



Novelty, conditioning and attentional bias to sexual rewards



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ABSTRACT

The Internet provides a large source of novel and rewarding stimuli, particularly with respect to sexually explicit materials. Novelty-seeking and cue-conditioning are fundamental processes underlying preference and approach behaviors implicated in disorders of addiction. Here we examine these processes in individuals with compulsive sexual behaviors (CSB), hypothesizing a greater preference for sexual novelty and stimuli conditioned to sexual rewards relative to healthy volunteers. Twenty-two CSB males and forty age-matched male volunteers were tested in two separate behavioral tasks focusing on preferences for novelty and conditioned stimuli. Twenty subjects from each group were also assessed in a third conditioning and extinction task using functional magnetic resonance imaging. CSB was associated with enhanced novelty preference for sexual, as compared to control images, and a generalized preference for cues conditioned to sexual and monetary versus neutral outcomes compared to healthy volunteers. CSB individuals also had greater dorsal cingulate habituation to repeated sexual versus monetary images with the degree of habituation correlating with enhanced preference for sexual novelty. Approach behaviors to sexually conditioned cues dissociable from novelty preference were associated with an early attentional bias to sexual images. This study shows that CSB individuals have a dysfunctional enhanced preference for sexual novelty possibly mediated by greater cingulate habituation along with a generalized enhancement of conditioning to rewards. We further emphasize a dissociable role for cue-conditioning and novelty preference on the early attentional bias for sexual cues. These findings have wider relevance as the Internet provides a broad range of novel and potentially rewarding stimuli.

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1. Introduction

Why is online surfing so compulsively engaging to many individuals? The Internet provides a large source of novel and potentially rewarding stimuli. Novelty-seeking, attentional bias and cue-conditioning are fundamental processes that may drive unconscious preference and approach decisions in daily life. These processes may also contribute to the development and

maintenance of disorders of addiction.

Novelty-seeking may be both a predictor and consequence of disorders of addiction. This trait, which is often assessed using the Zuckerman's sensation-seeking scale, has been repeatedly found elevated in diverse behavioral and substance addictions (Belin et al., 2011; Redolat et al., 2009). A suggested explanation for this strong relationship relies on the hypothesis that exposure to novelty may activate, at least in part, the same neural machinery that mediates the rewarding effects of drugs of abuse (Bardo et al., 1996). In rodent studies, novelty preference predicts a transition towards compulsive cocaine-seeking behaviors (Belin and Deroche-Gamonet, 2012). In human studies, sensation-seeking is

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associated prospectively with binge drinking in adolescents (Conrod et al., 2013).

Conditioned signals or cues in our environment may also significantly influence behavior. The smell of cigarettes, places or friends associated with drug use, or the sight of money may act as conditioned cues and may enhance reactivity and trigger cravings, urges and relapse in disorders of addiction (for review see (Childress et al., 1993)). These cues are neutral stimuli that may inadvertently acquire motivational significance through the process of conditioning with repeated pairing with either drug rewards or other biologically relevant natural rewards such as food (Jansen, 1998) or sex (Pfaus et al., 2001; Toates, 2009).

The processing of novelty and learning has been proposed to include a functional polysynaptic loop involving the hippocampus, ventral striatum, and midbrain dopaminergic region (Lisman and Grace, 2005). Detection of novelty, long-term memory encoding and learning involves dopaminergic activity that enhances hippocampal synaptic plasticity which, through glutamatergic projections to the ventral striatum, relays information to the ventral tegmental area (VTA) which then projects directly back to the hippocampus (Knight, 1996; Lisman and Grace, 2005). With repeated exposure, the hippocampus and midbrain dopaminergic responses to novelty decrease, conferring habituation when stimuli become familiar (Bunzeck and Duzel, 2006; Bunzeck et al., 2013). Converging primate and human studies also show that phasic dopaminergic activity encodes prediction error, a comparison between the actual and expected outcomes indicating an unexpected salient outcome, acting as a teaching signal underlying conditioning processes (Schultz et al., 1997). Mesolimbic dopaminergic cell bodies in the midbrain project to a network including the striatum, dorsal anterior cingulate cortex (dACC) and hippocampus (Williams and Goldman-Rakic, 1998). The dACC is implicated in attentional responding to novel and salient events and in processing reward anticipation and prediction error (Ranganath and Rainer, 2003; Rushworth et al., 2011).

In addition to novelty-seeking and cue-conditioning influences, the tendency to preferentially process cues related to the object of addiction (attentional biases) is also an important feature that characterizes disorders of addiction (Ersche et al., 2010; van Hemel-Ruiter et al., 2013; Wiers et al., 2011). The influence of emotional stimuli on attentional processes is widely reported both in healthy and clinical samples (Yiend, 2010). Attentional biases towards substance-related stimuli have been found in substance-use disorders for alcohol, nicotine, cannabis, opiates and cocaine (Cox et al., 2006). Moreover, a direct association between highly arousing sexual pictures and attentional interference has also been found in healthy individuals, which seems to be influenced by sexuality-related attitudes and sexual motivation (Kagerer et al., 2014; Prause et al., 2008). We have previously extended these findings to individuals with compulsive sexual behaviour (CSB) using a dot-probe task (Mechelmans et al., 2014).

With increasing access to the Internet, there is growing concern regarding the potential for excessive use. A study that assessed the predictive power of several types of Internet applications (gaming, gambling, email, etc.) on the development of compulsive Internet use suggested that online sexually explicit stimuli have the highest potential for addictive/compulsive use (Meerkerk et al., 2006). Online explicit stimuli are vast and expanding, and this feature may promote escalation of use in some individuals. For instance, healthy males viewing repeatedly the same explicit film have been found to habituate to the stimulus and find the explicit stimulus as progressively less sexually arousing, less appetitive and less absorbing (Koukounas and Over, 2000). However, subsequent exposure to a novel explicit film segment increases the levels of sexual arousal and absorption to the same previous levels prior to habituation,

suggesting important roles for novelty and habituation. Imaging studies have identified a specific network for the neural processing of sexual stimuli in healthy humans, comprising the hypothalamus, nucleus accumbens, orbitofrontal, occipital and parietal areas (Wehrum et al., 2013; Wehrum-Osinsky et al., 2014). This neural network, which is independent of general emotional arousal, is found both in men and women although men show overall stronger activations than women, which might be indicative of a stronger sexual responsiveness in men. The same neural network activates for stimuli conditioned sexual arousal, with a gender effect in the same direction (Klucken et al., 2009).

In our study, we assess novelty, attentional bias and cue-conditioning to online explicit sexual material in individuals with CSB. These processes are highly relevant to substance-use disorders and may also be relevant to CSB. Online sexually explicit stimuli have significant potential for compulsive use, and CSB is relatively common, occurring in 2–4% in community and college-based young adults and in psychiatric inpatients (Grant et al., 2005; Odlaug and Grant, 2010; Odlaug et al., 2013). CSB is associated with significant distress, feelings of shame and psychosocial dysfunction. Although a working group for the 11th edition of the International Classification of Diseases is currently proposing to include CSB as an impulse-control disorder (Grant et al., 2014), CSB was not included in DSM-5, albeit with some controversy (Toussaint and Pitchot, 2013), largely due to limited data. Thus, further studies are needed. Understanding the similarities and differences between CSB and other psychiatric disorders, particularly impulse-control disorders and addictions, may help with classification efforts as well as with the development of improved prevention and treatment approaches.

We have previously found that individuals with CSB demonstrate greater regional brain activation in response to explicit sexual cues in the ventral striatum, dorsal anterior cingulate cortex (dACC) and amygdala, regions implicated in drug cue reactivity and craving in disorders of addiction (Voon et al., 2014). Functional connectivity of this network, and particularly the dACC, was associated with greater sexual desire or motivation to explicit stimuli. We further observed that individuals with CSB, as compared to those without, demonstrate an early attentional bias towards sexually explicit cues (Mechelmans et al., 2014). This early attentional bias was proposed to reflect facilitatory mechanisms underlying the motivational effect of cues conditioned to sexual outcomes. Here, we deepen our research focus investigating the mechanisms underlying the development of enhanced attentional bias and cue reactivity in CSB by assessing both behavioral and neural responses to novelty and to cue-conditioning in response to explicit sexual stimuli.

We conducted two behavioral tasks outside of the scanner to assess choice preference for novel versus familiar sexual stimuli and choice preference for cues conditioned to Sexual, Monetary and Neutral stimuli. We hypothesized that CSB individuals relative to healthy volunteers (HVs) would have greater choice preference to novel relative to familiar images in the Sexual condition but not in the control condition. We further hypothesized that CSB subjects would have greater choice preference to the conditioned cues in the Sexual condition but not in the Monetary condition.

Participants also performed a functional magnetic resonance imaging (fMRI) conditioning and extinction task involving conditioning to Sexual, Monetary and Neutral images. Two neutral stimuli were randomly paired with different sexual images shown repeatedly during conditioning. In the outcome phase of the conditioning arm, neural habituation to the sexual images was assessed by evaluating the change in neural activity of each different sexual image over time focusing on the repeated exposure thereby dissociating the analysis of the conditioning and outcome

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