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Alterations in functional brain networks associated with loss-chasing in gambling disorder and cocaine-use disorder

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ABSTRACT

Background: Continued, persistent gambling to recover accumulating losses, or 'loss-chasing', is a behavioral pattern linked particularly closely to gambling disorder (GD) but may reflect impaired decision-making processes relevant to drug addictions like cocaine-use disorder (CUD). However, little is known regarding the neurocognitive mechanisms of this complex, maladaptive behavior, particularly in individuals with addictive disorders.

Methods: Seventy participants (25 GD, 18 CUD, and 27 healthy comparison (HC)) completed a loss-chase task during fMRI. Engagement of functional brain networks in response to losing outcomes and during decision-making periods preceding choices to loss-chase or to quit chasing losses were investigated using independent component analysis (ICA). An exploratory factor analysis was performed to examine patterns of coordinated engagement across identified networks.

Results: In GD relative to HC and CUD participants, choices to quit chasing were associated with greater engagement of a medial frontal executive-processing network. By comparison, CUD participants exhibited altered engagement of a striato-amygdala motivational network in response to losing outcomes as compared to HC, and during decision-making as compared to GD. Several other networks were differentially engaged during loss-chase relative to quit-chasing choices, but did not differ across participant groups. Exploratory factor analysis identified a system of coordinated activity across prefrontal executive-control networks that was greater in GD and CUD relative to HC participants and was associated with increased chasing persistence across all participants.

Conclusions: Results provide evidence of shared and distinct neurobiological mechanisms in substance and behavioral addictions, and lend insight into potential cognitive interventions targeting loss-chasing behavior in GD.

1. Introduction

'Loss-chasing', or continued gambling in an attempt to recover losses, is a behavioral pattern that is arguably unique to gambling relative to substance addictions (American Psychiatric Association, 2013), and may differentiate the most severely affected disordered gamblers from non-problem gamblers (Breen and Zuckerman, 1999; Corless and Dickerson, 1989; James et al., 2016; O'Connor and Dickerson, 2003; Toce-Gerstein et al., 2003). Loss-chasing has been linked to heightened impulsivity, reward and loss sensitivity, emotional regulation and decision-making (Bibby, 2016; Breen and Zuckerman, 1999; Lister et al., 2016; Ochoa et al., 2013; Parke et al., 2016). While loss-chasing represents as a significant feature of compulsive gambling, reflecting poor self-control and impaired decision-making (el-Guebaly et al., 2012; Robbins and Clark, 2015), the neural mechanisms underlying the behavior in individuals with addictive disorders remain unclear.

Loss-chasing is a salient feature of decision-making under risk and uncertainty even in non-gambling populations (Shafir and Tversky, 1995). Initial neurobiological investigations of loss-chasing behavior in minimally-experienced gamblers suggest contributions of distinct and dissociable neural systems (Campbell-Meiklejohn et al., 2011;

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Campbell-Meiklejohn et al., 2008). Decisions to discontinue (or 'quit') chasing losses is associated with activity in the dorsolateral prefrontal, anterior cingulate, striatum and parietal cortices (Campbell-Meiklejohn et al., 2008), regions that are commonly associated with networks of executive cognitive functioning (Niendam et al., 2012). By comparison, decisions to chase losses are associated with neural activity in ventral prefrontal regions, consistent with impulsive behavior and impaired decision-making (Fineberg et al., 2010; Hare et al., 2009). Furthermore, increased activity in the anterior cingulate following losing outcomes is associated with the subsequent decisions to quit loss-chasing (Campbell-Meiklejohn et al., 2008), suggesting terminating a chase is associated with increased emotional processing and cognitive conflict in response to loss outcomes (Kim et al., 2010). Similarly, dissociable and complementary contributions of serotonergic and dopaminergic mechanisms influence chasing behavior (Campbell-Meiklejohn et al., 2012; Campbell-Meiklejohn et al., 2011; Rogers et al., 2011). Together, these initial findings suggest that a complex of executive-control and impulsivity-related systems involved in decision-making and loss-processing may contribute to loss-chasing behavior in minimally experienced gamblers. In individuals with gambling disorder, and possibly addictive disorders more broadly, alterations in the neural mechanisms of executive control, impulsivity and reward/loss processing (Leeman and Potenza, 2012) may contribute to loss-chasing behavior.

As compared to general linear model (GLM) approaches to fMRI analysis, independent component analysis (ICA) allows examination of distinct, functionally integrated brain networks associated complex cognitive processes (Calhoun and Adali, 2006). ICA has been proposed to have several advantages over GLM, including less susceptibility to functional heterogeneity and the ability to separate inhibitory and excitatory influences on neuronal activity (Xu et al., 2015; Xu et al., 2016). ICA is a data-driven, network-based computational procedure that has been used to identify functional alterations in the multiple brain networks that contribute to cognitive control (Worhunsky et al., 2013), decision-making (Elton et al., 2017), and during resting-state (Ding and Lee, 2013) in individuals with substance-use disorders. Thus, the current study aimed to extend previous investigations of loss-chasing behavior by examining activity in functional brain networks in individuals with gambling disorder (GD), individuals with cocaine-use disorder (CUD) and a healthy comparison (HC) sample. Participants played a modified version of the loss-chase task (Campbell-Meiklejohn et al., 2008) during fMRI. that allows We hypothesized that ICA-identified networks associated with executive function and motivational processing would be functionally related, or 'engaged', in response to losing outcomes and during decision-making periods of the loss-chase task. We expected greater engagement of medial frontal and fronto-parietal networks in GD relative to HC during decision-making, and losing outcomes, preceding choices to quit compared to continue loss-chasing. We also expected ventromedial prefrontal and striatal networks would be more engaged in GD relative to HC during decision-making to continue loss-chasing compared to quit-chasing. It was expected that GD and CUD participants would exhibit shared, addiction-related, and distinct, disorder-specific, patterns of network engagement. Finally, we performed an exploratory factor analysis of engagement patterns of ICA-identified networks to examine differences between GD, CUD and HC individuals in coordinated network activity.

2. Methods

2.1. Participants

Participants were 25 individuals with GD, 18 with CUD and 27 HC individuals (Table 1) recruited from the local community. GD and CUD participants were non-treatment-seeking, and all participants were assessed using semi-structured clinical interviews according to DSM-IV criteria (SCID; (First et al., 2002)). Exclusion criteria included the presence or history of psychotic disorder or other serious mental, neurologic or general medical illness that would interfere with the ability to participate in fMRI procedures (e.g., implanted devices, claustrophobia). GD participants were excluded for a co-occurring current substance addiction (other than tobacco/nicotine), and CUD participants with gambling-severity scores indicative of probable problematic gambling (Lesieur and Blume, 1987) were excluded from the current analyses. Urine toxicology screening for cocaine, marijuana (THC), opiates, amphetamine/methamphetamine, methylenedioxymethamphetamine (MDMA), barbiturates, phencyclidine (PCP), and benzodiazepines (Integrated EZ Split Key Cup; Redwood Toxicology Laboratories, Santa Rosa, CA, USA) and alcohol breathalyzer screening (Alco-Sensor III; Intoximeters, Saint Louis, MO, USA) were performed at the time of scanning to confirm no recent substance use in GD and CUD participants. Study procedures were approved by the Yale Human Investigations Committee, and participants provided written informed consent.

Table 1
Participant characteristics and task performance.

	HC	GD	CUD	$F/t/\chi^2$ (P)
N	27	25	18	
Participant characteristics				
Gender, Female (%)	12 (44.4)	9 (36.0)	7 (38.9)	0.40 (0.82)
Age, years (SD)	33.6 (10.8)	38.4 (11.5)	43.7 (5.3)	5.48 (0.006)
IQ, estimated IQ (SD)	108 (9.9)	103.1 (13.2)	94.7 (9.4)	7.89 (0.001)
Tobacco user, N (%)	2 (7.4)	9 (36.0)	12 (66.7)	17.37 (< 0.001)
Disorder chronicity, years (SD)	–	13.5 (10.0)	14.4 (7.9)	0.30 (0.77)
Loss-chase performance				
Chase decision-time, ms (SD)	1477 (672)	1482 (674)	1736 (749)	0.91 (0.407)
Quit decision-time, ms (SD)	1661 (879)	1519 (668)	1727 (463)	0.49 (0.617)
Control reaction time, ms (SD)	1269 (684)	1167 (568)	1390 (487)	0.73 (0.487)
Chase depth (SD)	1.7 (0.2)	1.8 (0.2)	1.8 (0.2)	1.21 (0.306)
Quit depth (SD)	1.9 (0.5)	1.7 (0.4)	1.8 (0.3)	1.86 (0.164)
Chase value, $ (SD)	230 (48)	234 (51)	221 (40)	0.44 (0.644)
Quit value, $ (SD)	266 (96)	230 (88)	256 (49)	1.24 (0.296)
Chases won, per run (SD)	3.0 (1.4)	2.9 (1.4)	2.7 (1.4)	0.35 (0.707)
Maximum losses, per run (SD)	1.7 (0.7)	2.2 (1.3)	1.9 (1.4)	1.32 (0.273)

Abbreviations: HC, Healthy comparison; GD gambling disorder; CUD, cocaine-use disorder.

2.2. Loss-chase task

Participants completed a modified version of the loss-chase task (Fig. 1; (Campbell-Meiklejohn et al., 2008)). Prior to scanning, participants were instructed that they had been given a hypothetical $20,000 endowment to participate in a decision-making task. They were informed that, in groups of 10 consecutive participants, the individual with the largest amount remaining in their endowment would receive $50 in addition to research compensation. Participants completed a brief practice prior to scanning to ensure comprehension of the task structure and progression.

The loss-chase task was performed in two consecutive fMRI runs, each consisting of 12 'chasing' rounds and 6 'control' rounds. Chasing rounds began with the imposition of an initial loss ($40, $80, $160 or $320). Participants were given the option to either 'play' a double-or-nothing wager (to try to recover the loss) or to 'quit' the current round and surrender the loss. Within each chasing round, participants were allowed to continue double-or-nothing wagers (i.e., chase losses) until a maximum loss of $1280 was accrued, a winning outcome (i.e., recovery of accumulated losses) was delivered, or the option to terminate a chase