ventromedial prefrontal cortex will be thinner among individuals with CSB, reflecting lower neuronal resources for successful extinction. This thinning will be correlated with propensity to disrupted extinction effects measured with self-reported valence and arousal in response to erotic cues post-extinction. It will also be negatively correlated with experienced CSB symptoms.

3. Methods

3.1. Participants

Sixty-six right-handed heterosexual males participated in the study, among which 33 self-identified as struggling with CSB and 33 as healthy control (HC) subjects. Recruitment was done under supervision of a psychologist, and equally via therapist referrals, internet-based and social media advertisements. All participants underwent on-line screening with psychological questionnaires before the functional magnetic resonance imaging (fMRI) examination [*Brief Pornography Screener* (BPS, Kraus et al., 2020; 5-items scale created to assist in the assessment of problematic pornography use, scores equal or more than 4 is considered a positive screen for plausible problematic pornography use); *Sexual Addiction Screening Test* (SAST-R, Carnes, Green & Carnes, 2010; Gola et al., 2017b; 20-items scale created to assist in the assessment of sexually compulsive behaviors in sex addiction framework, measuring different kinds of sexual behaviors; 5 or more points can indicate the need for additional clinical interviews for CSB); *South Oaks Gambling Screen* (SOGS, Lesieur & Blume, 1987); *Criteria for Hypersexual Disorder* (HD, Kafka 2010; following aspects: (1) Persistent, intense sexual urges, fantasies, or behaviors lasting at least six months; (2) Repeated, unsuccessful efforts to control or reduce these sexual urges or behaviors; (3) Excessive time spent in sexual fantasies, urges, planning, or engaging in sexual behavior; (4) Continued involvement in sexual behaviors despite the risk of harm to oneself or others; (5) Clinically significant distress or impairment in social, occupational, or other important areas of functioning due to the behavior; Engagement in these sexual activities often occurs in response to dysphoric moods (e.g., anxiety, depression, boredom) or stressful life events); *Obsessive Compulsive Inventory* (OCI-R, Foa et al., 2002); *The Hospital Anxiety and Depression Scale* (HADS, Zigmond & Snaith, 1983); *Hypersexual Behavior Inventory* (HBI, Reid et al., 2011;19-item scale created to assesses different aspects of hypersexuality through three factors: control, coping, and consequences of sexual behaviors); *Alcohol Use Disorders Identification Test* (AUDIT, Babor et al., 1989; assess alcohol consumption, drinking behaviors, and alcohol-related problems.); *Impulsiveness Scale* (IS-12, Kahn et al., 2019; Szczypiński et al., 2021; measuring *cognitive impulsivity* and *behavioral impulsivity*)], and were also asked to report time spent on pornography consumption in the month prior to the examination. Sexual orientation was assessed using the Kinsey Scale Test (Kinsey, Pomery & Martin,

1948; Wierzba et al., 2015). Participants were also inquired about their history and level of education. Based on the inclusion criteria, subjects were assigned to either the CSB or HC group.

The inclusion criteria for the CSB group were: at least 4 out of 5 criteria of HD, BPS score 6 or more out of 10 points, SAST-R 6 or more out of 20, whereas for the HC group, the criteria were BPS score 3 or less, SAST-R 5 or less, and 1 or 0 criteria of HD. Additionally, both groups had to score SOGS 4 or less, in OCI-R 25 points or less out of 72 and in HADS 19 points or less out of 42. Other exclusion criteria were related to contradiction in taking part in magnetic resonance imaging examination, i.e. significant health issues, epilepsy, serious past head traumas, metal objects/implants in the body. Subjects were also informed to abstain from alcohol, caffeinated beverages, and psychoactive substances one day prior to the experiments, although they were informed that if caffeine is included in the morning routine, it is advised to follow it on that day. Additionally, subjects were asked to be well rested before the experimental session. The reliability of used questionnaires was computed using Cronbach's α procedure and reported in Section 4.1.

3.2. Conditioning and extinction tasks

During the fMRI examination, subjects engaged in an active conditioning and extinction procedure (extended task used by Kruse et al., 2017, see Figure 6). The conditioning task consisted of two fMRI runs (10 minutes each). It was followed by the extinction task that had exactly the same structure as the conditioning task (two fMRI runs, 10 minutes each), except that no matter how quick the response, subjects could never win any rewarding outcome (i.e. *Unconditioned Stimuli*: $UCS+_{erotic}$ or $UCS+_{cash}$) and were always presented with UCS- (scrambled picture). Each trial began with a fixation cross (6–10 seconds), followed by 1 of 3 possible simple shapes (6 seconds), which were the cues, informing about the category of a possible reward (i.e. $CS+_{erotic}$, $CS+_{cash}$, CS-). Next, for a randomized length of time (1–3 sec), a small circle was presented, followed by a larger circle during which subjects had to quickly react with a button click in order to win a reward. The window of opportunity was between 140 milliseconds and 500 milliseconds. For fast enough responses, the reward was displayed accordingly to trial type: either a pornographic

or erotic picture of women for erotic condition (UCS+$_{erotic}$), the amount (2–5 PLN) won in the given trial for the monetary condition (UCS+$_{cash}$), and a scrambled picture for control condition (UCS-). Reactions outside the window of opportunity always resulted in scrambled pictures (UCS-). After the reward presentation (2.5 seconds), a brief eye pictogram was displayed (3 seconds) to remind participants to blink during this period.

The strength of CS reinforcement was kept at around 70% (7 out of 10 trials of both CS+ condition types in each fMRI run) and was controlled by an adaptive window of opportunity length in which reactions would result in a reward. Each time a trial that was planned to be reinforced (by having a longer window of opportunity period) failed to be reacted upon, a next-in-queue non-reinforced trial was switched to be reinforced in addition to prolonging the window of opportunity length for all following reinforced trials (+20 milliseconds for all reinforced trials and -20 milliseconds for all non-reinforced trials, Kruse et al., 2017; Hahn et al., 2009). Likewise, trials that were planned to be non-reinforced and had faster-than-anticipated reaction time resulted in the shortening of future windows and re-queuing trial order so that, in the end, subjects ended up with a near 7:3 ratio of won-to-lost trials. The trial order was semi-randomized so that the same specific condition type and its reinforcement could never be presented twice in a row. Additionally, the first six trials in the first fMRI run were always presented such that in the first three trials, each of the conditions had to appear, and only one trial could be reinforced (either monetary or erotic); the second three trials also had to have one of each condition and the other condition would be reinforced. The order of those conditions and its reinforcement was randomized between subjects. Thus, the pace of conditioning was normalized between subjects at the beginning of the task. The connection between cue shape and reward type was randomized between subjects. Explicit erotic stimuli were selected from a subset of the Nencki Affective Picture System (NAPS-ERO) based on the highest arousal and valence scores (Wierzba et al., 2015).

Before entering the MRI and beginning the experiment, subjects underwent a brief training on the task to familiarize themselves with the procedure. Participants were instructed to react as fast as possible in the target period, regardless of cue

type. Subjects were compensated based on task performance, up to 120 Polish złotys (27 euros). Experimental protocol was displayed using a VisualSystem HD (NordicNeuroLab), and responses were collected using response grips held in the right hand (SmitLab).

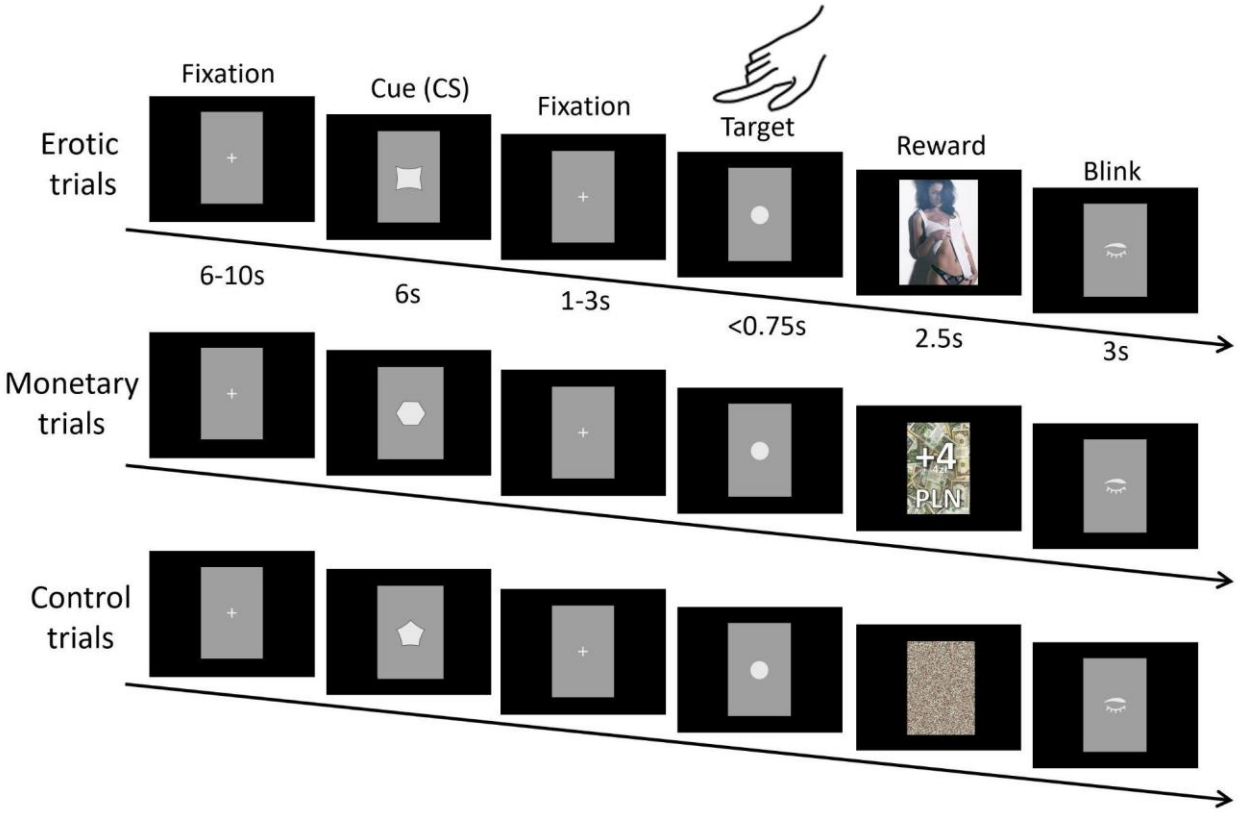

Figure 6. The design of trial in the conditioning and extinction task design.

To assess the behavioral effects of conditioning and extinction success, subjects were asked to rate their valence and arousal towards simple shapes (all three CS) in the form of a 7-point Self-Assessment Manikin (Bradley & Lang, 1994) at three time points: before the beginning of conditioning, after conditioning, and after extinction (see Figure 7).

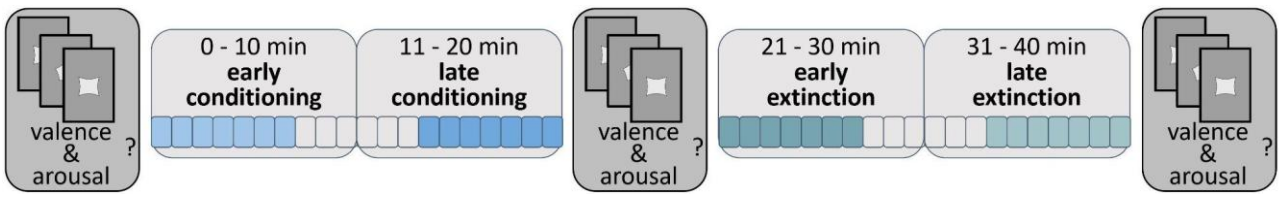

Figure 7. General experimental procedure protocol, including self-assessed valence and arousal towards (initially) neutral cues and length of each of the task phases. Before

entering the MRI room, subjects were asked to rate valence and arousal towards shapes used as the CS in the following tasks. Then, after finishing the conditioning task and after the extinction task, subjects were again asked to rate their CS-related valence and arousal. Conditioning and extinction tasks each lasted 20 minutes and were divided into early and late phases. To increase sensitivity to effects taking place during the early and late phases of the learning process, the first seven trials were taken into analysis for the early and the last seven for the late phase, colored blue for conditioning and turquoise for extinction.

3.3. Analysis of behavioral and self-assessment data

The effects of conditioning and extinction on subjective arousal and valence were analyzed using a three-way repeated-measures *Analysis of Variance* (ANOVA) with a within-subjects factor of Time (pre-conditioning, post-conditioning, and post-extinction), Condition Type (monetary and erotic), and a between-subjects factor of Group (CSB vs. HC). Reaction times were analyzed in two separate three-way ANOVAs (first for conditioning and second for extinction task): one with the effect of Time (early and late conditioning), Condition Type, and Group.

For data reduction purposes and to follow subtractive fMRI analysis logic, difference scores (Δ) of subjective ratings and reaction times between each CS+ relative to the CS- were used. Homogeneity of variance assumption was assessed by comparing variances in CSB and HC groups. There are several rules of thumb for acceptable between-group variance ratio, which should not violate the assumption (Dean & Voss 1999; Keppel, 1991). A cut-off variance ratio of 3 was used in the thesis following Dean & Voss (1999). The normality of residuals assumption was assessed graphically using a quantile-quantile plot. If either of the assumptions were not met the dependent variable was transformed using Yeo-Johnson transformation (Yeo & Johnson, 2000). If Mauchly's Test of Sphericity was significant, the Greenhouse – Geisser correction for Departure from Sphericity was applied. All post-hoc tests were adjusted for multiple comparisons using Holm's method unless stated otherwise. The generalized eta squared (η_G^2) was used as a measure of explained variance, as it is a preferable method in designs including within-subject factors (Bakeman, 2005). Consistent with Cohen's η^2 interpretation convention, "small" effect size range between .01 ≤ η_G^2 ≤ .06, "medium" .06 ≤ η_G^2 ≤ .14, and "large" η_G^2 ≥ .14 (Olejnik & Algina, 2003).

Further, a one-way Spearman correlation was performed to assess the relationship between BPS questionnaire measures of CSB symptoms especially connected to the pornography consumption and self-reported effects of conditioning and extinction towards $CS+_{erotic}$ in the CSB group. Statistical analyses were performed in R version 4.1.0 (R Core Team, 2021).

3.4. Image acquisition details

Neuroimaging data was collected at Bioimaging Research Center, Institute of Physiology and Pathology of Hearing, Poland, using a 3 Tesla Siemens Prisma MRI scanner (Siemens Medical Systems, Erlangen, Germany) equipped with a 64-channel phased-array RF head coil. Structural images were obtained using a T1-weighted 3D MP-Rage sequence (repetition time (TR) = 2400 milliseconds, inversion time (TI) = 1000 milliseconds, echo time (TE) = 2.74 milliseconds, 8° flip angle, field of view (FOV) = 256×256 millimeters, image matrix 320×320 millimeters, voxel size of 0.8×0.8×0.8 millimeters, 240 slices of 0.8 millimeters slice thickness, acquisition time = 6:52 minutes). Functional scans were acquired using a Multi-band Echo Planar Imaging (EPI) sequence (TR = 750 milliseconds, TE = 31 milliseconds, flip angle = 52°, FOV = 220×220 millimeters, 110×110 millimeters image matrix, 72 axial slices of 2 millimeters slice thickness, voxel size of 2×2×2 millimeters, Slice Acceleration Factor = 8, In-Plane Acceleration Factor = 1, integrated *Parallel Acquisition Techniques* = 8). Functional images were collected in paired runs with opposite phase-encoding directions (anterior-posterior and posterior-anterior) to compensate for phase-encoding direction distortions.

Resting-state functional data was acquired with two 7 minute and 30 seconds runs (over all 15 minutes), during which subjects were asked to look at the fixation cross. For the conditioning and extinction tasks, functional data was acquired in an overall four runs, each lasting 10 minutes. Therefore, the first two runs (20 minutes) were early and late conditioning, and the third and fourth run (20 minutes) were early and late conditioning.

Due to the overall length of the MRI procedure, the scanning session was divided into two parts. During the first, resting-state and structural T1-weighted imaging was performed (approximately 28 minutes). Then, subjects exited the MR room, were instructed about and briefly trained in the experimental task they were

going to perform in the second imaging part (approximately 3 minutes). After that, four runs of functional neuroimaging were conducted during the conditioning and extinction tasks (approximately 45 minutes).

3.5. Image preprocessing details

All functional scans had an even number of runs with the opposite phase coding direction (anterior-posterior and posterior-anterior). Spatial distortions were corrected with the *FSL topup* tool (Andersson et al., 2003) based on the average representation of the images in both directions. Further image preprocessing was done in *SPM12* (Ashburner & Friston, 2005), *CONN* toolbox (ver. 22.v2407, Whitfield-Gabrieli & Nieto-Castanon, 2012) and *Matlab* (ver. 2017b, Mathworks). Functional data was spatially realigned to the mean image, to which the structural image was then co-registered. Segmentation and normalization to the common MNI space were performed based on high-resolution structural images with resampling to 1 millimeter isometric voxels. The obtained transformation parameters were applied to the functional volumes with resampling to 2 millimeters isometric voxels. The data was 0.004 Hertz high-pass filtered.

Task-based and resting-state required additional denoising steps due to their correlational nature. For task-based functional connectivity, data was denoised with regressing out task-related effects (boxcar function of all task-related conditions convolved with canonical hemodynamic response function) and six head-movement parameters and their first order derivatives were modeled as nuisance regressors. The same temporal filtration was used, i.e. 0.004 Hertz high-pass. No spatial smoothing was used due to region-of-interest to region-of-interest (ROI-to-ROI) analysis undertaken in this study. For resting-state functional connectivity, data denoising included using data points outlier detection method *ArtToolbox* (as implemented in *CONN*, Whitfield-Gabrieli, Nieto-Castanon & Ghosh, 2011), with 'intermediate settings' (Global-signal z-value < 5; motion < 0.9 millimeters; Power et al., 2014; Nieto-Castanon, 2022). Additionally, to reduce physiological artifacts in the functional data, the *COMPCOR* approach (Behzadi et al., 2007; Chai et al., 2012) was utilized on white matter and cerebrospinal fluid masked Echo-Planar Imaging (EPI) signals to generate nuisance regressors related to (5 principal components for each mask). Then, the denoising was performed using general

linear model (GLM) regression and including 12 *COMPCOR*, 12 head-movement parameters (six and their first order derivatives) and data points detected as outliers as nuisance regressors. The data was filtered in the 0.008 to 0.09 Hertz band range. Also, no spatial smoothing was used due to ROI-to-ROI analysis undertaken.

3.6. Task-based brain activity

Functional images were analyzed using the general linear model in *SPM12* and using custom-made *Matlab* scripts (ver. 2017b, Mathworks). Blood-oxygenation-level-dependent (BOLD) responses evoked by each cue type ($CS+_{erotic}$, $CS+_{cash}$, CS-) and reward type ($UCS+_{erotic}$, $UCS+_{cash}$, UCS-) were modeled as separate regressors. Additionally, the first occurrence of CS of each trial type was modeled as a single regressor of no interest since it is required to present both the cue and the reward at least once to start the conditioning (and extinction) process (Phelps et al., 2004). The model also included six head motion-related nuisance regressors. All four fMRI runs (two conditioning and two extinction) were input into one model on the first level (for each subject). Both conditioning and extinction tasks were divided into early and late phases, naturally occurring in the first and second fMRI run of each task, similar to Kruse et al. (2017) and Banca et al. (2016), with a slight modification of modeling the first seven (out of 10) occurrences of given condition in the early phase and the last seven occurrences in the late phase to increase the potential effects specific to a given conditioning phase. This resulted in four time points: early conditioning, late conditioning, early extinction, and late extinction (see Figure 6). For the exploratory whole-brain analysis, the following CSB vs. HC contrasts were tested for each of the four stages: 1) $CS+_{erotic}$ vs. CS-; 2) $CS+_{cash}$ vs. CS- for a total of 8 contrasts of interest. Additionally, analogous whole-brain analysis was conducted without between-subject factor (no group division) for the purpose of general task activity visualization. Whole-brain group-level analyses used a voxel-level threshold of $p<.001$ and cluster-based correction $p_{FWEc}<.05$. The results of this exploratory analysis are included in supplementary materials, as they are outside the focus of this dissertation.

For the main task-based fMRI analysis, knowing that the effects of conditioning and reward anticipation in CSB on brain functioning are small (for a review, see Klein et al., 2022), a priori-hypothesized bilateral ROIs were chosen to

improve statistical test sensitivity. For ROI analysis, the following regions were used (see Figure 8):

1) ventral striatum (functionally defined mask from previous studies; Gola et al., 2017; Sescousse et al., 2013),

2) amygdala (structural mask derived from Harvard-Oxford atlas),

3) anterior and 4) posterior orbitofrontal cortex (structural masks derived AAL3 atlas; Rolls et al., 2020),

5) dorsal anterior cingulate cortex (functionally defined mask from Brainnetome Atlas, label *A32p*; Fan et al., 2016) and

6) ventromedial prefrontal cortex (structural mask derived from AAL3 atlas under the name *fronto-medial orbitofrontal cortex*).

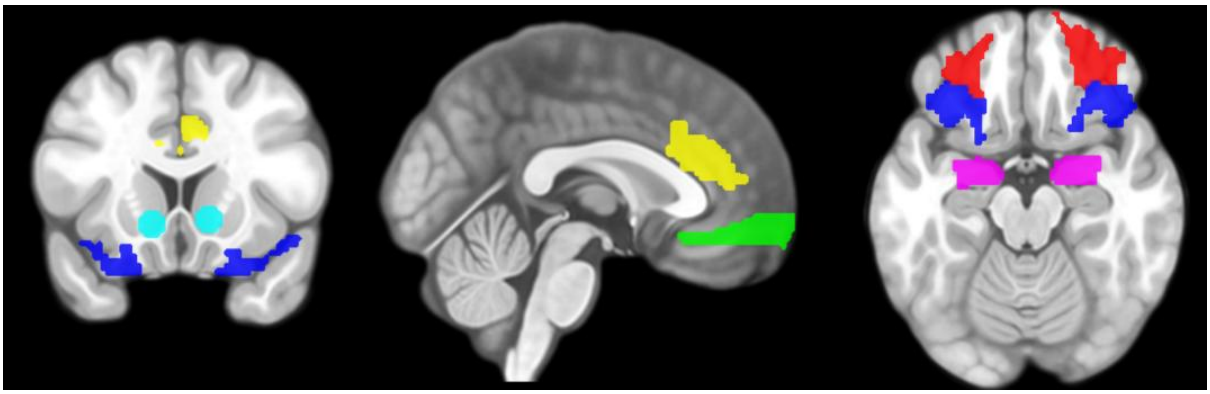

Figure 8. Visualization of ROIs chosen for analysis. The ventral striatum is colored in turquoise, amygdala in pink, dorsal anterior cingulate cortex in yellow, anterior and posterior orbitofrontal cortices in red, and blue and ventromedial prefrontal cortex in green.

The averaged contrasts of beta estimates of each CS+ vs. CS- for each condition of each task from the ROIs were extracted. In an analogous fashion to the reaction times analysis, ROI values were analyzed in two separate three-way ANOVAs for each ROI for conditioning and extinction task: with within-subject effects of Time and Condition Type, and a between-subject effect of Group. This includes the homogeneity testing and sphericity correction. All post-hoc tests were adjusted for multiple comparisons using Holm correction unless stated otherwise.

To test the hypothesis that pertained to the lack of differences in rewards (UCS+) processing in CSB vs. HC groups, a Bayesian equivalent to ANOVA was used instead on each of UCS+ vs. UCS- during early and late conditioning. Priors for mean and standard deviation were set to uninformative Jeffries priors, while priors for main effects and interactions were set as independent scaled inverse-chi-

square priors (Rouder et al., 2012). Bayes factors (BF) and $BFe_{xclusion}$ were reported for all main effects and interactions tested against the null (intercept only) model. This analysis tested a hypothesis of lack of differences against a null hypothesis about a presence of a difference, thus a higher value of a BF indicates an evidence in favor of lack of differences. The $BF_{exclusion}$ quantifies the change from prior inclusion odds to posterior exclusion odds and can be interpreted as the evidence in the data for excluding the predictor. Since BF can be an effect size on its own, no additional effect sizes were reported. All post-hoc tests were adjusted for multiple comparisons using Holm correction unless stated otherwise. Bayesian analysis was performed using the *BayesFactor* package (Morey & Rouder, 2023).

3.7. Functional connectivity during the task

To assess changes in functional connectivity within the reward system during the conditioning and extinction tasks, ROI-to-ROI generalized psychophysiological interaction analysis was performed, using *CONN* toolbox (Whitfield-Gabrieli & Nieto-Castanon, 2012), with bivariate regression approach. The connectivity analysis on subject-level was conducted for each of the six designated ROIs (seed regions) with the remaining ones (target regions). For each seed region, a generalized psychophysiological interaction term was defined as the product of the seed ROI's BOLD signal (physiological factor) and the boxcar signals characterizing each task phase (early and late) and condition ($CS+_{erotic}$ and $CS+_{cash}$), convolved with an SPM canonical hemodynamic response function (psychological factors). Alterations in connectivity between each seed ROI and all other target ROIs for each of the conditions characterized by the Fisher-transformed semipartial correlation coefficient of the psychophysiological interaction terms in each model. On group-level analysis, connectivity of selected ROI pairs in which changes in connectivity could be explained by either Group factor, Group x Time, Group x Conditioning or Group x Time x Condition factor interactions were analyzed. To this end, F-tests were performed, separately for conditioning and extinction. Post-hoc T-tests were applied to evaluate changes in coupling for each significant ROI-to-ROI connection pair. Results were reported using a false discovery rate threshold of p-FDR correction ($p < .05$). Only connections that survived the correction were considered statistically significant.

Additionally, to test the relationship between the self-reported effects of conditioning and extinction and altered connectivity during the task, general linear regression analysis was performed on ROI functional connectivity pairs that were significantly altered only in the CSB group. To focus on the CSB group and therefore reduce the amount of statistical tests, these analyses were conducted only within CSB subjects, and only considering the self-reported effects of arousal and valence for $CS+_{erotic}$ after the conditioning and after extinction.

3.8. Functional connectivity during resting state

Functional connectivity of the brain reward system during resting-state was assessed using the ROI-to-ROI approach. The connectivity matrices were estimated characterizing the patterns of functional connectivity with all six ROIs considered in previous analyses, i.e. ventral striatum, ventromedial prefrontal cortex, dorsal anterior cingulate cortex, anterior and posterior orbitofrontal cortices, separately for every subject (first-level analysis). Functional connectivity strength was represented by Fisher-transformed bivariate correlation coefficients from a weighted general linear model (Nieto-Castanon, 2020), defined separately for each pair of seed and target areas, modeling the association between their BOLD signal timeseries. Then, for group analysis (second-level analysis), for each individual connection a separate general linear model was estimated, with first-level connectivity measures at this connection as dependent variables, and groups (CSB and HC) as independent variables. Connection-level hypotheses were evaluated using multivariate parametric statistics with random-effects across subjects and sample covariance estimation across multiple measurements, as implemented in the *CONN* toolbox (Whitfield-Gabrieli & Nieto-Castanon, 2012) Inferences were performed at the level of individual ROIs. ROI-level inferences were based on parametric multivariate statistics, combining the connection-level statistics across all connections from each individual ROI. Results were thresholded using a familywise corrected p-FDR < 0.05 ROI-level threshold (Nieto-Castanon, 2020; Benjamini & Hochberg, 1995).

3.9. Cortical thickness of ventromedial prefrontal cortex

To obtain cortical thickness estimates of ventromedial prefrontal cortex regions, all subjects' structural T1-weighted data were processed and further analyzed using the *CAT12* toolbox (version r2583) within *SPM12*, running on *Matlab*

(ver. 2017b, Mathworks). Initially, the images are denoised using a spatially adaptive nonlocal means filter (Manjón et al., 2010) and resampled to achieve isotropic voxel sizes. Then, volumes were segmented using the thickness estimation option for ROI analysis.

Estimation of cortical thickness was performed in a single step utilizing the projection-based thickness method (Dahnke, Yotter & Gaser, 2013). This procedure included topology correction (Yotter et al., 2011), spherical mapping (Yotter, Thompson & Gaser, 2011), and spherical registration. After tissue segmentation, white matter distance was calculated, and local maxima were projected onto other gray matter voxels, using a neighbor relationship defined by the white matter distance (Dahnke, Yotter & Gaser, 2013). Additionally, all data underwent critical visual inspection. The sulco-gyral surface-based Destrieux cortical parcellation atlas (Destrieux et al., 2010) used for regional cortical thickness estimation. Cortical thickness was calculated for each orbitofrontal and ventromedial prefrontal ROI in native subject space, which increases the cortical thickness estimates (Gaser et al., 2020). As the volume-based ROI used in the task-based activity analyses does not have a one-to-one representation in the Destrieux cortical parcellation atlas, a series of independent samples *t*-tests were conducted for each ROI, comparing the CSB and healthy control groups. For visual inspection purposes, a surface projection of volumetric-based ventromedial prefrontal ROI was performed (Figure 16). Additionally, correlation analysis between cortical thickness and self-reported effects of conditioning (arousal and valence) towards $CS+_{erotic}$ was performed using Spearman *rho* method for each ROI.

To further explore the potential topology of cortical thinning among individuals with CSB, an exploratory full-cortex surface-based analysis was performed. For this purpose, co-registration of individualized surface meshes with *FreeSurfer* template using a 2D version of Dartel approach (Ashburner, 2007), and all the vertices were smoothed using a 12 millimeter Gaussian kernel (Gaser et al., 2020).

3.10. Ethics

Before taking part in the study, all subjects gave their written informed consent for participation and were screened for any contraindications to MRI. All participants have been informed that they can opt out of further participation in the

study at any time. The research protocol was approved by Nicolaus Copernicus University in Toruń, Poland ethical committee (consent number 2/2018) and was conducted in accordance with the Declaration of Helsinki. Structural brain images of participants were examined by a radiologist to potentially exclude subjects with pathological structural brain anomaly. None of the participants had significant structural anomalies that were deemed pathological by the radiologist.

4. Results

Due to numerous hypotheses stated in this dissertation, an indication of whether given analysis confirms each of the hypotheses will be placed after each of the sections of the results.

4.1. Psychological profile

The reliability of the used questionnaire scales was assessed with Cronbach's α procedure: Brief Pornography Screener (α=0.94), Sexual Addiction Screening Test (α=0.92), Hypersexual Behavior Inventory (α=0.98), Obsessive Compulsive Inventory (α=0.75), Impulsiveness Scale (α=0.77), The Hospital Anxiety and Depression Scale (α=0.81).

Group characteristics in terms of demographic and clinical variables are listed in Table 1. There was no significant difference in age between the CSB group and HC. However, the CSB group scored significantly higher on measures of problematic pornography use measured with BPS, sexual addiction measured with SAST-R and hypersexuality measured with HBI. The CSB group reported higher levels of anxiety and depression: HADS–Anxiety, and HADS–Depression. No significant differences were found between the groups on the OCI-R, AUDIT nor SOGS. Similarly, the impulsiveness measured with IS-12 did not show significant differences in Behavioral subscale and showed a tendency in the Cognitive subscale. Additionally, the CSB group reported significantly higher pornography consumption, averaging 6.67 hours per week (SD=6.66) compared to 1.08 hours per week (SD=1.16) in the HC group. These results indicate that individuals with CSB exhibit significantly higher levels of problematic pornography use, sexual addiction tendencies, hypersexual behavior, anxiety, and depression compared to healthy controls, slightly but not significantly elevated cognitive impulsiveness, and no significant differences were observed in behavioral impulsiveness or obsessive-compulsive symptoms between the two groups. Three subjects (two HC and one CSB) were removed from the analysis due to incomplete neuroimaging data.

Table 1. Demographic and clinical characteristics of the CSB and HC groups. Each variable was compared between the CSB and HC groups using an independent *t*-test. without correction for multiple comparisons.

Variable name	CSB (n = 32)	HC (n = 31)	*Test statistic*	*p*-value
Age, M (SD)	28.91 (7.07)	27.81 (5.62)	0.68	.498
BPS, M (SD)	8.31 (1.42)	1.29 (1.16)	21.42	**<.001**
SAST-R, M (SD)	11.56 (3.53)	1.94 (1.34)	14.23	**<.001**
HBI, M (SD)	60.94 (12.46)	24.13 (3.79)	15.75	**<.001**
HADS–Anxiety, M (SD)	6.66 (3.11)	4.00 (2.65)	3.65	**<.001**
HADS–Depression, M (SD)	4.28 (3.02)	2.39 (1.69)	3.06	**.003**
OCI-R, M (SD)	12.06 (5.90)	9.61 (6.44)	1.58	.120
IS-12–Cognitive, M (SD)	11.90 (2.19)	10.80 (2.76)	1.81	.076
IS-12–Behavioral, M (SD)	14.22 (3.53)	13.97 (3.58)	0.28	.781
AUDIT, M (SD)	7.09 (4.52)	7.48 (3.84)	0.34	.714
SOGS, M (SD)	1.03 (1.56)	0.81 (1.28)	0.63	.534
Pornography consumption (hours/week), M (SD)	6.67 (6.66)	1.08 (1.16)	4.60	**<.001**
Education, n (%)			-	.798
Primary	0	0		
Vocational	0	0		
High school	9 (28.1%)	11 (35.5%)		
Higher (unfinished)	6 (18.8%)	4 (12.9%)		
Higher (complete)	15 (46.9%)	16 (51.6%)		
Postgraduate	1 (3.1%)	0		
PhD	1 (3.1%)	0		

CSB—Compulsive Sexual Behaviors; HC—healthy control; BPS—Brief Pornography Screener; SAST-R—Sexual Addiction Screening Test; SOGS—South Oaks Gambling Screen; OCI-R—Obsessive Compulsive Inventory; HBI—Hypersexual Behavior Inventory;

AUDIT—Alcohol Use Disorders Identification Test; IS-12—Impulsiveness Scale. All numerical variables were compared using t-test; Education was compared using Fisher exact test.

4.2. Analysis of behavioral and self-assessment data

In the following subsections, hypotheses 3 and 7 were tested using self-assessed and behavioral effects of conditioning and extinction. These hypotheses pertained to the aberrant associative learning among individuals with CSB, i.e. enhanced conditioning and disrupted extinction.

4.2.1. Self-assessment analysis

The ANOVA results of the subjective valence rating difference (Table 2; Figure 9), between the conditioning and extinction tasks, showed a significant effect of Group, Time and Group x Time interaction. Post-hoc analysis of the Group effect showed a generally higher valence rating for both CS+ in the CSB group ($t=3.20$, $p=.002$), than in the HC group. Moreover, valence ratings were higher in the post-conditioning than in the pre-conditioning ($t=6.10$, $p<.001$) in post-extinction than in pre-conditioning ($t=2.99$, $p=.011$), and in post-conditioning than in post-extinction ($t=4.31$, $p<.001$). Post-hoc tests for the Group x Time interaction showed that the between-group difference was driven by the post-conditioning period ($t=2.81$, $p=.041$). Additionally, to check for the success of extinction, we tested pre-conditioning vs. post-extinction separately for each group, which yielded a significant difference for the CSB group ($t=3.81$, $p=.007$) and no significant difference in the HC group ($t=0.59$, $p>0.999$).

Table 2. Analysis of variance for differences in valence and arousal ratings.

	Difference in valence				Difference in arousal			
Effect	DF	F	η^2_g	p	DF	F	η^2_g	p
Group	1, 58	10.25	.047	**.002**	1, 58	10.78	.043	**.002**
Condition Type	1, 58	0.95	<.001	.333	1, 58	0.29	<.001	.593
Group:Condition Type	1, 58	0.37	<.001	.543	1, 58	3.60	.005	**.063**
Time	1.69, 97.76	24.64	.199	**<.001**	1.70, 98.61	27.25	.204	**<.001**
Group:Time	1.69, 97.76	4.63	.045	**.017**	1.70, 98.61	2.24	.021	.119
Condition Type:Time	1.79, 103.82	0.84	.001	.421	1.87, 108.29	0.57	.001	.553
Group:Condition Type:Time	1.79, 103.82	0.37	<.001	.669	1.87, 108.29	0.95	.002	.383

DF – degrees of freedom; η^2_g – generalized eta squared

Similarly, ANOVA for the difference in arousal ratings (Table 2; Figure 9) showed a significant effect of Group, Time, and a tendency for an interaction for Group x Condition Type. Post-hoc analysis for the Group effect showed a higher arousal rating for both CS+ in the CSB group than in the HC group (t=3.28, p=.002). Moreover, differences in arousal ratings were higher in the post-conditioning than in the pre-conditioning (t=6.63, p<.001), and in post-extinction than in pre-conditioning (t=3.61, p=.002), and in post-conditioning than in post-extinction (t=4.16, p=.001). Post hoc tests for the Group x Condition Type interaction showed that the between-group difference was present for $CS+_{erotic}$ (t=3.44, p=.004), but not for $CS+_{cash}$ (t=2.14, p=.110) Despite the lack of a significant Group x Time interaction, a hypothesis-driven direct check for the success of extinction in arousal, similar to valence, was performed. Therefore, pre-conditioning vs. post-extinction was tested separately for each group, averaged over Condition type (overall two post-hoc tests), which yielded a significant difference for the CSB group (t=4.11, p=0.003) and no difference in the HC group (t=1.15, p=0.977).

General successful conditioning and extinction reflected in the cue preference were shown in both of these ANOVA with a significant Time effect (Table 2). Post-hoc analyses showed no preference for neither of CS+ vs. CS- before conditioning, increased preference for both CS+ right after conditioning (arousal: t=7.31, p<.001, valence: t=6.87, p<.001), and a decrease in this preference after extinction (arousal: t=4.56, p<.001, valence: t=4.62, p<.001).

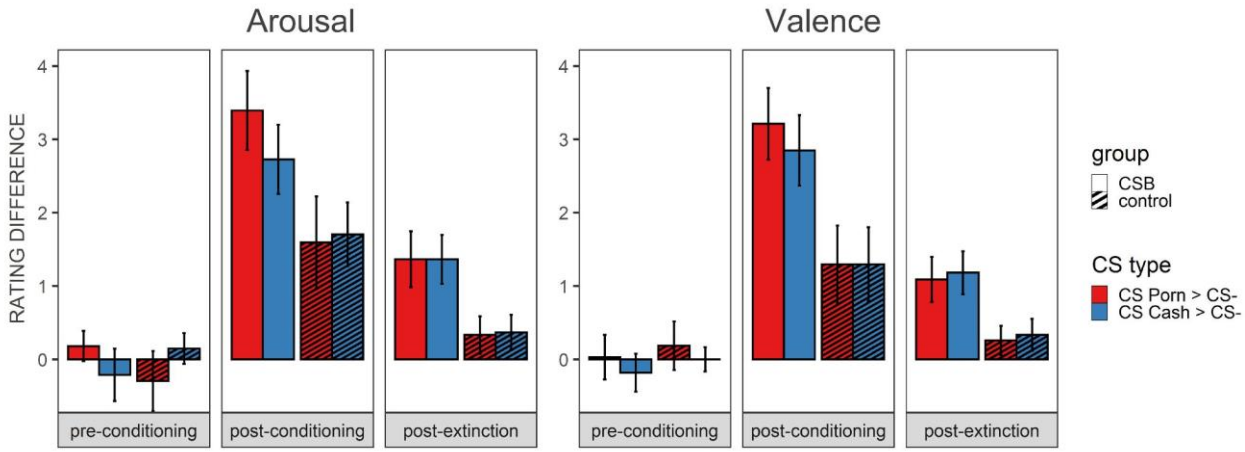

Figure 9. Differences in subjective arousal (left) and valence (right) towards both CS+ (relative to the CS-) before the beginning of the conditioning task, after conditioning, and

after the extinction task. The CSB group is denoted with plain bars and the HC with striped bars. The difference between $CS+_{erotic}$ vs. CS- is coded in red, and $CS+_{cash}$ vs. CS- is coded in blue. Error bars represent standard error.

4.2.2. Behavioral analysis

Differences in reaction times measured during conditioning were transformed with the Yeo-Johnson method since the residuals of the model did not follow a normal distribution. The ANOVA for differences in reaction times during conditioning (Table 3. Figure 10) showed a significant effect of Group, and an interaction for Group x Time. Post-hoc analysis of the Group effect showed faster reaction times for both CS+ in the CSB group (t=2.00, p=.050), and the Group x Time interaction showed that this difference was present during late conditioning period (t=3.11, p=.009), but not during the early conditioning period (t=0.07, p>.999). The ANOVA for reaction times during extinction showed no significant Group effect or interaction with Group effects (Table 3).

Table 3. Analysis of variance for differences in reaction times during conditioning and extinction phases.

		Conditioning			Extinction		
Effect	DF	F	η^2_g	p	F	η^2_g	p
Group	1, 56	5.02	.037	.029	0.79	.006	.379
Condition Type	1, 56	29.74	.056	**<.001**	24.82	.053	**<.001**
Group:Condition Type	1, 56	0.74	.001	.392	1.14	.003	.291
Time	1, 56	3.55	.023	**.065**	3.35	.015	**.073**
Group:Time	1, 56	6.10	.040	**.017**	0.59	.003	.444
Condition Type:Time	1, 56	0.40	<.001	.527	0.46	.001	.502
Group:Condition Type:Time	1, 56	0.00	<.001	.963	0.26	<.001	.612

DF – degrees of freedom; η^2_g – generalized eta squared

General heightened motivation, reflected by faster reaction times in both conditioning and extinction, was shown in both ANOVAs with a significant Condition Type effect (Table 3). Post-hoc analyses revealed longer reaction times for $CS+_{erotic}$ vs. $CS+_{cash}$ (conditioning: t=5.59, p<.001, extinction: t=4.98, p<.001).

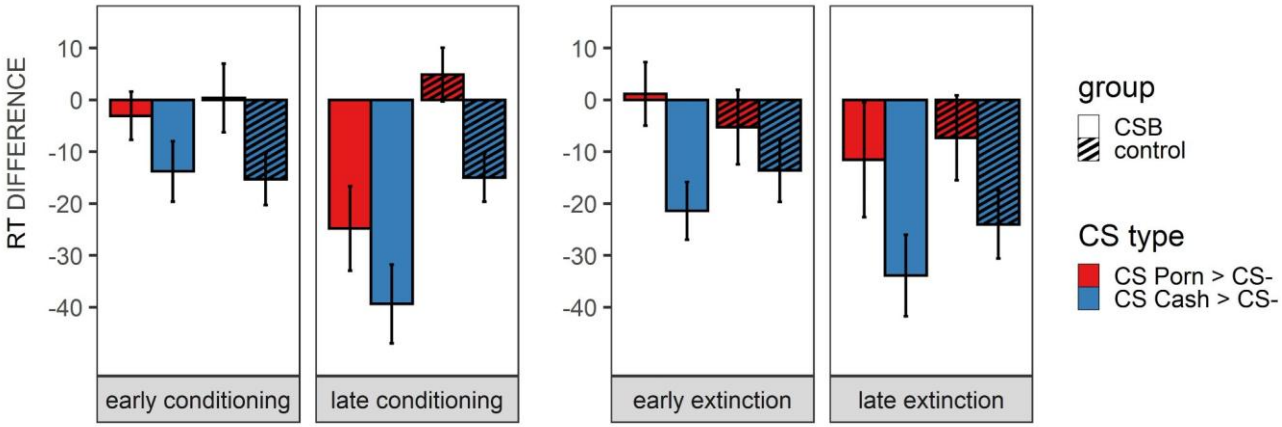

Figure 10. Differences in reaction times (ms) for both CS+ (relative to the CS-) during (left) conditioning and (right) extinction tasks are divided into early and late phases. The CSB group is denoted with plain bars and the HC with striped bars. The difference between $CS+_{erotic}$ vs. CS- is coded with red, and $CS+_{cash}$ vs. CS- is coded with blue color. Barplot was prepared using non-transformed data. Error bars represent standard error.

4.3.3. Correlational analysis

Results of correlation analysis are presented in Table 4. There was a significant positive correlation between score obtained in BPS and arousal (*rho*=0.42, p=.034) and tendency for BPS questionnaire and valence (*rho*=0.35, p=.074), as reported for $CS+_{erotic}$ in post-conditioning period.

Table 4. Correlation analysis of questionnaire measures and self-reported effects of conditioning and extinction in the CSB group.

	$CS+_{erotic}$ valence post-conditioning	$CS+_{erotic}$ arousal post-conditioning	$CS+_{erotic}$ valence post-extinction	$CS+_{erotic}$ arousal post-extinction
BPS	**0.35**#	**0.42***	-0.01	-0.02
SAST-R	0.14	0.02	-0.07	-0.16

*p < .05, #p < .075. Spearman correlation was used for all measures. Holm correction was used to control for multiple comparisons.

Therefore, hypothesis 3 is largely supported by the results, and hypothesis 7 is partially supported.

4.3. Task-based brain activity

In the following subsections, hypotheses 1 and 5 were tested using task-based brain activity analysis in ROI approach on six selected regions of brain reward system, i.e. ventral striatum, amygdala, ventromedial prefrontal cortex, dorsal anterior cingulate cortex and anterior and posterior orbitofrontal cortices. These hypotheses pertained to altered brain reward system activity among individuals with CSB during conditioning and extinction processes.

4.3.1. ROI analysis in conditioning

During conditioning, the ventral striatum yielded a significant interaction for Group x Time effects (Table 5). Post-hoc tests showed increased activity in late conditioning in the HC vs. CSB group (t=2.92, p=.017). Similarly, the anterior orbitofrontal cortex yielded an interaction for Group x Time effects (Table 5). Post-hoc testing showed increased activity in late conditioning in the CSB vs. HC group (t=2.7, p=.024) and an increase from the early to late conditioning phase in the CSB group (t=3.61, p=.002) but not in the HC group (t=-0.11, p>.999). The dorsal anterior cingulate cortex yielded an interaction for Group x Time effects (Table 5). Post-hoc testing showed decreased activity in late conditioning vs. early conditioning in the CSB group (t=3.06, p=.013) but no change in the HC group (t=1.22, p=.228). No

significant Group or interaction with Group effects were found in posterior orbitofrontal cortex, amygdala and ventromedial prefrontal cortex in conditioning. Significant (ventral striatum, dorsal anterior cingulate cortex and anterior orbitofrontal cortex) results are visualized in Figure 11.

Therefore, hypothesis 1 was partially supported by the results.

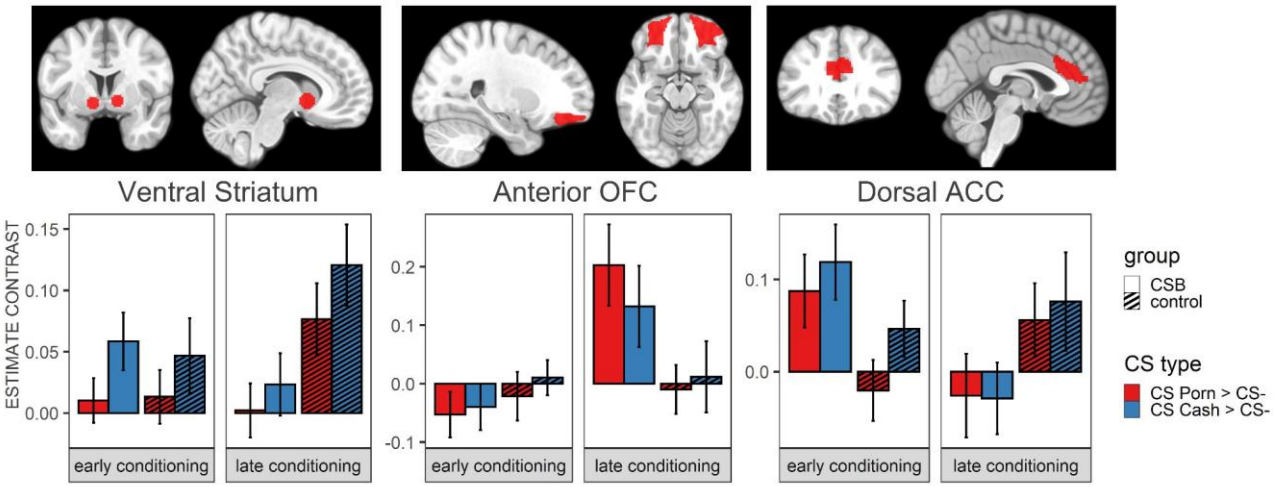

Figure 11. Brain activity during both CS+ (relative to the CS-) during conditioning is divided into early and late phases for three ROIs: (lower left) ventral striatum, (lower middle) anterior orbitofrontal cortex, and (lower right) dorsal anterior cingulate cortex), with significant Group or interaction with Group factors in the ANOVA model. The CSB group is denoted with plain bars and the HC with striped bars. The difference between $CS+_{erotic}$ vs. CS- is coded with red, and $CS+_{cash}$ vs. CS- is coded with yellow. Error bars represent standard error. The upper panel represents localization of the regions of interest (regions highlighted in red). OFC - orbitofrontal cortex; ACC - anterior cingulate cortex.

Table 5. Analysis of variance for differences in brain activity during conditioning phase for ventral striatum, anterior orbitofrontal cortex, and dorsal anterior cingulate cortex.

		Ventral Striatum			Anterior orbitofrontal cortex			Dorsal anterior cingulate cortex		
Effect	DF	F	η^2_g	p	F	η^2_g	p	F	η^2_g	p
Group	1, 61	3.81	.024	.056	1.95	.015	.167	0.00	<.001	.959
Condition Type	1, 61	9.91	.019	**.003**	<0.01	<.001	.957	1.84	.005	.180
Group:Condition Type	1, 61	0.03	<.001	.859	2.20	.003	.143	0.47	.001	.496
Time	1, 61	1.28	.008	.263	6.80	.043	**.011**	1.63	.009	.207
Group:Time	1, 61	4.73	.029	**.034**	6.03	.039	**.017**	9.08	.048	**.004**
Condition Type:Time	1, 61	0.15	<.001	.698	2.39	.002	.127	1.32	.002	.256
Group:Condition Type:Time	1, 61	0.82	.001	.369	1.47	.001	.231	0.03	<.001	.863

DF - degrees of freedom; η^2_g - generalized eta squared

Table 6. Analysis of variance for differences in brain activity during conditioning phase posterior orbitofrontal cortex, ventromedial prefrontal cortex and amygdala.

		Posterior orbitofrontal cortex			Ventromedial prefrontal cortex			Amygdala		
Effect	DF	F	η^2_g	p	F	η^2_g	p	F	η^2_g	p
Group	1, 61	0.46	.003	.502	<0.01	<.001	.984	2.25	.011	.139
Condition Type	1, 61	2.33	.004	.132	0.17	<.001	.681	0.34	<.001	.561
Group:Condition Type	1, 61	0.33	<.001	.570	0.10	<.001	.753	0.38	<.001	.538
Time	1, 61	0.70	.004	.406	0.02	<.001	.901	0.05	<.001	.825
Group:Time	1, 61	0.02	<.001	.888	2.32	.013	.133	2.84	.021	.097
Condition Type:Time	1, 61	0.05	<.001	.819	1.33	.002	.253	0.01	<.001	.936
Group:Condition Type:Time	1, 61	1.16	.002	.286	0.31	<.001	.579	0.44	<.001	.510

DF - degrees of freedom; η^2_g - generalized eta squared

4.3.2 ROI analysis in extinction

In extinction, ventral striatum yielded an interaction for Group x Time x Condition Type effects (Table 7). Post-hoc tests showed larger activity for $CS+_{cash}$ vs. $CS+_{erotic}$ in late extinction in the CSB group (t=3.41, p=.007) but not in the HC group (t=0.52, p>.99) and no differences between $CS+_{cash}$ vs. $CS+_{erotic}$ in early extinction (separately for CSB and HC). Additionally, we found a significantly decreased activity for $CS+_{erotic}$ in late vs. early extinction in the CSB group (t=2.89, p=.033), but not for $CS+_{cash}$ (t=0.44, p>.99), and no differences between either $CS+_{erotic}$ or $CS+_{cash}$ in late vs. early extinction in the HC group (t=-0.33, p>.99; t=1.12, p>.99). We did not find any direct difference between the CSB and HC group. The dorsal anterior cingulate cortex yielded a Group effect (Table 7). Post-hoc tests showed generally higher activity in the CSB group vs. HC (t=2.2, p=.031). No significant Group or interaction with Group effects were found in amygdala (Table 8). The ventromedial prefrontal cortex yielded a weak tendency in Group x Time x Condition Type effects (Table 8); however, post-hoc tests showed no significant group differences in comparisons of interest. Significant (ventral striatum, dorsal anterior cingulate cortex) results are visualized in Figure 12.

Therefore, hypothesis 5 was partially supported by the results.

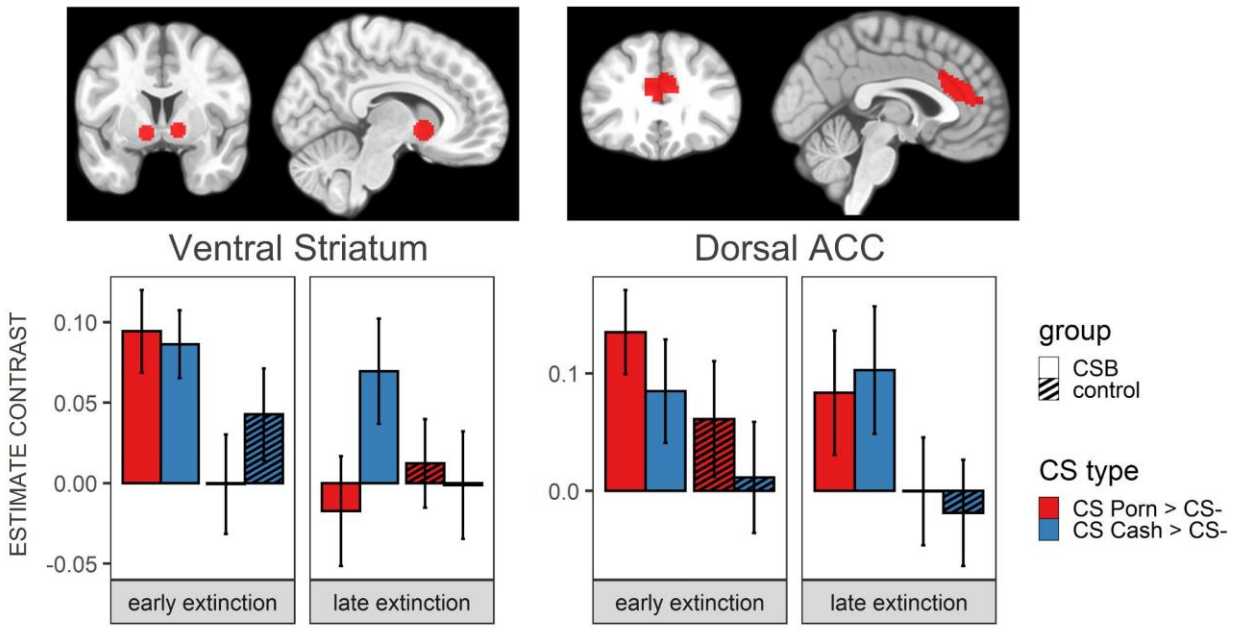

Figure 12. Brain activity during both CS+ (relative to the CS-) during extinction is divided into early and late phases for 2 ROIs: (lower left) ventral striatum and (lower right) dorsal anterior cingulate cortex with significant Group or interaction with Group factors in the

ANOVA model. The CSB group is denoted with plain bars and the HC with striped bars. The difference between $CS+_{erotic}$ vs. CS- is coded in red, and $CS+_{cash}$ vs. CS- is coded in blue. Error bars represent standard error. The upper panel represents localization of the regions of interest (regions highlighted in red). ACC - anterior cingulate cortex.

Table 7. Analysis of variance for differences in brain activity during extinction phase for ventral striatum, anterior orbitofrontal cortex, and dorsal anterior cingulate cortex.

		Ventral striatum			Anterior orbitofrontal cortex			Dorsal anterior cingulate cortex		
Effect	DF	F	η^2_g	p	F	η^2_g	p	F	η^2_g	p
Group	1, 61	3.69	.022	.059	0.47	.003	.497	4.86	.033	**.031**
Condition Type	1, 61	5.11	.008	**.027**	0.01	<.001	.925	1.68	.003	.200
Group:Condition Type	1, 61	1.04	.002	.312	0.79	.002	.379	0.24	<.001	.628
Time	1, 61	2.78	.018	.100	2.67	.014	.107	0.77	.004	.385
Group:Time	1, 61	1.04	.007	.313	1.34	.007	.252	0.16	<.001	.687
Condition Type:Time	1, 61	0.49	.001	.488	0.03	<.001	.854	1.39	.003	.243
Group:Condition Type:Time	1, 61	7.76	.016	**.007**	0.98	.002	.326	0.20	<.001	.659

DF - degrees of freedom; η^2_g - generalized eta squared

Table 8. Analysis of variance for differences in brain activity during extinction phase posterior orbitofrontal cortex, ventromedial prefrontal cortex and amygdala.

	Posterior orbitofrontal cortex				Ventromedial prefrontal cortex			Amygdala		
Effect	DF	F	η^2_g	p	F	η^2_g	p	F	η^2_g	p
Group	1, 61	2.63	.018	.110	0.54	.003	.465	0.46	.002	.502
Condition Type	1, 61	0.54	.002	.465	0.00	<.001	.986	0.54	.001	.465
Group:Condition Type	1, 61	1.14	.003	.291	0.93	.002	.338	2.94	.007	.091
Time	1, 61	0.72	.004	.398	0.96	.006	.332	0.73	.006	.398
Group:Time	1, 61	0.14	<.001	.714	2.63	.015	.110	0.18	.001	.677
Condition Type:Time	1, 61	1.01	.001	.320	0.15	<.001	.696	0.34	<.001	.559
Group:Condition Type:Time	1, 61	2.19	.003	.144	3.30	.006	**.074**	1.58	.003	.214

DF - degrees of freedom; η^2_g - generalized eta squared.

4.5. Outcome (reward) processing

In the following section, hypothesis 4 was tested using task-based brain activity analysis in ROI approach on six selected regions of brain reward system, i.e. ventral striatum, amygdala, ventromedial prefrontal cortex, dorsal anterior cingulate cortex and anterior and posterior orbitofrontal cortices. This hypothesis pertained to consummatory reward processing, as opposed anticipatory cue processing, among individuals with CSB.

Brain activity during the outcome stimuli presentation, i.e. rewards, was compared between CSB and HC groups in each of the six ROIs. Both erotic and monetary conditions were considered but only during conditioning (both early and late), as in the extinction task rewards were no longer presented. Similarly to cue processing analysis, six separate Bayesian equivalent to ANOVA were conducted on each ROI.

The Bayesian ANOVAs indicated that the observed results support the hypothesis of no difference between CSB and HC groups in either Group or any interaction with Group factors (see Tables 9, 10 and 11).

Therefore, hypothesis 4 was supported.

Table 9. Bayesian analysis of variance for differences in brain activity during reward presentation in ventral striatum, and anterior orbitofrontal cortex.

		Ventral striatum					Anterior orbitofrontal cortex				
Effect	P(prior)	P(posterior)	BF_{10}	BF_{excl}	$P(posterior)_{excl}$	error	P(posterior)	BF_{10}	BF_{excl}	$P(posterior)_{excl}$	error
Group	.13	.36	3.93	16.11	.70	.06%	.48	6.42	3.29	.32	.08%
Condition Type	.13	.01	0.04	0.02	<.01	<.01%	.07	0.55	0.15	.02	.01%
Group:Condition Type	.13	.50	7.06	29.04	.81	.09%	.49	6.69	3.44	.33	.08%
Time	.13	.10	0.79	3.12	.31	.01%	.41	4.93	2.49	.26	.07%
Group:Time	.13	.51	7.22	29.73	.81	.09%	.50	7.02	3.61	.34	.09%
Condition Type:Time	.13	.47	6.16	25.33	.78	.08%	.50	7.09	3.65	.34	.09%
Group:Condition Type:Time	.13	.49	6.60	27.17	.80	.08%	.50	7.13	3.67	.34	.09%

BF – Bayesian Factor

Table 10. Bayesian analysis of variance for differences in brain activity during reward presentation dorsal anterior cingulate cortex and posterior orbitofrontal cortex.

		Dorsal anterior cingulate cortex					Posterior orbitofrontal cortex				
Effect	P(prior)	P(posterior)	BF_{10}	BF_{excl}	$P(posterior)_{excl}$	error	P(posterior)	BF_{10}	BF_{excl}	$P(posterior)_{excl}$	error
Group	.13	.31	3.09	1.1e+5	1.00	.05%	.50	6.90	1.3e+15	1.00	.09%
Condition Type	.13	<.01	<0.01	<0.01	<.01	<.01%	<.01	<0.01	<0.01	<.01	<.01%
Group:Condition Type	.13	.50	6.91	2.6e+6	1.00	.09%	.51	7.21	1.4e+15	1.00	.09%
Time	.13	.48	6.55	2.5e+6	1.00	.08%	.41	4.83	9.3e+14	1.00	.07%
Group:Time	.13	.27	2.55	9.7e+5	1.00	.04%	.39	4.42	8.5e+14	1.00	.06%
Condition Type:Time	.13	.20	1.70	6.4e+4	1.00	.03%	.20	1.73	3.3e+14	1.00	.03%
Group:Condition Type:Time	.13	.49	6.60	2.5.e+6	1.00	.08%	.50	6.99	1.3e+15	1.00	.09%

BF – Bayesian Factor

Table 11. Bayesian analysis of variance for differences in brain activity during reward presentation in ventromedial prefrontal cortex and amygdala.

	Ventromedial prefrontal cortex						Amygdala				
Effect	P(prior)	P(posterior)	BF_{10}	BF_{excl}	$P(posterior)_{excl}$	error	P(posterior)	BF_{10}	BF_{excl}	$P(posterior)_{excl}$	error
Group	.13	.15	1.20	1.7e+09	1.00	.02%	.31	3.09	3.8e+30	1.00	.05%
Condition Type	.13	<.01	<0.01	<0.01	<.01	<.01%	<.01	<0.01	0.0e+00	<.01	<.01%
Group:Condition Type	.13	.47	6.25	8.8e+09	1.00	.08%	.51	7.21	8.8e+30	1.00	.09%
Time	.13	.49	6.77	9.5e+09	1.00	.09%	.49	6.76	8.3e+30	1.00	.09%
Group:Time	.13	.51	7.24	1.0e+10	1.00	.09%	.32	3.26	4.0e+30	1.00	.05%
Condition Type:Time	.13	.46	5.89	8.3e+09	1.00	.08%	.51	7.24	8.9e+30	1.00	.09%
Group:Condition Type:Time	.13	.48	6.47	9.1e+09	1.00	.08%	.50	6.90	8.5e+30	1.00	.09%

BF – Bayesian Factor

4.6. Functional connectivity during the associative learning

To test the hypotheses 2 and 6 of altered functional connectivity between reward system's regions during conditioning and extinction tasks, generalized psychophysiological interaction analysis was conducted. Similarly to behavioral and task-based activity, separate F-tests were conducted on conditioning and extinction tasks, and only on the cues (i.e. $CS+_{erotic}$ and $CS+_{cash}$). Additionally, correlational analyses were performed on functional connectivity altered in CSB group, and self-reported effects of conditioning and effectiveness of extinction (i.e. arousal and valence towards $CS+_{erotic}$).

4.6.1. Functional connectivity during conditioning

In the conditioning task, significant interaction of Group x Condition was observed, indicating altered functional connectivity between ventral striatum and anterior orbitofrontal cortex among the CSB group (F=5.44, p=.005). Post-hoc analysis revealed stronger connectivity between these regions during $CS+_{erotic}$ in CSB group (t=3.24; p=.002) and larger positive difference between $CS+_{erotic}$ and $CS+_{cash}$ in CSB vs. healthy control group (t= 2.41; p=.019), indicating stronger bias towards erotic cues in the CSB group. No differences in $CS+_{cash}$ between groups were significant.

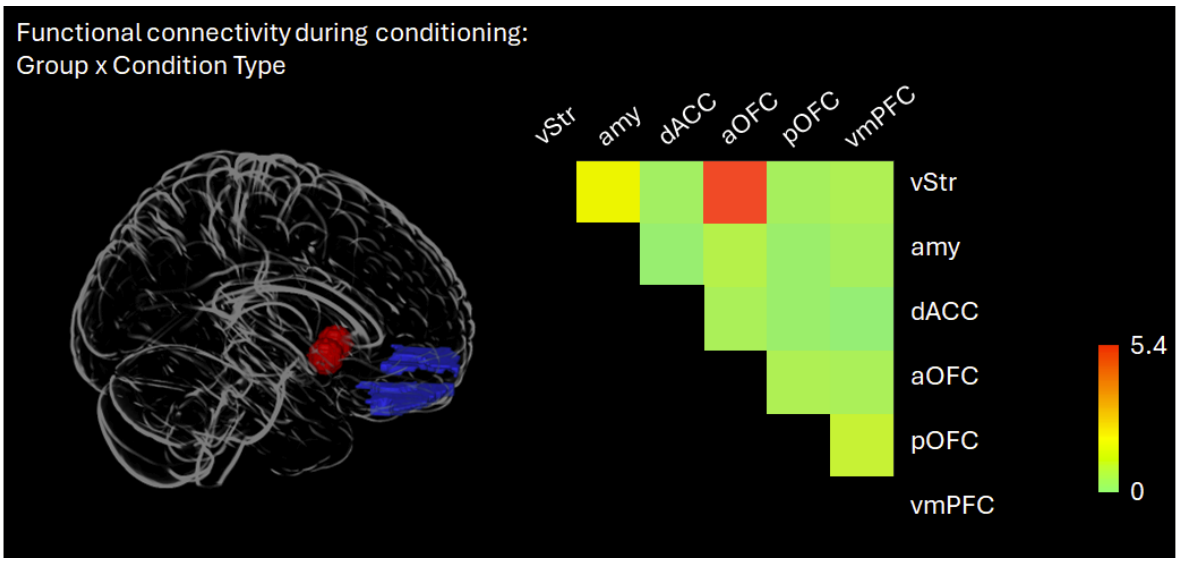

Figure 13. Group x Condition Type interaction in functional connectivity during conditioning task. Depicted on the right side is the connectivity matrix between pairs of brain reward system regions, mapping F statistics of Group x Condition Type interaction. On the left side a glass brain with pairs of regions displaying significant interaction, i.e. ventral striatum (red)

and anterior orbitofrontal cortex (blue), confirmed in subsequent post-hoc analysis. vStr - Ventral striatum; amy – amygdala; dACC - dorsal anterior cingulate cortex, aOFC/pOFC – anterior/posterior orbitofrontal cortex; vmPFC - ventromedial prefrontal cortex.

The relationship between the effects of conditioning and extinction (measured with self-reported valence and arousal) and the ventral striatum and anterior orbitofrontal cortex functional connectivity strength during early and late conditioning was tested in the CSB group. To focus on the effects of interest and therefore reduce the amount of statistical tests only, effects for $CS+_{erotic}$ were analyzed. Functional connectivity between these two regions was picked based on the significant alterations demonstrated in CSB vs. healthy control. Based on the fact that functional connectivity was stronger between these regions in the CSB group, positive association between the connectivity strength of ventral striatum and anterior orbitofrontal cortex and the conditioning, and negative with extinction measures was assumed, i.e. that the stronger the connectivity during conditioning the more appetitive the cues, and the stronger the connectivity during conditioning, the less effective the extinction success. This amounted to eight statistical tests.

Table 12. Correlation analysis of functional connectivity between ventral striatum and anterior orbitofrontal cortex and self-assessed valence and arousal ratings in towards $CS+_{erotic}$ (vs. CS-) CSB group.

vStr - aOFC connectivity	$CS+_{erotic}$ valence post-conditioning	$CS+_{erotic}$ arousal post-conditioning	$CS+_{erotic}$ valence post-extinction	$CS+_{erotic}$ arousal post-extinction
early conditioning	-.12	-.05	<.01	.28
late conditioning	.05	.13	.14	**.39#**

#p < .075 (Holm corrected). Pearson correlation was used for all measures. Holm correction was used to control for multiple comparisons. vStr - ventral striatum; aOFC - anterior orbitofrontal cortex; CS+ - conditioned stimulus.

The one relationship found to have tendency of significance (after Holm correction), was between ventral striatum and anterior orbitofrontal cortex functional connectivity and self-reported extinction success in arousal, i.e. the stronger the

connectivity during CS+$_{erotic}$ processing, the less effective the subsequent extinction of arousal towards that cue (see Table 12). No relationship was found between functional connectivity between the ventral striatum and anterior orbitofrontal cortex during conditioning and self-assessed conditioning effects.

Additionally, no relationship between the functional connectivity of ventral striatum and anterior orbitofrontal cortex during conditioning and CSB symptoms measured with BPS nor SAST-R was found to be significant. Exploratory analysis on other connectivity pairs also yielded no significant relationships.

4.6.2. Functional connectivity during extinction

In the extinction task, significant interaction of Group x Condition was observed, indicating altered functional connectivity between the ventral striatum and ventromedial prefrontal cortex among the CSB group (F=4.95, p=.01). Post-hoc analysis revealed weaker functional connectivity between these regions during CS+$_{erotic}$ in CSB group than HC (t=3.15, p=.002). No significant differences in CS+$_{cash}$ between groups were observed.

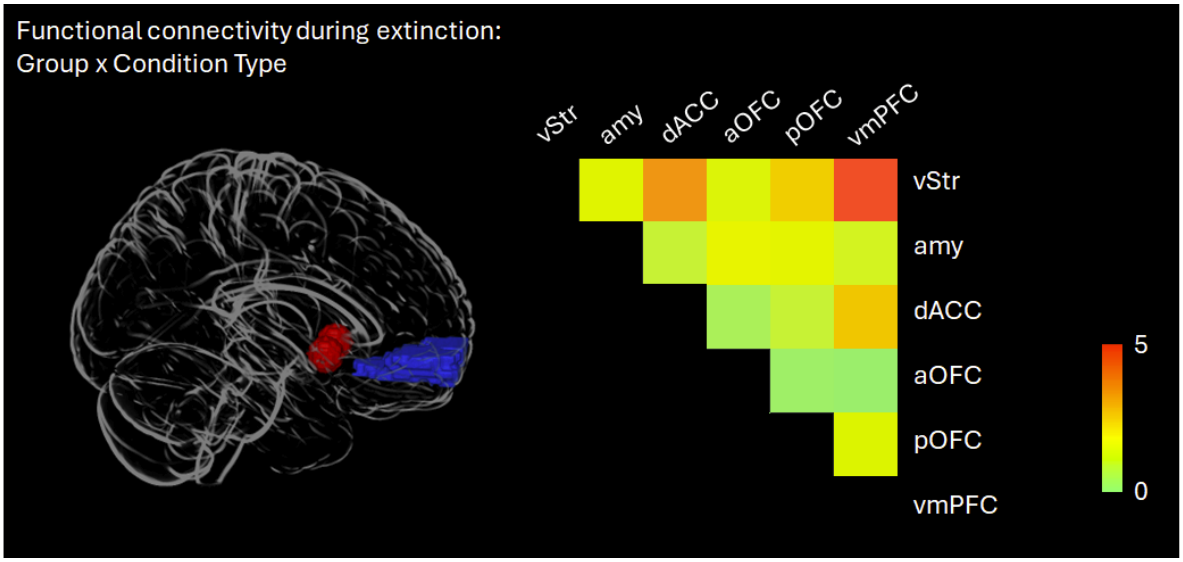

Figure 14. Group x Condition Type interaction in functional connectivity during extinction task. Depicted on the right side is the connectivity matrix between pairs of brain reward system regions, mapping F statistics of Group x Condition Type interaction. On the left side a glass brain with pairs of regions displaying significant interaction, i.e. ventral striatum (red) and ventromedial prefrontal cortex (blue), confirmed in subsequent post-hoc analysis. vStr - Ventral striatum; amy – amygdala; dACC - dorsal anterior cingulate cortex, aOFC/pOFC – anterior/posterior orbitofrontal cortex; vmPFC - ventromedial prefrontal cortex.

Additionally, Group x Time interaction was observed, also in the connection between the ventral striatum and ventromedial prefrontal cortex among the CSB group (F=7.19, p=.002). Post-hoc analysis revealed weaker functional connectivity between these regions during early extinction among the CSB group (t=3.8, p<.001). No differences in late extinction between groups were significant.

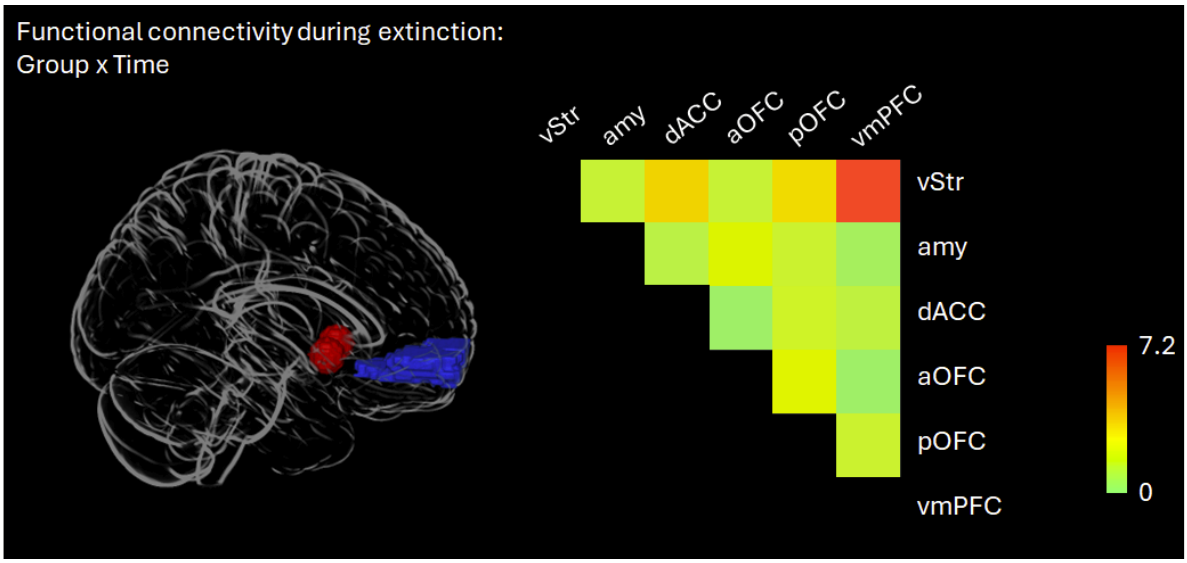

Figure 15. Group x Time interaction in functional connectivity during extinction task. Depicted on the right side is the connectivity matrix between pairs of brain reward system regions, mapping F statistics of Group x Time interaction. On the left side a glass brain with pairs of regions displaying significant interaction, i.e. ventral striatum (red) and ventromedial prefrontal cortex (blue), confirmed in subsequent post-hoc analysis. vStr - Ventral striatum; amy – amygdala; dACC - dorsal anterior cingulate cortex, aOFC/pOFC – anterior/posterior orbitofrontal cortex; vmPFC - ventromedial prefrontal cortex.

Similarly to conditioning, the relationship between the effects of conditioning and extinction (measured with self-reported valence and arousal) and the ventral striatum and ventromedial prefrontal cortex functional connectivity strength during early and late extinction was tested in the CSB group. Only effects for $CS+_{erotic}$ were analyzed. Functional connectivity between these two regions was picked based on the significant alterations demonstrated in CSB vs. healthy control. Based on the fact that functional connectivity was weaker between these regions in the CSB group, negative association between the connectivity strength of ventral striatum and ventromedial prefrontal cortex and conditioning, and positive with extinction measures was assumed, i.e. that the more appetitive the cues, the weaker the

connectivity during extinction, and the weaker the connectivity during extinction, the less effective the extinction success. This amounted to eight statistical tests, mirroring the functional connectivity analysis during conditioning.

Table 13. Correlation analysis of functional connectivity between ventral striatum and ventromedial prefrontal cortex and self-assessed valence and arousal ratings in towards $CS+_{erotic}$ (vs. CS-) CSB group.

vStr - vmPFC connectivity	$CS+_{erotic}$ valence post-conditioning	$CS+_{erotic}$ arousal post-conditioning	$CS+_{erotic}$ valence post-extinction	$CS+_{erotic}$ arousal post-extinction
early extinction	**-.48***	-.35	-.11	.03
late extinction	.18	.05	-.01	-.33

*p < .05 (Holm corrected). Pearson correlation was used for all measures. Holm correction was used to control for multiple comparisons. vStr - ventral striatum; vmPFC - ventromedial prefrontal cortex; CS+ - conditioned stimulus.

The one relationship found to be significant (after Holm correction), was between self-assessed effects of conditioning in valence towards $CS+_{erotic}$ (see Table 13), i.e. the stronger the self-reported effects of conditioning in valence, the weaker the connectivity during extinction. Although arousal displayed a similar correlation, it did not survive correction for multiple comparisons ($r= -.35$, $p_{uncorrect} =.026$). Similarly, while a correlation between ventral striatum and ventromedial prefrontal cortex functional connectivity and self-assessed extinction success in arousal, i.e. the weaker the connectivity during $CS+_{erotic}$ processing, the less effective the subsequent extinction of arousal towards that cue, was found, it did not survive multiple-testing correction ($r= -.33$, $p_{uncorrect} =.033$).

No relationship between ventral striatum and ventromedial prefrontal cortex during extinction and CSB symptoms measured with BPS nor SAST-R was found to be significant. Exploratory analysis on other connectivity pairs also yielded no significant relationships.

4.6.3. Summary of functional connectivity during both tasks

To summarize the results from both conditioning and extinction tasks:

1) In conditioning, anterior orbitofrontal cortex and ventral striatum functional connectivity was stronger in the CSB group compared to the HC group for $CS+_{erotic.}$

2) In extinction, ventromedial prefrontal cortex and ventral striatum cortex functional connectivity was weaker in the CSB group compared to healthy control for $CS+_{erotic}$ in both early and late extinction phases, and weaker during both $CS+_{erotic}$ and $CS+_{cash}$ in early extinction.

3) The stronger the ventral striatum and anterior orbitofrontal cortex functional connectivity during late conditioning, the worse the subsequent arousal extinction effectiveness (tendency after correction).

4) The stronger the conditioning effects in valence (and arousal when uncorrected), the weaker the ventral striatum and ventromedial prefrontal cortex connectivity during early extinction.

5) The weaker the ventral striatum and ventromedial prefrontal cortex connectivity in late extinction, the worse the arousal extinction effectiveness (uncorrected).

Therefore, hypothesis 2 was largely supported, excluding the assumed relationships with amygdala and functional connectivity correlation with CSB symptoms. Hypothesis 6 was also largely supported, also excluding the assumed relationships with amygdala and functional connectivity correlation with CSB symptoms.

4.7. Resting-state functional connectivity

To test hypothesis 8, pertaining to altered brain reward system communication among individuals with CSB without any task or erotic context, functional connectivity of brain reward system's regions - ventromedial prefrontal cortex, orbitofrontal cortex, dorsal anterior cingulate cortex, amygdala and ventral striatum - was analyzed using ROI-to-ROI approach. Additionally, the correlations between strength of these connections and self-reported effects of conditioning and extinction were tested in the CSB group. This allowed investigation of the relationship between resting reward system functioning and the propensity for altered associative learning in individuals with CSB.

No group differences between selected reward system regions in the strength of functional connectivity was found. Additionally, no association between functional

connectivity and self-reported effects of conditioning and extinction was found in the CSB group.

Therefore, hypothesis 8 was not supported.

4.8. Cortical thickness of orbitofrontal and prefrontal cortices

To test hypothesis 9, pertaining to morphological changes in the ventromedial prefrontal cortex and its relationship with disrupted extinction among individuals with CSB, a surface-based morphometry analysis was performed. As the volume-based ROI used in the task-based activity analyses does not have a one-to-one representation in the surface-based Destrieux cortical parcellation atlas, a series of independent sample *t*-tests were conducted for each orbitofrontal and ventromedial prefrontal ROI, comparing the CSB and healthy control groups (Figure 16).

Reduction in cortical thickness in the CSB group was only observed in the right orbital olfactory sulcus ($t=3.449$, $p<.001$). However, this cortical area is not part of the ventromedial prefrontal cortex, which was hypothesized to be thinner in the CSB group (Figure 16). No correlations were found between cortical thickness and self-assessed extinction effectiveness.

Therefore, hypothesis 9 was not supported.

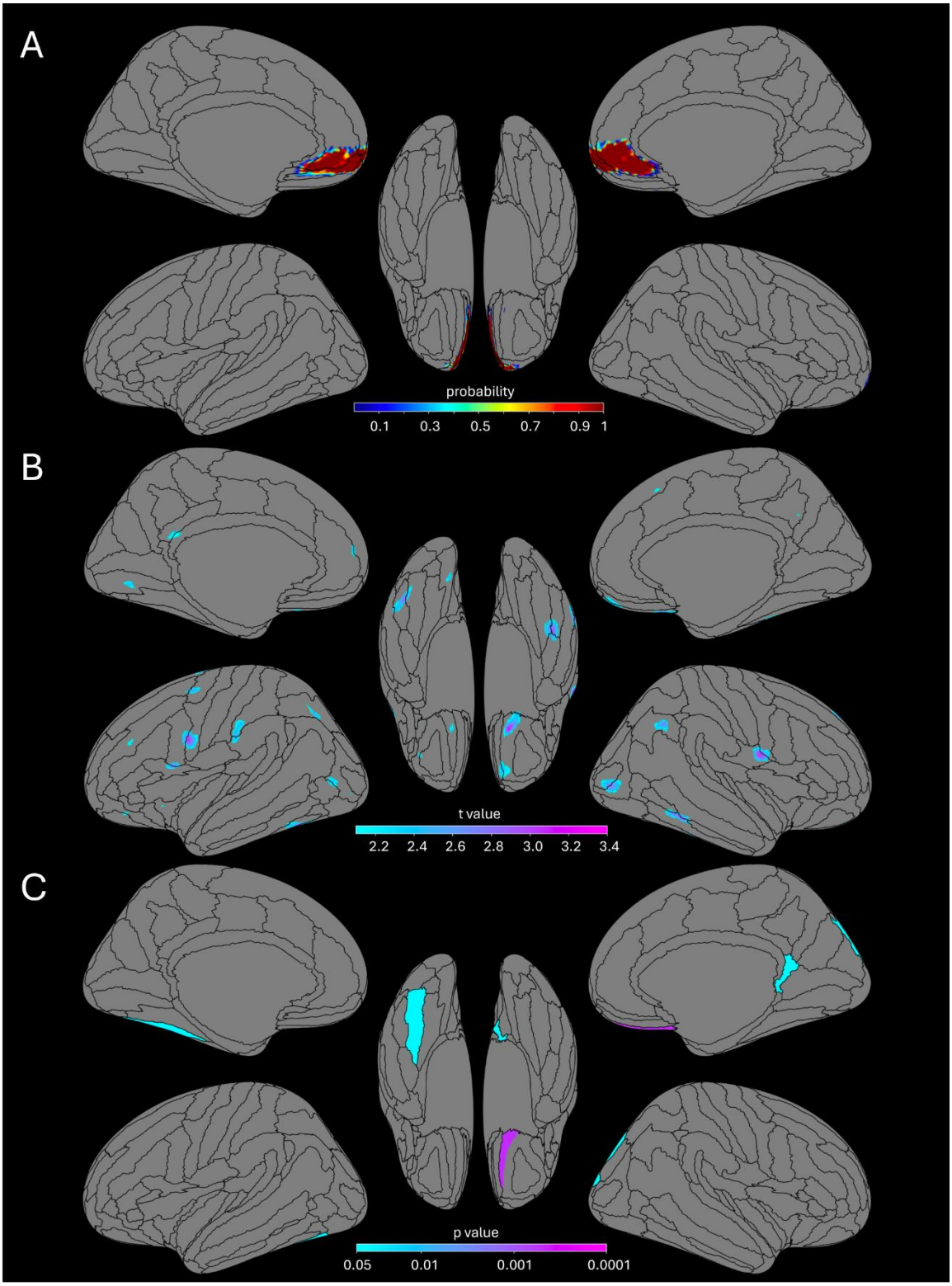

Figure 16. Cortical thickness reduction among individuals with CSB compared to healthy control subjects in a parcellated approach with overlaid contours of parcellation using Destrieux sulco-gyral atlas. A) for visualization purpose, projection of volume-based ventromedial prefrontal cortex region of interest onto the surface. B) Whole-brain surface-based mapping of group differences in cortical thickness. The statistical threshold used here is uncorrected p<.01. C) Surface-based group differences using individualized brain

parcellation and region-of-interest analysis approach, thresholded using uncorrected p<.05. For visualization purposes, all the regions and their corresponding *p* values were plotted. Color bar represents: (a) probability of vertex representation of the volume-based ventromedial prefrontal cortex region of interest; (b) *t*-value and (c) *p*-value of between-groups differences tests.

5. Discussion

In this dissertation, signs of appetitive associative learning processes dysfunctions with their neurobiological substrates within the reward system were explored among men struggling with CSB symptoms, e.g. problematic pornography use. As postulated by the Incentive Sensitization Theory model, appetitive associative learning—conditioning and extinction in particular—are key processes in the development and maintenance of addictive behavior (Robinson & Berridge, 1993, 2001, 2008; Berridge & Robinson, 2016). This model is also the most widely discussed view of CSB symptoms emergence and persistence in neuroimaging studies (Antons & Brand 2020; Golec et al., 2021; Gola et al., 2017; Draps et al., 2022; Seok & Sohn 2020; Sinke et al. 2020; Starcke et al., 2018; Liberg et al. 2022; Voon et al., 2014; Wang et al., 2024; Wang & Dai 2020; Wang & Li, 2023; Wang, Chen & Zhang, 2021; for review see: Klein et al., 2021). To date, however, no comprehensive evaluation has been conducted on the role of appetitive learning and underlying alterations in reward system functioning in reference to CSB. This work therefore aims to fill this gap, by providing detailed examination of acquisition and extinction of appetitive conditioned responses, reward-related specificity of these processes and their neurobiological underpinnings among men struggling with CSB.

Several hypotheses have been stated in present research, each of which concerned either self-assessed, behavioral or neuronal level of appetitive learning and its alterations among individuals with CSB. For clarity, see Table 14 for a summary of research questions and whether hypotheses related to them were supported by the results.

Table 14. Summary of posed research questions and hypotheses with indication of degree to which they were supported by the results.

	Hypotheses confirmation	Research question posed
Research question 1		Do individuals with CSB exhibit incentive salience sensitization via appetitive associative learning specific to erotic cues during active conditioning.
Hypothesis 1	Partially supported	
Hypothesis 2	Largely supported	
Hypothesis 3	Largely supported	
Research question 2		Does altered reactivity of the reward system in individuals with CSB also manifests during the actual processing of rewards, both erotic and monetary
Hypothesis 4	Fully supported	
Research question 3		Do individuals with CSB exhibit impaired extinction of sensitized cue-driven responses, and if such impairments are specific to erotic stimuli or more generalized.
Hypothesis 5	Largely supported	
Hypothesis 6	Largely supported	
Hypothesis 7	Partially supported	
Research question 4		Do individuals with CSB exhibit functional alterations in the brain's reward system during resting state, independent of task engagement or exposure to sexual stimuli
Hypothesis 8	Not supported	
Research question 5		Does structural alterations in ventromedial prefrontal regions of the reward system underlie observed disruption in extinction
Hypothesis 9	Not supported	

5.1. Enhanced conditioning in CSB

The primary research question of this dissertation aimed to determine whether individuals with CSB exhibit incentive salience sensitization via appetitive associative learning specific to erotic cues during active conditioning. Specifically, it was sought to understand if this sensitization is particular to cues of erotic rewards or reflects a generalized dysfunction of the reward system affecting other types of cue-outcome, such as monetary incentives.

On the self-assessed and behavioral level, in comparison to the control group, **CSB group expressed stronger subjective arousal and valence and shorter reaction times to cues of stimuli reinforced by both erotic and monetary rewards. These effects were not reflected within reward system's regions in fMRI whole-brain analysis**, which is in line with previous studies that reported no robust CSB-specific alterations of activity patterns in the whole-brain analysis (for review: Klein et al., 2022). **More sensitive region-of-interest analyses indicated specific effects**, which are discussed in detail in the following sections.

5.1.1. Behavioral and self-reported effects of conditioning

Previous studies on CSB reported mixed results regarding self-assessed and behavioral reactions during conditioning tasks. Such ambiguity may be related to differences in studied populations (diagnosed with CSBD according to the ICD-11 criteria, subclinical or/and general population), implemented different reward modalities (monetary, erotic, or/and both) and different tasks used (Pavlovian vs. instrumental conditioning). Enhanced transfer of motivational value to an initially neutral cues (measured via self-assessment or behaviorally via reaction times) was observed in three studies, out of which two used Pavlovian conditioning and all three used an erotic-type rewards (Hoffman et al., 2014; Snagowski et al., 2016; Banca et al., 2016).

The study of Banca et al. (2016) was the only study to use both monetary and erotic reward, and, similar to results presented in this dissertation, Authors observed strengthened conditional responses to both of them. Both the study presented in this dissertation and Banca's et al. (2016) study suggest that individuals with CSB might present general, unspecific strengthening of reward-based associative learning. On the other hand, Snagowski et al. (2016), who (like

Banca et al., 2016) used Pavlovian-to-instrumental conditioning task (i.e. transfer of motivational salience from conditioned stimulus to instrumental reaction) using only cues of monetary rewards, did not observe that transfer. One possible explanation for this discrepancy is the fact that Snagowski et al. (2016) studied a general male population sample that was median-split based on Online Sexual Behaviour questionnaire scores, while Banca et al. (2016) and the study presented in this dissertation studied men struggling with CSB symptoms. In study by Klucken et al. (2016) however, no CSB vs. control group differences were present in either self-assessed arousal, valence or sexual arousal towards cues of erotic outcome, nor in the psychophysiological arousal measured with galvanic skin response. Perhaps instrumental action-outcome, goal-directed behavior is an important component of motivational and affective transfer in CSB, as in the Klucken et al. (2016) study classical conditioning procedure was used.

Self-assessment results (see Sections 4.2.1 and 4.2.2) indicated that subjective motivational (arousal) and value-related (valence) transfer from outcome reward to cues was enhanced in CSB. The motivational transfer was more reward-specific towards erotic cues, whereas value-related transfer was non-reward-specific, although both (erotic and monetary) followed a similar pattern among the CSB group. Since the used task design included elements of instrumental conditioning (receipt of the reward depended on the speed of performed button press), it was also possible to objectively measure motivational aspects of rewards to cues transfer with analysis of reaction times. The conditioning (and extinction) tasks used in the presented study were divided into early and late phases to capture the learning progression and accompanied changes in brain activity. In the late phase of conditioning, the reaction times to both cues of rewarding outcomes were shorter in the CSB group, but with no bias toward cues of erotic rewards. The latter result is inconsistent with subjective self-assessment of arousal described above and not in line with expectations inferred from the literature. Based on previous studies on explicit cue-reactivity (Gola et al., 2017; Golec et al., 2021; Draps et al., 2021), it was hypothesized that once the cue-outcome contingency was established by the participants in the late conditioning, the motivation measured via reaction times would be selectively increased for erotic cues only. However, the latter studies used explicit cues in the form of naked woman pictograms, which might have elicited further enhanced reactions towards cues, in contrast to inherently neutral cues used

in the studies presented in this dissertation. Additionally, all three of the latter studies (Gola et al., 2017; Golec et al., 2021; Draps et al., 2021) had two additional dimensions of complexity to the experimental task used, i.e. cues were signaling magnitude (small vs large reward) and probability (25%, 50% or 75%) of obtaining the outcome reward, which might overlay additional cognitive processes on the simplified cue-reactivity framework. Indeed, in the study of Golec et al. (2021) it was demonstrated that individuals with CSB have altered processing of magnitude and probability of the upcoming appetitive outcome stimuli.

Moreover, a positive correlation was observed between self-reported conditioning effects (valence and arousal ratings toward cues of erotic outcomes) and CSB symptoms severity of *Problematic Pornography Use*, as assessed by the *Brief Pornography Screener* (Kraus et al., 2020). This correlation implies that individuals with higher severity of CSB symptoms exhibited stronger conditioning effects, reinforcing the notion that enhanced associative learning toward erotic cues is linked to the behavioral manifestations of CSB. Interestingly, this correlation was not present in the *Sexual Addiction Screening Test*. Correlations of the latter CSB symptoms measures were also not detected with neither valence nor arousal self-reported extinction effects. It is important to note, that both CSB symptoms and self-reported effects of tasks are self-assessed, which are prone to higher than behavioral measurement errors (Ainsworth et al., 2021) and therefore would suffer from low statistical power with present study's sample size, and that lack of statistically significant result does not equate to lack of effect. Nevertheless, detected correlation specifically between severity of problematic pornography use and its impact on individuals with CSB and their self-reported propensity to stronger conditioning effects warrants further research efforts. Indeed, some researchers argue that while most individuals diagnosed with CSB suffer from Problematic Pornography Use, it might be a separate clinical phenomenon from broader CSB (Antons & Brand, 2021; Gola, 2024; Antons et al., 2022; Briken et al., 2024). The observed result of correlation between increased self-assessed conditioning effects and Problematic Pornography Use symptom severity is therefore an interesting premise in the discussion about CSB and its subtypes, but warrants replication on larger, and more diverse sample in terms of CSB symptomatology.

Attentional biases have been linked to CSB symptoms, with several studies demonstrating a correlation between CSB an increased attentional processing and

cue sensitivity for erotic content (Pekal et al., 2018; Mechelmans et al., 2014; Albery et al., 2017; Draps et al., 2021; 2024; Wang et al., 2021; Banca et al., 2016; Gola et al., 2017a; Liberg et al., 2022). Consequently, it was expected that stronger conditioning effects will be present for trials with erotic rewards. However, the results only partially (on the level of self-assessment in arousal, but not in valence nor reaction times) corroborate this anticipated effect. This discrepancy can also support the hypothesis that the CSB group might exhibit a non-specific enhancement of appetitive conditioning. The vulnerable individuals, through continual exposure to various experiences, could develop a preference for certain erotic stimuli and, upon repeated exposure to these stimuli, begin to demonstrate specific effects manifesting as attentional biases towards erotic stimuli. Given that the task used was designed to assess immediate and transient associative learning, it was not feasible to detect the whole process. To address this gap in knowledge, future research should focus on longitudinal effects of associative learning and careful examination of development of conditional responses to both CSB specific and non-specific stimuli.

5.1.2. Brain activity during conditioning

It was expected that regions previously documented as functionally altered in CSB and related to motivational (dorsal anterior cingulate cortex and ventral striatum), value-related (anterior orbitofrontal cortex, posterior orbitofrontal cortex and ventromedial prefrontal cortex) and affective processing (amygdala) to be differentially engaged during conditioning in the CSB group.

The presented neuroimaging results do not fully corroborate two of the previous neuroimaging studies of conditioning in CSB (Klucken et al., 2016; Banca et al., 2016). These studies used Pavlovian tasks with either erotic or erotic and monetary rewards. In Banca et al. (2016), no group differences in any of the cues' processing were observed in the whole-brain analysis, but authors, contrary to the study in presented dissertation, did not use any hypothesis-driven region-of-interest analysis, hindering potential observable effects due to low statistical power. In Klucken et al. (2016), researchers used the occipital cortex, insula, orbitofrontal cortex, ventral striatum, and amygdala as their regions of interest, and only in the amygdala they detected increased activity related to erotic cues as the group difference. In contrast, changes in amygdala activity in the CSB group were not

detected in the study presented in this dissertation. However, the conditioning task used in the study presented in this dissertation included instrumental (active) elements, and amygdala was documented to be more often engaged in Pavlovian than instrumental conditioning (Chase et al. 2015), which may explain the differences in the obtained results.

Also in contrast to Klucken et al. (2016), in the study presented in this dissertation, altered activity in anterior orbitofrontal cortex and ventral striatum was detected, further adding to the importance of the experimental task design. The anterior orbitofrontal cortex has previously been implicated in a study on cue-reactivity in the CSB (Golec et al., 2021), in which the authors interpreted its activation as involved in aberrant salience attribution to the stimuli related to the addiction, drawing parallels with Gambling Disorder and similarly altered posterior orbitofrontal cortex activity (Sescousse et al., 2013a). Corroborating that, presented results indicate that the effect is not specific to cues of erotic rewards in associative learning context, and may underlay non-specific enhancement of appetitive conditioning. Interestingly, the division of posterior and anterior orbitofrontal cortex and their role in processing of primary (e.g. sex, food) and secondary (social, wealth) types of reward's values, accordingly, has been previously demonstrated (Sescousse et al., 2013b). Countering the intuition, in Gambling Disorder, the posterior orbitofrontal cortex has increased activity during monetary cue processing (Sescousse et al., 2013a), and in CSB the anterior orbital cortex demonstrated increased activation during erotic cue processing (Golec et al., 2021). This phenomenon has been interpreted as increased neural value-processing resources directed towards sensitized incentive in each of the disorders in a mirroring fashion. However, both of the latter studies used explicit cues of upcoming rewards, without the associative learning context, whereas in the study presented in this dissertation, simple shapes were used as cues, which nevertheless altered the anterior orbitofrontal cortex activity in the CSB group in the late stage of conditioning.

Unexpectedly, in present study it was demonstrated that ventral striatum activity was dampened in the CSB group in comparison to the healthy subjects during late conditioning towards cues of both (erotic and monetary) rewarding outcomes. Not only do these results suggest that the activity was altered in a non-specific fashion, but importantly, that active conditioning engages these brain regions in a more complex way than the passive Pavlovian counterpart, as well as

tasks based on explicit cue-reactivity without conditioning aspects used in the previous studies on the CSB (Gola et al., 2017a; Golec et al., 2021). However, the functional connectivity between ventral striatum and anterior orbital cortex was observed to be stronger in CSB group towards cues of erotic outcome stimuli during both (early and late) conditioning phases. Moreover, this neurodynamic interplay between ventral striatum and anterior orbital cortex was found to be moderately correlated with subsequent extinction success, i.e. that stronger connectivity was followed by less effective extinction measured by self-reported arousal, while simultaneously not correlating with self-reported conditioning effects. This interesting finding suggests that the persistence of erotic-oriented appetitive responses in CSB subjects is associated with increased functional interplay between the ventral striatum and the anterior orbitofrontal cortex. Moreover, although the activity changes in these regions were observed in opposite directions during late conditioning (ventral striatum activity of CSB group was decreased as opposed to anterior orbitofrontal cortex), their enhanced functional connectivity indicates a more complex underlying mechanism which was not captured by traditional activity-based analysis. Notably, functional connectivity approaches have been shown to provide insights into the dynamic interactions between brain regions that extend beyond what can be inferred from classical task-based contrasts (Friston, 2011; Fox & Raichle, 2007). Furthermore, while the task-based activation patterns observed in the present study imply non-reward-specific alterations, the functional connectivity measures suggest that this effect may be more reflective of an erotic-specific bias in appetitive processing.

The role of the dorsal anterior cingulate cortex in associative learning, and more specifically in learning goal-directed actions via motivational processing, has been extensively studied in rodents and, to some extent, in humans (Shenhav, Botvinick & Cohen, 2013; Yee et al., 2021). It was demonstrated that the dorsal anterior cingulate cortex plays a crucial role in learning, and it exhibits stronger activity during early exploring phases of tasks and is positively related to the learning rate (Heilbronner & Hayden, 2016). In his seminal work on anterior cingulate cortex, Botvinick (2007) argued that the dorsal anterior cingulate cortex generates a teaching signal, resulting from monitoring the contingencies in the environment. The activity of the dorsal anterior cingulate cortex is therefore also involved in general-domain reward monitoring and reward-motivated behaviors, enabling reward-

related choices to be transferred into motor actions (Bush et al., 2002; Rushworth & Behrens, 2008). In line with hypothesis, the activity of the dorsal anterior cingulate cortex was altered in CSB: hyperactive in early conditioning and hypoactive during late conditioning when the cue-reward relationship was already established. The observed results again presented non-reward-specific activity alteration. Interestingly, it was expected that both dorsal anterior cingulate cortex and ventral striatum to be hyperactive in late conditioning in erotic trials in the CSB group on the grounds of documented heightened reactivity towards cues of erotic rewards in tasks with explicit cue-reward relationships (Gola et al., 2017a; Golec et al., 2021). However, despite expected similarities of both tasks in that regard (i.e. the existence of anticipation of already known reward), the context of associative learning via conditioning influenced the reactivity of dorsal anterior cingulate cortex in the CSB group such that it activated more strongly during the novelty-driven exploring phase of the conditioning rather than the exploitative phase.

As demonstrated, the results of analyses used in the study presented in this dissertation paint a complex, but incomplete picture. Behavioral and self-assessed measures of conditioning point towards non-reward-specific enhanced bias towards anticipatory stimuli in the CSB group. Similarly, task-based activity in several key regions of the brain reward system also supports this view. This, especially in the late phase of conditioning, when the associations between conditioned stimuli and outcomes were learned, was an unexpected result, as bias towards cues of erotic outcomes was anticipated based on most of the very limited body of research in this domain. However, using task-based functional connectivity approach, bias towards conditioned stimuli of erotic outcomes was present in the CSB group between two of the three anticipated brain reward regions, i.e. ventral striatum and anterior orbitofrontal cortex—regions crucial for cue reactivity. These results open new perspective and call for further research into specificity of associative learning and cue-reactivity among CSB, enriched with analytical methods beyond classical task-based activity.

5.2. Extinction disruption in CSB

One of the central research questions in this dissertation was whether individuals with CSB exhibit impaired extinction of sensitized cue-driven responses, and if such impairments are specific to erotic stimuli or more generalized. According

to the Incentive Sensitization Theory (Berridge & Robinson, 2016; Robinson & Berridge, 2008), persistent motivational salience assigned to addiction-related cues can impede the natural extinction processes, maintaining compulsive behaviors even in the absence of reward.

In the self-assessment, in comparison to the control group, **CSB group expressed disrupted subjective arousal and valence towards cues of stimuli previously reinforced by both erotic and monetary rewards**. **These effects were not reflected in fMRI whole-brain analysis, nor in reaction times during the extinction procedure. More sensitive region-of-interest analyses indicated specific effects**, which are discussed in detail in the following sections.

5.2.1. Behavioral and self-reported effects of extinction

The extinction process is considered crucial to clinical approaches and cognitive behavioral therapy of addiction (Lovibond, 2004; Goode & Maren, 2019). In chemical addictions, e.g. alcohol, heroin and cocaine, aberrant associative learning present in both conditioning and extinction translates to a high rate of relapse after therapeutic interventions (Yang et al., 2019; Sinha & Li 2007; O'Brien et al. 1993; Zhang et al., 2019; Torregrossa & Taylor, 2013; Izquierdo & Jentsch, 2021). As there were previously no studies on behavioral or self-assessment effects of extinction in the CSB, presented results provide first insights into this aspect of associative learning disruption in the context of behavioral addiction in the men struggling with CSB. It is important to note that surprisingly little is known about the neurobiology of *appetitive* extinction in humans, as most of the studies focus on negative/fear extinction processing, despite its key role in managing addictive behaviors (Konova et al., 2019).

The observed persistence of subjective arousal and valence towards both cues of rewarding outcomes in the CSB group, despite the absence of rewards, suggests a heightened incentive salience attributed to the cues in a non-specific fashion. This enduring "wanting" could reflect a maladaptive learning process in which individuals continue to assign high motivational value to the cues, consistent with the Incentive Sensitization Theory description of addiction's impact on the reward system (Robinson & Berridge, 2003). From a therapeutic perspective, this may mean two things. First, typical therapeutic techniques based on habituation processes, e.g. behavioral experiments in the Cognitive Behavioral Therapy (CBT)

framework, working on habituation of the response to the trigger, could be less effective or secondly, it could indicate the potential importance of relearning processes and thus require increased exposure to the stimulus, similarly as it has been demonstrated before in the case of nicotine addiction (Conklin & Tiffany, 2002; Waters et al., 2004; McClernon et al., 2005). Moreover, these findings add to the validity of view that interventions for men with CSB might need to incorporate strategies that directly target the incentive salience of cues, potentially employing *cognitive restructuring* from Cognitive Behavioral Therapy or mindfulness-based approaches designed to reduce the maladaptive motivational value assigned to these cues (Hallberg et al., 2017; Brem et al., 2017; Bowen, Chawla, & Marlatt, 2010; Kober & Mell, 2015; Garland, 2016).

5.2.2. Brain activity during extinction

The only previous neuroimaging study on the extinction process in the CSB was by Banca et al. (2016), in which they found no neuronal alteration in CSB, although they used stringent statistical thresholding adequate for whole-brain fMRI analysis and no analysis on region-of-interest level. Increased sensitivity granted by the region-of-interest analysis used in the study presented in this dissertation allowed to find functional alterations in the dorsal anterior cingulate cortex and ventral striatum in the CSB group. The dorsal anterior cingulate cortex activity in the CSB group was heightened throughout early and late extinction towards cues of both (erotic and monetary) rewarding outcomes. The latter effect again suggests non-reward-specific activity alteration. This is consistent with the altered activity observed in the early novelty-driven exploring phase in conditioning and the impaired extinction demonstrated by self-assessment, suggesting prolonged exploration after the reward was no longer attainable. Indeed, in recent study on appetitive extinction in general population sample, Kurse et al. (2020) found that dorsal anterior cingulate cortex was activated towards cues of previously rewarding outcomes (monetary) only during early phase of extinction, attributing it outcome expectancy, which in the late phase of extinction was no longer driven by the discontinued cue-outcome association. Moreover, the reward monitoring role of the dorsal anterior cingulate cortex was also demonstrated in response to rewards that could have been obtained, but were not (Hayden, Pearson & Platt, 2009). While drawing conclusion about neurocognitive processes based on neuroimaging results

may be prone to bias (Rugg & Thompson-Schill, 2013), the heightened dorsal anterior cingulate cortex during the entirety of extinction among individuals with CSB may therefore reflect the continued salience of cues despite the awareness of discontinued paring with the outcome rewards. However, this assertion will require further examination in future research.

The ventral striatum, which plays a crucial role in both conditioning and extinction (Kruse et al., 2020), exhibited high activity in the early extinction for both cues of rewarding outcome, but in the late extinction phase, the activity for the erotic cue diminished, while for the monetary cue it remained elevated. This nuanced pattern may reflect a differential process of salience reduction for different types of rewards over the course of extinction. Indeed, ventral striatum has been demonstrated to be more sensitive to secondary (e.g. monetary or social) than primary (e.g. food or sex) rewards (Sescousse et al., 2013). Surprisingly, hypothesized alterations of activity in the ventromedial prefrontal cortex were not observed with task-based activation analysis, contrary to substance addiction studies in cocaine users (Konova et al., 2019; Bechara, 2005). However, examining functional connectivity during extinction provided evidence of an altered pattern of cue processing among individuals with CSB between ventral striatum and ventromedial prefrontal cortex, in line with predicted directionality of connectivity change. In animal models, ventromedial prefrontal cortex has been demonstrated to be a central extinction memory storage in fear extinction studies, and it was postulated that the expression of new updated associations are realized in concert with basolateral amygdala and nucleus accumbens (key part of ventral striatum), to which ventromedial prefrontal cortex has rich projections (Kalivas, Peters & Knackstedt, 2006; Peters, Kalivas & Quirk, 2009). Corroborating this in human neuroimaging, ventromedial prefrontal cortex was found to be related to appetitive Pavlovian extinction success by its functional connectivity strength with amygdala, but not on its own as observed via task-based activity (Ebrahimi et al., 2017). The connection between ventromedial prefrontal cortex and ventral striatum could be attributed to instrumental reaction required in the task used in the study presented in this dissertation, in line with animal models of drug self-administration and its extinction (Millan, Marchant & McNally, 2011). This interesting result is neatly in-line with interpretation put forward in recent study by Konova et al. (2017), in which authors speculate that while ventromedial prefrontal cortex play role in updating the

value of cues of the outcome stimuli during extinction, it crucially depend on communication with either amygdala (in case of aversive stimuli) or ventral striatum (for appetitive stimuli) to combine motivational characteristics of conditioned stimulus processed therein.

No activity alteration among individuals with CSB in the amygdala was found, despite previous studies suggesting that it might play an important role in the extinction process (Kruse et al., 2019) and documented altered activity in CSB during Pavlovian conditioning (Klucken et al., 2016). Importantly, the extinction, similarly to conditioning, had an instrumental component (required action, albeit no longer consequential), therefore the role of potentially disrupted amygdala processing might have been less pronounced than in Pavlovian design (Chase et al., 2015). Another crucial aspect in neuroimaging of amygdala using functional MRI in humans is the heterogeneity of functional and structural connectivity (Amunts et al., 2005; Bzdok et al., 2013) of this region along with its relatively small volume and influence of non-neuronal arterial signal interference that is often correlated with general fluctuations in arousal, and therefore with experimental tasks (Boubela et al., 2015). Indeed, in a recent study on resting-state in CSB, Adamus et al., (in review) demonstrated that based on signal-information-based functional parcellation of the amygdala into dorsomedial and ventrolateral subregions, individuals with CSB differ from healthy control sample of population in terms of volumes of the subregions, i.e. that left dorsomedial and right ventrolateral parts of amygdala were smaller and vice versa for right dorsomedial and left ventrolateral in CSB group. Taken together, this underscores the complexity and potential variability of results and interpretation of the amygdala role in both task-based and resting-state functional activity.

Similarly to the conclusions of the conditioning part of the study presented in this dissertation, the results of analyses during extinction also provide a complex picture of extinction disruption among individuals with CSB. Based on self-assessed measures, i.e. arousal and valence toward cues, the CSB group displayed weaker extinction effectiveness in a non-reward-specific manner, suggesting generalized aberrant associative learning. While the increased activity of dorsal anterior cingulate cortex supports this view, ventral striatum and its weakened functional connectivity with ventromedial prefrontal cortex provide an account of impaired

extinction processing biased toward sensitized cues of previously erotic outcome stimuli.

5.3. Reward processing

The second research question posed in the dissertation investigates whether altered reactivity of the reward system in individuals with CSB also manifests during the actual processing of rewards, both erotic and monetary. This question is crucial for understanding the neurobiological underpinnings of CSB, especially within the framework of the Incentive Sensitization Theory (Robinson & Berridge, 1993, 2001, 2008; Berridge & Robinson, 2016). According to this model, addiction is primarily driven by an excessive "wanting" or craving in response to cues associated with rewards, rather than alterations in the "liking" or pleasure derived from the rewards themselves. Assuming the Incentive Sensitization Theory postulates, it was hypothesized that the consummatory “liking” will not be affected among individuals with CSB.

In the current study, brain activity during the presentation of appetitive unconditioned outcome stimuli, i.e. the actual erotic pictures or monetary gains, was measured and compared between the CSB group and healthy control group across the same set of key brain reward system’s regions of interest as the cue phase of the conditioning and extinction tasks, i.e. orbitofrontal cortex, ventromedial prefrontal cortex, dorsal anterior cingulate cortex, amygdala and ventral striatum. **The analysis in the Baysian framework revealed evidence for no differences between the CSB and healthy control groups in brain activity during the processing of reward stimuli in any of the specified brain regions. This was consistent for both erotic and monetary rewards**. It suggests that individuals with CSB might not exhibit altered neural responses when actually receiving rewards, whether erotic or monetary. This result also aligns with the hypothesis derived from Incentive Sensitization Theory, which posits that addiction-related behaviors are driven by heightened sensitivity to cues (conditioned stimuli) associated with cues predictive of rewards rather than the rewards themselves. **These findings indicate that the hyper-reactivity of the reward system in CSB is more pronounced in the anticipation cue processing rather than the consummatory processing of appetitive stimuli.** This potential specificity underscores the importance of targeting

cue-induced cravings in therapeutic interventions for CSB, modifying maladaptive cue-reward associations (Gola, 2024).

However, it is important to note that erotic stimuli used in the study presented in this dissertation were static images. While most of the previous studies on cue-reactivity and associative learning used similar type of erotic rewarding stimulation (Gola et al., 2017; Golec et al., 2021; Banca et al., 2016; Klucken et al., 2016; Brand et al., 2016; Prause et al., 2015), it might be argued that static images are not on-par with the pornographic material used nowadays to fulfill the autoerotic behaviors, i.e. high-fidelity and wide variety of pornographic videos materials. Adding to this, individuals with CSB tend to select more intense materials as the CSB progresses, which is interpreted as countering habituation (Wordecha et al., 2018). Indeed, in a study by Voon et al. (2014), by examining brain reactivity towards short videos of explicit sexual materials compared to non-sexual exciting materials like sports, it was demonstrated that individuals with CSB are characterized by increased reactivity of dorsal anterior cingulate cortex, ventral striatum and amygdala. Interestingly, authors also compared video materials that were not explicit, but rather erotic/suggestive, and brain reactivity towards those videos compared to non-sexual exciting videos did not differ between CSB and control groups. While stimuli used in the current study were chosen from a database based on high rating of arousal and valence of participants who rated various explicit and non-explicit erotic photographs (Wierzba et al., 2015), it might nevertheless be that the discrepancy between stimulation intensity elicited by still images and actual videos dampens the excitement otherwise experienced by individuals with CSB (Gola, 2024; Wierzba et al., 2015). Clearly this area of neuroimaging research is still scarce and hence it would be premature to draw definitive conclusions, but assuming that appetitive outcome stimuli used in the current study were not as exciting for individuals with CSB as the materials regularly consumed by them, the appetitive conditioning and anticipatory processes were nevertheless significantly altered, adding to the view of increased motivational “wanting” sensitization in CSB.

5.4. Reward system outside the associative learning

The fourth research question sought to determine whether individuals with CSB exhibit functional alterations in the brain's reward system during resting state, independent of task engagement or exposure to sexual stimuli. Specifically, it was

hypothesized that individuals with CSB would display altered baseline functional connectivity among key regions implicated in reward processing. It was posited that these alterations might reflect fundamental changes in reward system functioning associated with CSB and could correlate with the behavioral effects observed during conditioning and extinction tasks. **Contrary to the stated hypothesis, the analysis of resting-state functional connectivity revealed no significant differences between the CSB and healthy control groups**. Using a region-of-interest approach, functional connectivity between ventromedial prefrontal cortex, orbitofrontal cortex, amygdala, dorsal anterior cingulate cortex and ventral striatum was examined. The analysis did not detect any group differences in the strength of connectivity between these regions. **Additionally, within the CSB group, no significant associations were found between reward system's resting-state functional connectivity patterns and the self-assessed effects of conditioning and extinction in arousal and valence towards cues of erotic outcome stimuli**. These findings suggest that, at rest, individuals with CSB do not exhibit alterations in functional connectivity within the reward system. The absence of resting-state functional connectivity differences indicates that the neurobiological alterations associated with CSB may be more context-dependent, emerging primarily during task engagement or in response to specific stimuli rather than as a persistent baseline state. This aligns with prior research suggesting that functional dysregulations in CSB are often observed in response to explicit sexual cues or during active engagement in reward-related tasks (Gola et al., 2017; Klucken et al., 2016).

The lack of association between resting-state functional connectivity within the brain reward system and self-assessed measures of associative learning further supports the idea that baseline functional connectivity of reward system might not directly predict individual differences in conditioning or extinction effects among individuals with CSB. It is possible that dynamic changes in reward system functional connectivity in response to sensitized stimuli or contexts related to them underlie the neurobiological mechanisms contributing to CSB symptoms. Task-based functional connectivity analyses in the current study did reveal significant group differences during conditioning and extinction tasks, suggesting that functional neural alterations in CSB are more pronounced during active processing of appetitive anticipatory processing. Indeed, based on previous studies on cue

reactivity in CSB, in recent study by Engels et al. (2023) authors discuss lack of expected alteration in resting-state functional connectivity of ventral striatum with the rest of the brain in CSB, as less robust in default state than in substance use disorder, similarly to previously discussed analogy in other behavioral addictions as seen in meta-analysis approach (Tolomeo & Yu, 2022).

The final research question pertained to whether structural alterations in ventromedial prefrontal regions of the reward system underlie observed disruption in extinction. The ventromedial prefrontal cortex has been linked to successful extinction learning, with both its thickness and reactivity, predicting how effectively individuals suppress outdated or maladaptive associations (Ebrahimi et al., 2019; Milad & Quirk, 2012; Phelps et al., 2004). It plays a distinct role in integrating contextual information, updating expectations when outcomes change, and inhibiting responses that are no longer beneficial. Such adaptive control mechanisms are essential for maintaining behavioral flexibility. In addiction, where behavior often remains rigid despite negative outcomes, structurally affected ventromedial prefrontal cortex may prevent effective context updating and extinction of harmful habits (Konova & Goldstein, 2019). **However, based on the results in the study presented in this dissertation, this hypothesis could not be supported. While minor reductions in cortical thickness were noted in certain orbitofrontal subregions, the ventromedial prefrontal cortex did not show significant structural differences.** This outcome contrasts with findings in substance use disorders, where structural changes in prefrontal regions often accompany chronic dysregulation and neurotoxic effects of substances (Mackey et al., 2019). That result might not be specific to CSB. A recent meta-analysis study by Zeng et al. (2023) did not discover structural alterations within the ventromedial prefrontal cortex among various behavioral addictions. However, the measure of morphometry used in the latter study was voxel-based and it assessed gray matter volume, which—while being partially correlated with each other—convey different information about the morphometry of the cortex than cortical thickness (Winkler et al., 2010). The absence of robust structural alterations in CSB may suggest that the neuroadaptations driving the pathology are more functional (e.g., aberrant connectivity or neurotransmitter signaling) than anatomical, at least at the macrostructural level. Furthermore, only subtle structural differences in orbitofrontal regions between CSB and control group in this study were found, which were not in

the actual ventromedial prefrontal cortex. Additionally, no correlations of these regions' thickness and altered extinction effects among individuals with CSB were found, further adding to the argument that ventromedial prefrontal cortex thickness might not be the central culprit in disruption of associative learning in CSB.

5.4. Summary and conclusions

This study provides new insights into behavioral and brain reward system functioning aspects of appetitive conditioning and extinction in CSB. Both monetary and erotic rewards were included in the experimental design to study the specificity of associative learning alterations. Obtained results show that men struggling with CSB are prone to short-term general conditioning and extinction alterations towards cues of both erotic and monetary rewards. These alterations were present in self-assessment, reaction times, and reactivity of the ventral striatum, anterior orbitofrontal cortex, and dorsal anterior cingulate cortex. Intriguingly, the notion of generalized aberrant associative learning, however, was not supported by task-based functional connectivity analyses, which provided an account of erotic-biased processing of appetitive cues in both conditioning and extinction.

These findings contribute to the ongoing debate regarding the classification of CSB. While CSB shares phenomenological similarities with substance use disorders and other behavioral addictions, such as heightened cue reactivity and compulsive engagement despite adverse consequences (Kraus et al., 2016; Gola & Potenza, 2018), the neurobiological underpinnings may differ between substance use disorders and CSB. The absence of resting-state functional connectivity changes in key brain reward regions and morphological alterations in ventromedial prefrontal cortex suggest that CSB might involve different neural mechanisms than those seen in substance use disorders or that the neuroadaptations are more subtle and context specific.

In conclusion, in line with Incentive Sensitization Theory, the present findings contribute to the growing evidence that CSB may share certain neurobiological characteristics with addictive disorders, particularly regarding enhanced conditioning, cue-reactivity and disrupted extinction learning. However, methodological and conceptual limitations, as well as mixed results across previous studies, highlight the need for further research. As demonstrated in the study presented in this dissertation, analytical approach towards neurobiological

underpinnings of CSB drawing on functional connectivity complementing the classically used task-based activity analysis, in tandem with self-reported and behavioral indices, may provide a richer view of this complex disorder.

5.5. Limitations

Several limitations of the presented study should be considered. First, the recruited sample consisted of white Caucasian, heterosexual males, which limits results interpretations to this specific subpopulation. The choice of such composition of the studied sample was dictated by the effort to minimize potential heterogeneity and therefore results variability to in turn increase the statistical power. One such source of variability is the type of stimuli used in the experimental procedure. Exclusion of potential participants was undertaken, based on ongoing problems with alcohol and substance abuse and high OCI-R scores, which measure OCD symptoms. It has been noted that the general CSB population has increased OCI-R scores (Draps et al., 2021); therefore, some of the subpopulation was cut off. Additionally, this study was planned and conducted before the official introduction of CSBD criteria in ICD-11, hence the sample cannot be considered as clinically diagnosed with CSBD, despite similar CSB symptoms characteristics as measured by BPS and SAST-R, and large overlap with Hypersexuality Disorder criteria as proposed in DSM-5. Secondly, an active conditioning task design with only one response possibility was used. This limits the ability to interpret the results in light of more traditional instrumental conditioning approaches widely studied in animal models. Future studies should focus on studying instrumental conditioning with multiple choices during fMRI examination. A third limitation is related to the fact that the extinction was performed immediately after the conditioning. A more ecological approach would be to study extinction after a consolidation period (Hyman et al., 2006; Kruse et al., 2019). Importantly, while sample size studied in the presented dissertation was reasonable for task-based neuroimaging, functional connectivity and morphometric studies with between-subject factors display more robust results with sample size. Especially brain-behavior studies require larger samples (Marek et al., 2022), and therefore the results presented in this dissertation should be replicated accordingly. Sample size in the study presented in this dissertation was dictated by the funding granted by Polish National Science Centre via Preludium 11 grant, awarded to the author of this dissertation.

5.6. Future directions

Future studies using standardized diagnostic criteria, more ecologically valid stimuli, and longitudinal designs may provide deeper insight into the mechanisms of CSB and the relevance of incentive sensitization within this context. As demonstrated in the study presented in this dissertation, a more nuanced analytical approach to the neuroimaging data may further help to better describe the neurobiology of emergence of not only CSB, but also other addictive behaviors.

As self-assessed measures are inherently prone to variability and biases, it would be interesting to pursue psychophysiological forms of arousal tracking, i.e. using galvanic-skin response or pupillometry as indices of sympathetic and parasympathetic nervous systems activity. That would additionally allow for analysis in a single-trial manner, further elucidating the relationship between functional connectivity of brain reward system and psychophysiological reactivity.

Another critical avenue of future research directions is to study the neurobiology of CSB in a longitudinal design, e.g. examining the effects of a therapy or other interventions aimed at reducing the CSB symptoms severity. Based on results presented in this dissertation, it would be worthwhile to assess the effects of exposure therapy in managing cue reactivity.

Further studies of appetitive extinction should also include postponed extinction after a consolidation period, and perhaps even more importantly, include reinstatement procedure, i.e. remission of conditioned response after being exposed to unexpected reward. This approach inherently requires longitudinal study design, but understanding these processes and their neurobiological underpinnings could significantly advance the knowledge about the mechanisms behind CSB and potentially expedite therapeutic efforts.

Finally, as CSB is debilitating not only in heterosexual males, it is imperative to expand the research into more diverse groups, such as homosexual males, heterosexual and homosexual women and other minority sexual groups. Currently, there is a severe lack of studies of neurobiology of CSB in these groups. Adding to this call, the severity of CSB symptoms in women seems to manifest in different aspects of problematic sexual behaviors. By collecting data on these various groups struggling with CSB, a clearer picture of common neurobiological underpinnings may be unveiled.

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Publications

Publications directly underlying or related to this PhD thesis are marked with emphasis.

1. **Wojciechowski, J.,** Draps, M., Kublik, E., Dubiejko, P., Wolak, T., & Gola, M. (sent: 2024). Enhanced conditioning and disrupted extinction processes in men struggling with compulsive sexual behaviors. *Journal of Behavioral Addictions*.

2. **Wojciechowski, J.**, Jurewicz, K., Dzianok, P., Antonova, I., Paluch, K., Wolak, T., & Kublik, E. (2024). Common and distinct BOLD correlates of Simon and flanker conflicts which can (not) be reduced to time-on-task effects. *Human Brain Mapping*, *45*(1), e26549.

3. Golec-Staśkiewicz, K., **Wojciechowski, J.**, Haman, M., Wolak, T., Wysocka, J., & Pluta, A. (2024). Unveiling the neural dynamics of the Theory of Mind: a fMRI Study on Belief Processing Phases. *Social Cognitive and Affective Neuroscience*, nsae095.

4. Bryłka, M., **Wojciechowski, J.**, Wolak, T., & Cygan, H. B. (2024). Frontal Deactivation and the Efficacy of Statistical Learning: Neural Mechanisms Accompanying Exposure to Visual Statistical Sequences. *Journal of Cognitive Neuroscience*, 1-20.

5. Malinowska, U., **Wojciechowski, J.**, Waligóra, M., & Rogala, J. (2024). Performance of game sessions in VR vs standard 2D monitor environment. an EEG study. *Frontiers in Physiology*, *15*, 1457371.

6. Dzianok, P., **Wojciechowski, J.**, Wolak, T., & Kublik, E. (accepted: 2024). Alzheimer's disease-like features in resting state EEG/fMRI of cognitively intact and healthy middle-aged APOE/PICALM risk carriers. *Journal of Alzheimer's Disease.*

7. Pluta, A., Mazurek, J., **Wojciechowski, J.**, Wolak, T., Soral, W., & Bilewicz, M. (2023). Exposure to hate speech deteriorates neurocognitive mechanisms of the ability to understand others' pain. *Scientific Reports*, *13*(1), 4127.

8. Komorowski, M. K., Rykaczewski, K., Piotrowski, T., Jurewicz, K., **Wojciechowski, J.**, Keitel, A., Dreszer, J., & Duch, W. (2023). ToFFi–Toolbox for frequency-based fingerprinting of brain signals. *Neurocomputing*, *544*, 126236.

9. Żygierewicz, J., Janik, R. A., Podolak, I. T., Drozd, A., Malinowska, U., Poziomska, M., **Wojciechowski, J.**, Ogniewski, P., Niedbalski, P., Terczynska, I., & Rogala, J. (2022). Decoding working memory-related information from repeated psychophysiological EEG experiments using convolutional and contrastive neural networks. *Journal of Neural Engineering*, *19*(4), 046053.

10. Golec-Staśkiewicz, K., Pluta, A., **Wojciechowski, J.**, Okruszek, Ł., Haman, M., Wysocka, J., & Wolak, T. (2022). Does the TPJ fit it all? Representational similarity analysis of different forms of mentalizing. *Social Neuroscience*, *17*(5), 428-440.

11. Dzianok, P., Antonova, I., **Wojciechowski, J.**, Dreszer, J., & Kublik, E. (2022). The Nencki-Symfonia electroencephalography/event-related potential dataset: Multiple cognitive tasks and resting-state data collected in a sample of healthy adults. *GigaScience*, *11*, giac015.

12. Sato, W., Rymarczyk, K., Minemoto, K., **Wojciechowski, J.**, & Hyniewska, S. (2019). Cultural moderation of unconscious hedonic responses to food. *Nutrients*, *11*(11), 2832.

Conference publications

13. Malinowska, U., **Wojciechowski, J.**, Waligóra, M., Wróbel, A., Niedbalski, P., & Rogala, J. (2019, July). Spectral analysis versus signal complexity methods for assessing attention related activity in human EEG. In *2019 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)* (pp. 4517-4520). IEEE.

Supplementary Materials

Whole-brain neuroimaging results

Group differences

Exploratory whole-brain analysis revealed significant differences between CSB and control group only during late conditioning (Fig. S1). The CSB group had lower activity in bilateral calcarine for both $CS+_{erotic}$ vs. CS- and $CS+_{cash}$ vs. CS- in the late conditioning phase, but for $CS+_{erotic}$ vs. CS-, additionally, part of the precuneus, right middle temporal gyrus, right insula, right parahippocampal gyrus and a cluster spanning left hippocampus, fusiform gyrus, and parahippocampal gyrus had lower activity. In $CS+_{erotic}$ vs. CS-, the CSB group additionally had higher activation in a cluster located in the right cerebellum and inferior temporal gyrus. Results are presented in Table S1 and S2.

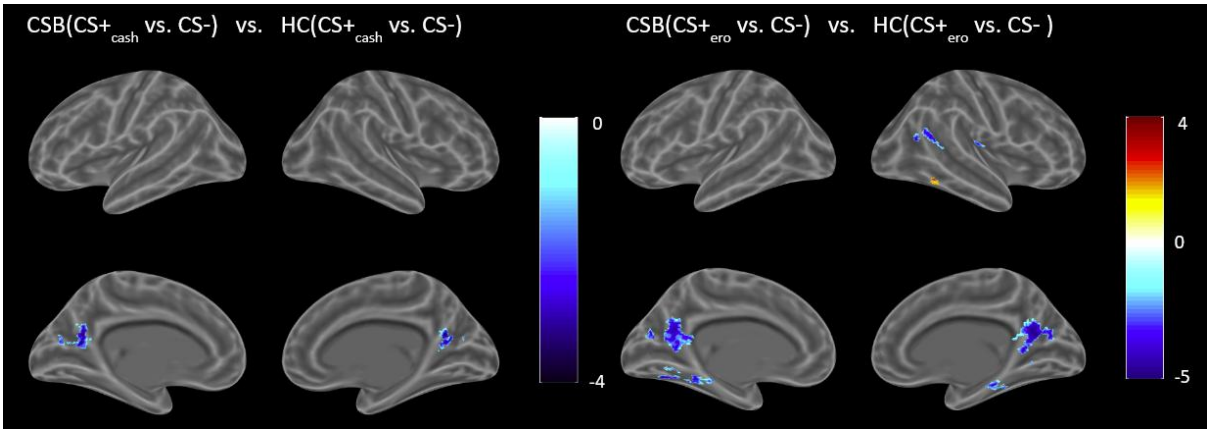

Figure S1. Group differences in BOLD activity in (left) $CS+_{cash}$ vs. CS- and (right) $CS+_{erotic}$ vs. CS- contrasts between the CSB and control groups in late conditioning. The results were obtained using a voxel-level threshold of p<.001 and an FWE-corrected cluster-forming threshold of p< .05. Color bars represent the *t*-values.

Table S1. Whole-brain results of group differences between CSB and HC in $CS+_{erotic}$ vs. CS- contrast.

					MNI Coordinates		
	Region Name	Side	Cluster size	*t*-value	x	y	z
CSB > HC	Cerebellum 6	R	326	4.97	40	-66	-24
	Inferior Temporal Gyrus	R	326	4.06	60	-54	-16
	Cerebellum (Crus 1)	R	326	3.84	54	-54	-38
HC > CSB	Precuneus	R	1144	5.07	12	-56	18
	Calcarine Gyrus	L	1144	4.22	-16	-56	10
	Middle Temporal Gyrus	R	240	4.87	40	-52	18
	Insula Lobe	R	124	4.84	32	-20	22
	Fusiform Gyrus	L	311	4.82	-28	-38	-10
	ParaHippocampal Gyrus	L	311	4.37	-24	-20	-18
	ParaHippocampal Gyrus	R	135	4.64	30	-28	-14

Cluster extent-based correction (FWEc) p< .05. The AAL3 atlas was used to denote region names. Clusters with peaks more than 8mm apart have indicated several regions per cluster.

Table S2. Whole-brain results of group differences between CSB and HC in $CS+_{cash}$ vs. CS- contrast.

					MNI Coordinates		
	Region Name	Side	Cluster size	*t*-value	x	y	z
HC > CSB	Calcarine Gyrus	R	186	4.77	8	-60	18
	Calcarine Gyrus	L	234	4.75	-4	-64	14

Cluster extent-based correction (FWEc) p< .05. The AAL3 atlas was used to denote region names.

General conditioning effects

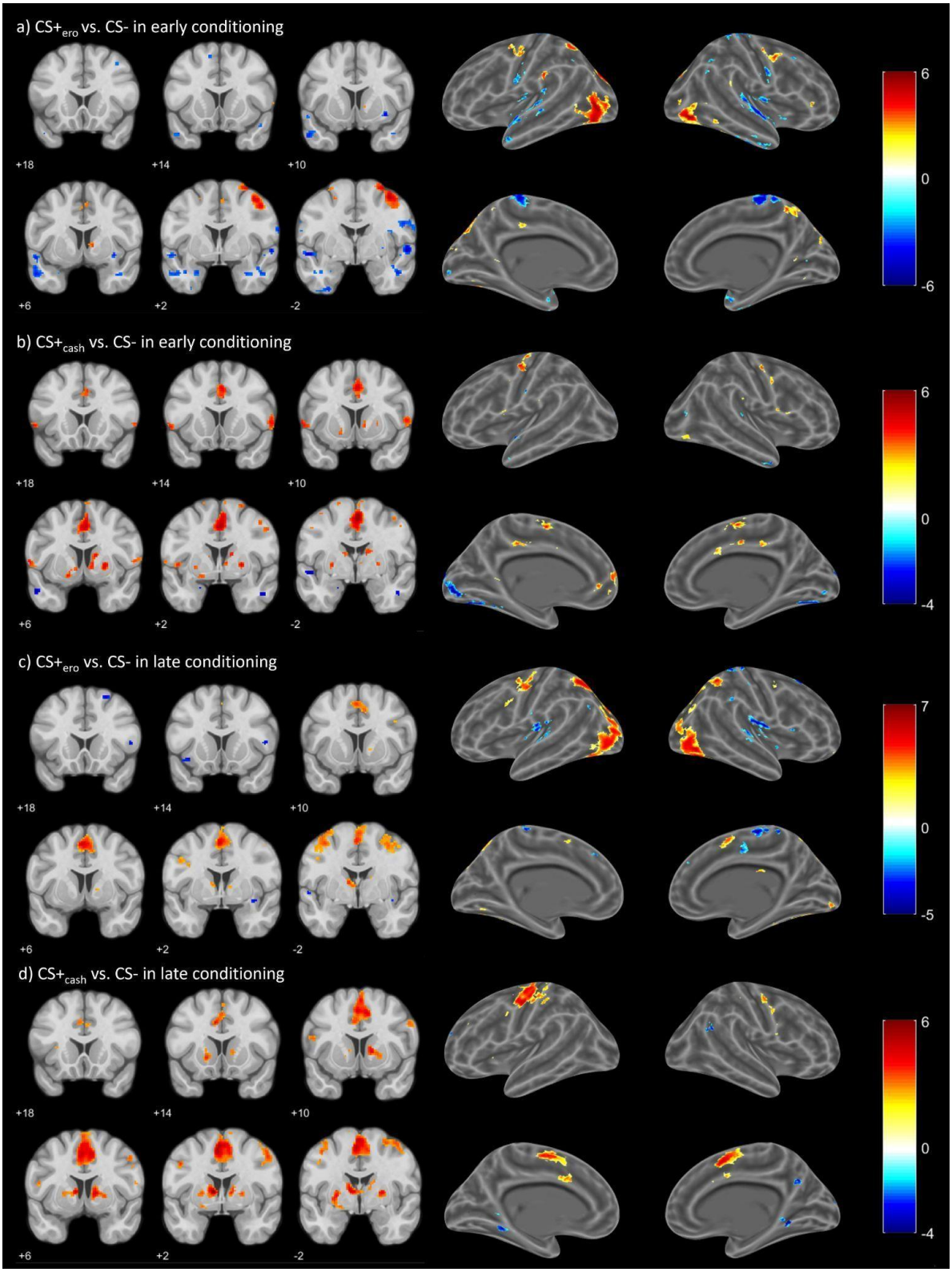

Figure S2. Effects of conditioning on BOLD activity for four analyzed contrasts (a-d), for all participants pooled together. For each contrast, left panels present coronal planes of volumetric representation of subcortical activity (see x coordinates in MNI space below each map); right panels present a surface render of cortical activity. Color bars represent *t*-values for both volumetric and surface visualizations; threshold used is p< .001.

General extinction effects

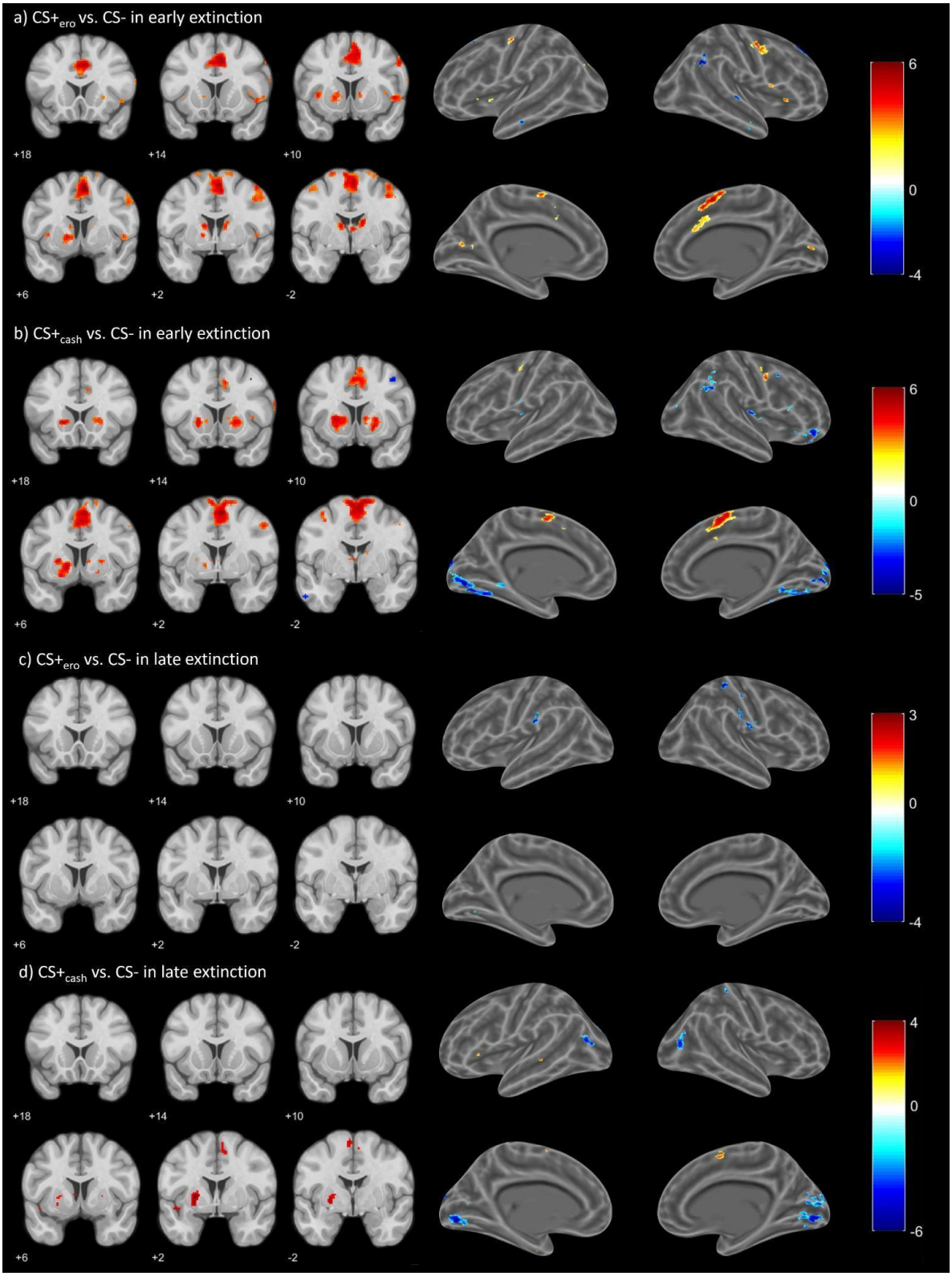

Figure S3. Effects of extinction on BOLD activity for four analyzed contrasts (a-d), for all participants pooled together. For each contrast, left panels present coronal planes of volumetric representation of subcortical activity (see x coordinates in MNI space below each map); right panels present a surface render of cortical activity. Color bars represent *t*-values for both volumetric and surface visualizations; threshold used is p< .001.