Addictive Behaviors 47 (2015) 86–90

Contents lists available at ScienceDirect

Addictive Behaviors

Short Communication

Cue-induced craving in patients with cocaine use disorder predicts cognitive control deficits toward cocaine cues

Gregory J. DiGirolamo [a,b,*], David Smelson [b,c], Nathan Guevremont [b]

[a] Department of Psychology, College of the Holy Cross, 1 College Street, Worcester, MA 01610, USA
[b] Department of Psychiatry, Medical School, University of Massachusetts, 55 Lake Avenue North, Worcester, MA 01605, USA
[c] Edith Nourse Rogers Memorial Veterans Hospital, Bedford, MA

HIGHLIGHTS

- CDPs make more antisaccade errors to cocaine cues than neutral.
- High cravers make more errors than low cravers to cocaine cues.
- Impulsivity is a predictor of general errors.
- Cue-induced craving is a specific predictor of errors toward cocaine cues.
- Cognitive control is disrupted in CDPs.

ARTICLE INFO

Available online 1 April 2015

Keywords:
Cocaine
Craving
Antisaccades
Cognitive control
Addiction

ABSTRACT

Introduction: Cue-induced craving is a clinically important aspect of cocaine addiction influencing ongoing use and sobriety. However, little is known about the relationship between cue-induced craving and cognitive control toward cocaine cues. While studies suggest that cocaine users have an attentional bias toward cocaine cues, the present study extends this research by testing if cocaine use disorder patients (CDPs) can *control* their eye movements toward cocaine cues and whether their response varied by cue-induced craving intensity.
Methods: Thirty CDPs underwent a cue exposure procedure to dichotomize them into high and low craving groups followed by a modified antisaccade task in which subjects were asked to *control* their eye movements toward either a cocaine or neutral drug cue by looking away from the suddenly presented cue. The relationship between breakdowns in cognitive control (as measured by eye errors) and cue-induced craving (changes in self-reported craving following cocaine cue exposure) was investigated.
Results: CDPs overall made significantly more errors toward cocaine cues compared to neutral cues, with higher cravers making significantly more errors than lower cravers even though they did not differ significantly in addiction severity, impulsivity, anxiety, or depression levels. Cue-induced craving was the only specific and significant predictor of subsequent errors toward cocaine cues.
Conclusion: Cue-induced craving directly and specifically relates to breakdowns of cognitive control toward cocaine cues in CDPs, with higher cravers being more susceptible. Hence, it may be useful identifying high cravers and target treatment toward curbing craving to decrease the likelihood of a subsequent breakdown in control.

1. Introduction

Cocaine dependence is a significant public health problem with a severe illness course, moderately successful psychosocial interventions (Dutra et al., 2008), and no FDA-approved medications (Alvarez et al., 2010). Craving is a prominent feature in cocaine addiction, recently added to DSM-V, and often serves as a target in pharmacotherapy (Childress & O'Brien, 2000). Craving exists despite the negative outcomes associated with abuse (Robinson & Berridge, 2008; Tiffany, 1990). Unfortunately, the field still struggles to understand the mechanisms that directly or indirectly precipitate cue-induced craving (CIC) and drive subsequent behavior (Garavan et al., 2000; Volkow et al., 2006). Understanding the relationship between CIC and breakdowns in cognitive control is further complicated by inter-subject variability (Avants et al., 1995; Smelson et al., 1998; Smelson et al., 2001). In some cocaine use disorder patients (CDPs), exposure to evocative cocaine cues results in increased craving (Childress, McLellan, & O'Brien, 1993; Childress et al., 1999; Maas et al., 1998; O'Brien et al., 1990). Craving can also arise through stress, emotions, perceived availability, and drug priming (Mahoney et al., 2007; Sinha et al., 2000; Yamamoto

* Corresponding author at: Department of Psychology, College of the Holy Cross, 1 College Street, Worcester, MA 01610, USA. Tel.: +1 508 793-3595.
E-mail address: gdigirol@holycross.edu (G.J. DiGirolamo).

http://dx.doi.org/10.1016/j.addbeh.2015.03.025
0306-4603/

et al., 2007). Cue type also affects the variability of the craving intensity, with more personal cues engendering higher craving (Wexler et al., 2001; Johnson et al., 1998). What remains unknown, however, is whether higher craving translates into greater loss of cognitive control toward cocaine cues.

Lack of cognitive control has frequently been measured as the amount of attention given to drug stimuli (for a review, see, Field & Cox, 2008), amount of time looking at drug cues (Franken, Kroon, & Hendriks, 2000), or delays in responding (Hester, Dixon, & Garavan, 2006; Copersino et al., 2004). CDPs demonstrate an attentional bias for cocaine-related stimuli, with greater bias predicting poorer outcomes during drug-treatment programs (Carpenter et al., 2006). While these types of studies have investigated CDPs' preferences or attentional biases toward cocaine pictures or words, they have not asked CDPs to control their behavior toward cocaine cues. A hallmark of drug use cessation and relapse prevention (Marhe et al., 2013) is the ability to control behavior toward cocaine cues (Volkow et al., 2010; Volkow et al., 2013; Dalley, Everitt, & Robbins, 2011). Therefore, the current study investigated the ability of CDPs to control their eye movements toward generic neutral and cocaine cues, and familiarized neutral and cocaine cues, and examined directly the relationship between high versus low CIC and cognitive control. In short, does cocaine CIC explain subsequent cue-elicited breakdowns in cognitive control toward cocaine cues?

2. Materials and methods

2.1. Participants and assessments

Thirty CDPs, identified by clinicians as cocaine dependent and not actively psychotic, were recruited from in-patient addiction treatment centers. CDPs provided informed consent and completed assessments included demographics, quantity and frequency of cocaine use, the Voris Cocaine Craving Scale (VCCS, Voris, Elder, & Sebastian, 1991), the Beck Depression Inventory (BDI, Beck, Steer, & Carbin, 1988), the Beck Anxiety Inventory (BAI, Beck et al., 1988), the Severity of Dependence Scale (SDS, Gossop et al., 1995), and the Barratt Impulsiveness Scale (BIS, Patton, Stanford, & Barratt, 1995). One patient did not complete the VCCS, and his data was not used when craving was included as a factor in the analyses. As Table 1 shows, the majority of the participants were crack cocaine users, with only 5 of the 30 CDPs using solely powder cocaine.

2.2. Cue-induced craving procedure

Following assessments, CDPs completed a relaxing computer task and the VCCS. CDPs handled either the five cocaine-related (e.g., crack pipe, lighter, vial) or the five neutral (e.g., shell, pine cone, twig) cues in a block design (counterbalanced for order effects). Each object in the group (drug or neutral) was handled for 30 s, and after handling all five objects in that group (for a total of 150 s of handling cocaine cues, or 150 s of handling neutral cues), participants rated their craving. For cocaine cues, CDPs recalled the last time they had used such an object while taking cocaine. For neutral cues, they recalled the last time they had encountered such an object. CDPs completed the VCCS before and after handling each group of cues. Pictures of CDPs' hands holding the neutral and cocaine cues were digitized and then used in the antisaccade task. Because these cues were shown and handled by the patients (and now included their own hands in the images), we call these cues familiarized drug or familiarized neutral. The cue exposure procedure ended with a relaxation exercise (see also, Smelson et al., 2013).

Table 1
Demographics, drug history, psychological assessments, and cocaine craving scores in cocaine use disorder patients.

Assessment	*N*	*M*	SE
Gender (male)	23 of 30		
Race (Caucasian)	23 of 30		
Crack as primary drug	25 of 30		
Age	30	37.87	1.59
Days of use (last 30 days)	30	14.00	3.44
Years of use	30	16.27	1.92
Previous drug treatments	30	17.00	3.08
Severity of Dependence Scale (SDS)	30	11.43	0.40
Barratt Impulsivity Scale (BIS)	30	82.23	2.82
Beck Depression Index (BDI)	30	23.67	2.19
Beck Anxiety Index (BAI)	30	18.20	2.12
Cue-induced craving increase after cocaine cue exposure	29	15.45	2.42

2.3. Antisaccade task

The antisaccade task included pictures of generic neutral and cocaine cues as well as the familiarized neutral and cocaine cues taken previously for each participant. Eye movements were recorded (SR Research Eyelink 1000) while CDPs faced a computer screen with their heads in a chin rest. Each trial began with two white boxes (8.19° of visual angle, VA) presented to the left and right (7.7° VA) of a central fixation. The fixation (and boxes) remained until CDPs had fixated for 200 ms. The fixation then disappeared, and the cue (8.10° VA) appeared 400 or 700 ms later (balanced and randomized across cue type) to prevent predictability in cue onset. CDPs were instructed to make an eye movement to the opposite location (an antisaccade). The picture remained on the screen for 800 ms and was followed by a 500 ms blank screen. An eye movement was classified as a saccade when its velocity reached 30°/s, or its acceleration had reached 8000°/s^2. Trials in which the eye movements were executed under 80 ms after the onset of the go signal were considered anticipations and discarded (Wenban-Smith & Findlay, 1991), as were trials where an eye blink occurred. The speed of the eye movement (saccadic reaction time; sRT) was calculated from the onset of the cue until the initiation of the eye movement. For every trial, the first saccade following the cue onset was labeled either an error if the eye moved toward the cue or a correct response if the eye moved toward the box opposite the cue.

The antisaccade task used a block design. Blocks consisted of 20 generic and 5 familiarized cues from one category (e.g., cocaine), and 5 generic cues from the other category (e.g., neutral), with these 30 cues randomly intermixed and repeated twice. Hence, each block consisted of 60 trials, with 50 trials of one cue type and 10 trials of the other cue type. The task consisted of 8 (4 neutral and 4 cocaine) blocks, with the block order randomized and counterbalanced across CDPs. A 30 s fixation period was included after every other block.

2.4. High vs. low cravers

Because our specific aim was to examining the role of high and low cue-induced craving in breakdowns in cognitive control toward cocaine cues, we analyzed the data in two ways. First, we dichotomize the 30 CPDs into two groups (high and low cravers) based on a median split of changes in self-reported cocaine cue-induced craving (Voris Cocaine Craving Scale; Q1) from baseline to after handling the cocaine cues. Second, we performed regression analyses on error rates treating increased cue-induced craving as a continuous variable. Note, we intentionally have not included a control group in this study. Our main analyses were to directly examine the relationship between CIC craving and breakdowns in cognitive control toward cocaine cues. Any non-cocaine using group would show no CIC to cocaine cues and would not be included in either of our two main analyses. Moreover, the CDPs would likely significantly differ from any control group on the other main assessments in Table 1; hence, we would be unable to differentiate cocaine craving from psychological differences in depression, anxiety, or impulsivity if any differences were found between the CDPs and a