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Altered neural correlates of reward and loss processing during simulated slot-machine fMRI in pathological gambling and cocaine dependence☆

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ABSTRACT

Background: Individuals with gambling or substance-use disorders exhibit similar functional alterations in reward circuitry suggestive of a shared underlying vulnerability in addictive disorders. Additional research into common and unique alterations in reward-processing in substance-related and non-substance-related addictions may identify neural factors that could be targeted in treatment development for these disorders.
Methods: To investigate contextual reward-processing in pathological gambling, a slot-machine fMRI task was performed by three groups (with pathological gambling, cocaine dependence and neither disorder; $N = 24$ each) to determine the extent to which two groups with addictions (non-substance-related and substance-related) showed similarities and differences with respect to each other and a non-addicted group during anticipatory periods and following the delivery of winning, losing and 'near-miss' outcomes.
Results: Individuals with pathological gambling or cocaine dependence compared to those with neither disorder exhibited exaggerated anticipatory activity in mesolimbic and ventrocortical regions, with pathological-gambling participants displaying greater positive possible-reward anticipation and cocaine-dependent participants displaying more negative certain-loss anticipation. Neither clinical sample exhibited medial frontal or striatal responses that were observed following near-miss outcomes in healthy comparison participants.
Conclusions: Alterations in anticipatory processing may be sensitive to the valence of rewards and content-disorder-specific. Common and unique findings in pathological gambling and cocaine dependence with respect to anticipatory reward and near-miss loss processing suggest shared and unique elements that might be targeted through behavioral or pharmacological interventions in the treatment of addictions.

1. Introduction

Individuals with gambling and substance-use disorders (SUDs) exhibit neurobiological similarities, particularly in reinforcement/reward/motivation circuitry (Leeman and Potenza, 2012; Potenza, 2008). Specifically, aberrant ventral striatal and ventrocortical function appear common across disorders and is consistent with models of addiction that encompass substance-related and non-substance-related behaviors (Potenza, 2013). However, the extent to which increased or blunted activation of reward circuitry is observed in pathological gambling (PG; gambling disorder in DSM-5) and SUDs has been debated, with data suggesting that context (e.g., gambling for PG or substances for SUDs) may determine whether increased or blunted activation is observed (Leyton and Vezina, 2013; Limbrick-Oldfield et al., 2013; van Holst et al., 2012b). Continued research into shared and unique alterations in

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reinforcement-related processes in PG and SUDs that consider such contexts may help identify neural factors that could be targeted in treatment development for these disorders (Insel et al., 2010; Potenza, in press; Potenza et al., 2011).

Electronic gambling machines (EGMs), popularly termed slot machines, are a prevalent form of gambling that some have argued is the most addictive form of gambling (Schüll, 2012), although this has been debated (Dowling et al., 2005). Specific features of EGMs have been cited as potentially addictive in that they may influence or interact with gambling-related cognitions and contribute to reinforcement learning and persistent gambling (Potenza, in press; Schüll, 2012). One such feature is the 'near-miss' phenomenon, a gambling-related experience that is typically encountered during EGM gambling. Defined as losing outcomes that are perceived as 'close' to being successful (Reid, 1986), near-miss outcomes occur when all but one of the reels display matching symbols (e.g., AAB). Although the monetary value of near-miss outcomes are equivalent to other losses, near-miss outcomes are associated with increased physiological arousal (Clark et al., 2012; Dixon et al., 2011), and in laboratory situations, can lengthen the duration of gambling sessions in both occasional and regular players (Côté et al., 2003; Dixon and Schreiber, 2004; Kassinove and Schare, 2001; MacLin et al., 2007). Models of how near-miss outcomes may encourage continued gambling suggest these events may promote erroneous gambling-related beliefs related to skill and illusions of control (Billieux et al., 2012; Clark et al., 2012) and activate appetitive mechanisms through activity in reward/reinforcement circuitry (Chase and Clark, 2010; Dixon et al., 2013).

Previous research in which occasional and at-risk gamblers participated in simulated slot-machine gambling has found that the delivery of near-miss outcomes relative to full-losses (e.g., slot-machine outcomes where no symbols match) is associated with increased activity within reward/reinforcement circuitry including the ventral striatum, insula, and midbrain (Chase and Clark, 2010; Clark et al., 2009). Similarly, individuals with problem gambling also exhibited increased activity in reward-related regions following the delivery of a near-miss (Habib and Dixon, 2010), suggesting near-miss outcomes may promote continued gambling through positive reinforcement (despite being monetary losses). However, in individuals with PG or SUDs, groups that have been found to exhibit altered patterns of neural activations during monetary reward/loss processing (Balodis et al., 2012; Goldstein et al., 2007; Jia et al., 2011; Peters et al., 2011; Reuter et al., 2005; Wrase et al., 2007), it is unclear if neural function underlying the processing of near-miss events will be similar or different across the groups with non-substance and substance addictions.

Previous fMRI investigations of near-miss experiences have focused upon differences between neural signals evoked by winning, losing and near-miss outcomes (Chase and Clark, 2010; Clark et al., 2009; Habib and Dixon, 2010). However, reinforcement-related neural responses develop through conditioned learning of predictive stimuli, and this association is expressed during anticipatory states (Fiorillo et al., 2008; Montague et al., 1996; Roesch et al., 2010; Schultz et al., 1997). PG and SUDs are associated with differences in anticipatory reward-processing (Balodis et al., 2012; Choi et al., 2012; Jia et al., 2011; van Holst et al., 2012a; Wrase et al., 2007) and thus warrant investigation.

In the current experiment, fMRI was used to investigate neural activity associated with reward-anticipation and near-miss outcomes while individuals with PG, cocaine dependence (CD; cocaine-use disorder in DSM-5) and neither disorder performed a simulated 'three-wheel' slot-machine fMRI task. We examined between-group differences in whole-brain activity associated with two types of near-miss outcomes (non-sequential and sequential near-misses, see Section 2.2.) as compared to other losing events. We had competing hypotheses. Consistent

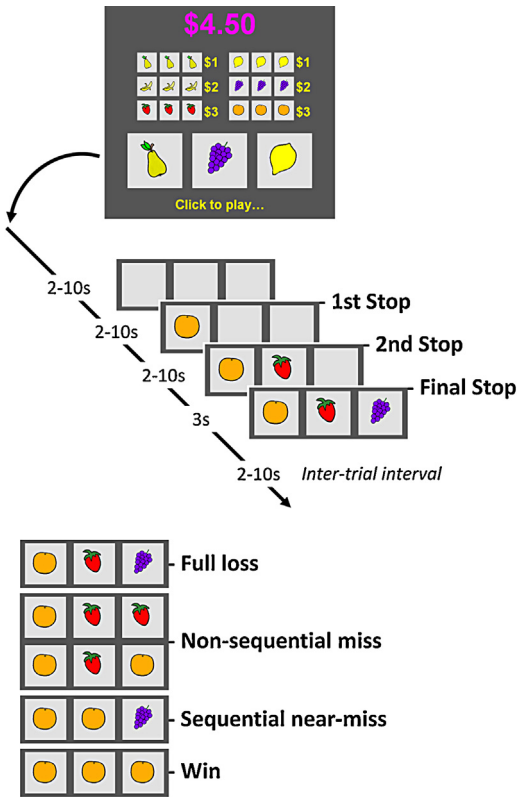

Fig. 1. Simulated slot-machine task design and example outcome types.

with models of gambling-related cue and reward hypersensitivity in PG (Leyton and Vezina, 2013; Limbrick-Oldfield et al., 2013; van Holst et al., 2012b), we hypothesized that individuals with PG would exhibit increased reward-anticipation and near-miss activity in striatal and ventrocortical circuitry as compared to CD and healthy comparison (HC) participants. Alternatively, if reward/reinforcement/motivation processes were shared across PG and CD, we had a competing hypothesis that both groups would demonstrate increased reward-anticipation and near-miss activity in striatal and ventrocortical circuitry as compared to HC participants.

2. Materials and methods

2.1. Participants

Participants included 24 individuals with PG, 24 with CD, and 24 HC individuals (Table 1) recruited from the local (New Haven, CT) community. All participants were assessed for DSM-IV diagnoses using semi-structured clinical interviews (SCID; (First et al., 2002)). Exclusion criteria included the presence or history of a psychotic disorder or general medical illness that would interfere with the ability to participate in screening, assessment or fMRI protocols. Urine toxicology screening for illicit substances was performed at the time of scanning. All study procedures were approved by the Yale Human Investigations Committee. Participants provided written informed consent.

2.2. Simulated slot-machine task

Participants performed a computer-simulated, three-reel slot-machine task designed for fMRI (Fig. 1). On each play, participants pushed a button after which all three 'reels' began randomly changing through six different fruit symbols every 200 ms to simulate spinning slot-machine reels. To maximize the expectancy and impact of the near-misses and other outcomes, the reels stopped in sequential order from left to right (Strickland and Grote, 1967). Colinearity of events was minimized by using durations of reel spins and inter-trial intervals that were pseudo-randomly presented between 2 and 10 s, with an average of 6 s, for an average total single play length of 18 s.

Outcomes were presented in one of four predetermined pseudorandom orders (balanced across groups), delivering approximately 17% (according to a variable ratio of 1:6) winning (e.g., AAA), sequential near-miss (e.g., AAB) and non-sequential