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Examining the interaction between cognitive control and reward sensitivity in substance use dependence

Kathleen Charles-Walsh, Daniel J. Upton, Robert Hester*

Melbourne School of Psychological Sciences, University of Melbourne, Melbourne, Australia

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ABSTRACT

Background: Drug dependence is characterized by altered reward processing and poor cognitive control, expressed as a preference for immediate rewards and impaired inhibitory control, respectively. To examine the interaction between reward processing (via the presence or absence of reward) and mechanisms of inhibitory control in drug dependence, the current study used the Monetary Incentive Control Task (MICT) to examine whether a group of opiate dependent persons demonstrated greater difficulty exerting control over immediate rewards compared to neutral stimuli.
Methods: The MICT is a Go/Stop paradigm that examines inhibitory control over immediate rewards. Performance of 32 opiate dependent individuals was compared to 29 healthy controls.
Results: Opiate users demonstrated poorer inhibitory performance than controls, irrespective of cues signaling immediate reward. Whereas control participants' responses were modulated by probability cues, the opiate group did not show a capacity to up-regulate their cognitive control performance.
Conclusions: The present results suggest a general decrease in cognitive control in opiate dependence, accompanied by a reduced ability to optimally modulate behavior in accordance with external cues. Opiate users and controls did not differ in the interaction between cognitive control and reward. The study highlights important issues for future research to consider when further examining this interaction in drug dependence.

1. Introduction

Drug dependence is a disorder of impulsivity, characterized by impaired control over substance use (Feil et al., 2010; Nigg et al., 2006). Impulsivity can be both a heightened sensitivity to bottom up, reward driven processes, and a failure of top down regulatory mechanisms (Grant and Chamberlain, 2014). Current drug dependence models suggest bottom up 'reward' processes are altered through repeated exposure to drugs of dependence, via their influence on learning and attentional mechanisms (Belin et al., 2013; Carpenter et al., 2015; Goldstein and Volkow, 2011; Robinson and Berridge, 2008; Volkow et al., 2010). Top-down cognitive control processes are also impaired (Garavan and Stout, 2005; Garavan et al., 2013), which may result in an impaired ability to exert effortful control over incentive, or reward driven processes (Belin et al., 2013; Goldstein and Volkow, 2011; Robinson and Berridge, 2008; Volkow et al., 2010).

Drug dependent groups show altered responses to reward anticipation and acquisition. They tend to have a stronger preference for smaller immediate rewards over and above larger delayed rewards compared to non-dependent groups (Bickel and Marsch, 2001; Kirby et al., 1999; Mitchell and Wilson, 2012). This altered processing has also been examined using the Monetary Incentive Delay (MID) task, which separates reward anticipation from acquisition to distinguish motivational and hedonic reward components (Balodis and Potenza, 2014; Knutson et al., 2000). These investigations have shown altered neural activity in the anticipation of reward, relative to control groups (Balodis and Potenza, 2014).

Cognitive control processes are often investigated via inhibitory control; the process by which rule guided action overrides ongoing, pre-potent responses. Inhibitory control is typically measured using the Go/NoGo and Stop Signal tasks (Boucher et al., 2007; Logan et al., 1997; Simmonds et al., 2008). These tasks establish a pattern of responding, then require the individual to quickly shift response type or stop an initiated response. Whilst drug dependent groups typically show poorer inhibitory performance on these tasks than healthy controls (Fillmore and Rush, 2002; Garavan and Stout, 2005; Gruber et al., 2007; Lee et al., 2005; Li et al., 2009), there can be some variation in patterns of inhibitory impairment according

* Corresponding author at: Melbourne School of Psychological Sciences, University of Melbourne, Parkville, Victoria, 3010, Australia.
E-mail address: hesterr@unimelb.edu.au (R. Hester).

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Table 1
Sample statistics for the recruited and final analysis groups.

	Recruited Groups (M, *SD*)		Final Analysis (M, *SD*)		
	Opiate (N = 36)	Control (N = 32)	Opiate (N = 32)	Control (N = 29)	Statistical Comparison
Age	35.79 *(9.23)*	41.21 (*10.74*)	35.16 (*8.62*)	40.76 (*10.65*)	$t(59) = -2.27^{*}$
Education	11.52 *(1.79)*	14.83 (*2.69*)	11.53 (*1.81*)	14.72 (*2.67*)	$t(48.61) = -5.41^{**}$
Premorbid-IQ	109.42 *(1.15)*	113.81(*5.74*)	109.20 (*7.77*)	113.66 (*5.79*)	$t(56.94) = -2.56^{*}$
BDI	15.24 *(10.83)*	4.97 (*1.85*)	15.56 (*10.84*)	4.97 (*1.88*)	$t(33.05) = 5.44^{**}$
STAI	37.85 *(9.84)*	2.97 (*2.16*)	38.31 (*9.62*)	3.03 (*2.16*)	$t(34.44) = 20.19^{**}$
PANAS pos	27.23 *(7.38)*	31.50 (*8.11*)	27.42 (*7.51*)	31.90 (*7.78*)	$t(58) = -2.27^{*}$
PANAS neg	12.59 *(3.85)*	11.50 (*2.62*)	12.48 (*3.86*)	11.59 (*2.72*)	$t(58) = 1.04$, *ns*
AUDIT	6.45 *(6.62)*	4.10 (*5.16*)	6.66 (*6.62*)	4.17 (*5.23*)	$t(59) = 1.61$, *ns*
SOWS	4.92 *(6.45)*	–	4.75 (*6.59*)	–	–
SODS	4.92 *(6.45)*	–	7.41 (*4.94*)	–	–

Statistical comparisons were performed only for final groups after applying exclusion criteria. Tests for unequal variances reported where appropriate. *ns* = not significant. Beck Depression Inventory (BDI); Stait Trait Anxiety Inventory (STAI); Positive and Negative Affect Scale (PANAS) – positive and negative measures; Alcohol Use Disorders Identification Test (AUDIT); Symptoms of Opiate Withdrawal Scale (SOWS); Symptoms of Opiate Dependence Scale (SODS).

* $p < 0.05$.

** $p < 0.001$.

to specific substance types (Smith et al., 2014; Constantinou et al., 2010).

Reward sensitivity and inhibitory control seem naturally interrelated concepts, yet studies of their interaction have been limited. O'Connor et al. (2012) found that healthy individuals optimize inhibitory performance in the face of reward, up-regulating inhibitory control to optimize monetary reward outcomes. Nondependent alcohol abusers, however, demonstrate a reduced capacity to up-regulate inhibitory control performance in the same way, despite similar inhibitory performance to controls under neutral conditions (Rossiter et al., 2012). On a similar task, nicotine dependent participants show patterns of neural activity suggestive of more cognitive 'effort' to achieve similar behavioral performances to controls (Luijten et al., 2013). Together, these studies suggest the interaction between inhibitory mechanisms and reward in drug abuse may differ from healthy populations.

The present study investigated interactions between reward and inhibitory control processes in drug dependence; specifically, whether drug-dependence is associated with increased difficulty in controlling responses to immediately rewarding stimuli. The experimental task modified the MID, adding an inhibitory control component to create a Monetary Incentive Control Task (MICT). The MICT (1) provides an anticipatory cue regarding the type of upcoming trial (reward/neutral, and lower/higher chance of a Stop target); (2) requires fast responding to 'Go' targets and inhibition of 'Stop' targets; (3) gives feedback about performance. The task therefore examines the modulation of cognitive control in accordance with reward incentives, whilst attempting to minimize other possibly confounding cognitive demands (e.g., risk-taking, working memory load).

The MICT was administered to Opiate-dependent participants, with previous evidence to suggest they have impaired cognitive control processes and heightened reward sensitivity (Forman et al., 2004; Hommer et al., 2011; Yücel et al., 2007). Opiate users were expected to have significantly poorer inhibitory control performance than controls, and demonstrate significantly poorer inhibitory control over immediate rewards, relative to neutral stimuli, compared to the control group.

2. Method

2.1. Participants

36 opiate dependent participants (12 female; mean age = 35.44; SD = 8.95) and 32 nondependent healthy control subjects (8 female; mean age = 40.47; SD = 10.54) were recruited. The opiate dependent group had previously received a diagnosis of Substance Use Dependence and been maintained on opiate substitution therapy (methadone or suboxone) for a minimum of 3 months. Control participants had no current or previous history of dependence on substances other than nicotine. Both groups had no: history of head injury with loss of consciousness >30 min; known neurological abnormalities or disorders; mania, schizophrenia, or non-substance induced psychosis; known diagnoses of HIV or metabolic disorders; uncorrected visual disturbances.

Opiate dependent participants were recruited as part of a larger neuroimaging study via advertisements placed in pharmacies delivering methadone treatment, and at inner city drop-in centers. Participants from previous research were also contacted, and asked to utilize existing social networks for further recruitment. Controls were recruited via advertisements online at public domain sites (e.g., Gumtree), and at the University of Melbourne campus. All participants provided written informed consent prior to participating in the study, as approved by the University of Melbourne human ethics committee (ID 0930976).

Control participants were matched to the sample of opiate users meeting eligibility for neuroimaging, but not the larger behavioral sample used in this study (which included participants ineligible for imaging because of handedness, metal implants, etc.). As such, key demographics matched approximately, but there were several measures that significantly differed between the two groups. This is outlined in Table 1 and discussed in the results section.

The majority of opiate dependent participants were poly-drug users, with 80.6% reporting a current or previous history of dependence on at least one drug other than heroin: 72.2% on cannabis, 50% on psycho-stimulants, (e.g., amphetamine, methamphetamine). 88.9% of the sample reported primary intravenous administration of opiates. Mean age of first opiate use was 20.47 years (SD = 5.50), and regular use was 22.21 (SD = 5.76). Years of regular opiate use was split between 1–5 years and 10–20 years (prevalence each of 27.8%). 50% reported one or more previous drug overdoses. 10 participants had been abstinent from opiates (excluding substitution therapy) for the past 3 months, 7 continued to use heroin on a monthly basis, and 7 were currently using heroin daily or almost daily. Mean number of years on opiate substitution therapy was 2.79 (SD = 2.88, range = 0–14 years). On the day of participation, 50% of the sample reported use of alcohol, opiates, barbiturates, or cannabis, within the past 24 hrs. No participant was administered cognitive tasks if they presented in an intoxicated state. Further details of substance use history are provided in the supplementary materials.

After applying performance-based exclusion criteria (detailed in the statistical analysis section), four opiate users and three control subjects were excluded, resulting in a final sample of 32 opiate