Addictive Behaviors 39 (2014) 1217–1223

Contents lists available at ScienceDirect

Addictive Behaviors

Laboratory-induced cue reactivity among individuals with prescription opioid dependence

Sudie E. Back [a,b,*], Daniel F. Gros [a,b], Jenna L. McCauley [a], Julianne C. Flanagan [a], Elizabeth Cox [c], Kelly S. Barth [a], Kathleen T. Brady [a,b]

[a] Medical University of South Carolina, Department of Psychiatry and Behavioral Sciences, Clinical Neuroscience Division, Charleston, SC 29425, United States
[b] Ralph H. Johnson Veterans Affairs Medical Center, Charleston, SC 29401, United States
[c] University of North Carolina, Department of Psychiatry, Chapel Hill, NC 27514, United States

HIGHLIGHTS

- Prescription opioid (PO) dependence is a critical health problem.
- Drug cue reactivity paradigms have advanced the understanding of substances.
- Present study assessed PO drug cue in PO dependent and healthy participants.
- PO group demonstrated pre to post cue increases in subjective/physiological indices.
- Findings support utility of a PO specific drug cue paradigm for understanding PO.

ARTICLE INFO

Available online 12 April 2014

Keywords:
Prescription opioids
Opiates
Prescription drugs
Drug cue reactivity
Drug cue paradigm

ABSTRACT

Prescription opioid (PO) dependence is a critical health problem. Although examination of drug cue reactivity paradigms has advanced the understanding of risk factors for relapse for a variety of substances (e.g., cocaine, alcohol, nicotine), no PO specific drug cue paradigm has been developed. The current study addressed this gap in the literature and evaluated the ability of a newly developed PO drug cue paradigm to elicit subjective, physiological, and neuroendocrine changes among PO-dependent participants ($n = 20$) as compared to controls ($n = 17$). The drug cue paradigm included an induction script, viewing and handling paraphernalia (e.g., bottle of oxycontin pills, pill crusher) and watching a video depicting people using POs as well as places related to POs (e.g., pharmacies). Consistent with hypotheses, the PO group demonstrated significant pre- to post-cue increases on subjective ratings of craving, difficulty resisting POs, stress, and anger. The control group did not demonstrate significant changes on any of the subjective measures. Both the PO group and the control group evidenced significant pre- to post-cue increases in physiological responses (e.g., blood pressure, skin conductance), as expected given the arousing nature of the drug cue stimuli. The PO group, but not the control group, evidenced a significant pre- to post-cue increase in heart rate and salivary cortisol levels. The development and validation of a drug cue paradigm for POs may help inform future research and treatment development efforts for patients with PO dependence.

Published by Elsevier Ltd.

1. Introduction

Prescription opioid (PO) dependence represents a critical health concern in the U.S. and internationally (Dhalla, Persaud, & Juurlink, 2011; Fischer, Nakamura, Rush, Rehm, & Urbanoski, 2010). PO dependence has increased significantly over the past two decades (Bagot, Heishman, & Moolchan, 2007) and recent surveys suggest that PO use is more commonly initiated than any other drug except marijuana (SAMHSA, 2012). Approximately 14% of individuals in the U.S. general population endorse lifetime non-medical use of POs (Back et al., 2010), a figure totaling nearly two million individuals (SAMHSA, 2011). The rapid rise of PO dependence in recent years is also of great concern due to its associations with serious negative outcomes, particularly unintentional overdose fatalities (Haug, Sorensen, Gruber, & Song, 2005; Veilleux, Colvin, Anderson, York, & Heinz, 2010). In fact, PO dependence is implicated in more overdose fatalities than heroin and cocaine combined (Warner, Chen, Makuc, Anderson & Miniño, 2011).

* Corresponding author at: Department of Psychiatry and Behavioral Sciences, Clinical Neuroscience Division, Medical University of South Carolina, 67 President Street, MSC861, Charleston, SC 29425, United States. Tel.: +1 843 792 5215; fax: +1 843 792 0528.
E-mail address: backs@musc.edu (S.E. Back).

http://dx.doi.org/10.1016/j.addbeh.2014.04.007
0306-4603/Published by Elsevier Ltd.

1.1. Advances in treatment and challenges associated with PO dependence

Recovery from PO dependence is a significant challenge for clinicians across health care fields. Nearly 10% of individuals seeking treatment for a substance use disorder report current PO abuse or dependence, amounting to a tenfold increase during the past decade (SAMHSA, 2010). The societal costs of PO use disorders in the U.S. are estimated at over $55 billion. Opioid dependence generally, and PO dependence specifically, are particularly challenging to treat due to a variety of factors, including: withdrawal from opioid use may be long-lasting and characterized by substantial discomfort; increased prescribing of POs for legitimate use has increased the availability of POs for distribution in the community; and dependence on POs may develop following legitimate use under a physician care (Joranson et al., 2000; Katz et al., 2007; Zacny, Bigelow, Compton, Foley, Iguchi, & Sannerud, 2003). Because many individuals who struggle with PO dependence initiated PO use to manage chronic pain conditions under a physician's care, the cessation of PO use may exacerbate one's discomfort and decrease motivation to maintain abstinence (Back et al., 2011; Barth et al., 2013; Joranson et al., 2002). While many individuals are able to complete detoxification and abstain from PO use for short periods of time, relapse remains highly prevalent (Tkacz, Severt, Cacciola, & Ruetsch, 2012). For example, in a recent study by Weiss et al. (2011), 30% of the treatment-seeking sample of individuals with PO dependence had received treatment prior to the current intervention. At week 16, 74% of participants had relapsed and by week 24, 91% had relapsed. Indeed, the essential feature of successful treatment for opioid dependence lies with relapse prevention rather than facilitating the initial cessation of use (O'Brien, Childress, Ehrman & Robbins, 1998; Stewart, 2003; Tkacz, Severt, Cacciola, & Ruetsch, 2012). In summary, PO dependence is a chronic and relapsing disease characterized by complex barriers to treatment.

One critical advancement in the treatment of opioid dependence over the past several decades is the use of pharmacological interventions. Clinical trials investigating the efficacy of several medications (e.g., Buprenorphine, Suboxone) alone and in combination with psychotherapy have yielded promising results (Carroll et al., 2001; Tkacz et al., 2012; Weiss et al., 2011). However, the generalizability of these findings to PO-dependent individuals may be limited because they have focused primarily on heroin-dependent individuals. Considering that PO dependence is currently 20 times more prevalent than heroin use, and approximately twice as many individuals seek treatment for PO dependence than heroin dependence (Office of Applied Studies, 2010), there is a great need for investigations to identify factors that exacerbate drug craving and predict drug consumption among PO dependent individuals.

1.2. Cue reactivity and relapse

Cue reactivity is a laboratory methodology in which an individual's subjective, behavioral, biological, and/or physiological responses to drug-related cues are measured. Previous laboratory studies have shown that exposure to drug-related cues, as compared to neutral cues, increases craving and induces changes in mood states and physiological measures (Carter & Tiffany, 1999a, 1999b; Shi et al., 2009; Yu et al., 2007). Importantly, cue reactivity in the laboratory has been found to predict relapse to drug use outside of the laboratory among cocaine and nicotine-dependent individuals (Back et al., 2010; Sinha, 2009).

Studies of cue reactivity have given rise to a variety of theoretical models, most of which use classical conditioning principles to explain drug cue-elicited craving and reactivity (O'Brien et al., 1998; See, 2002; Siegel, 1999; Siegel & Ramos, 2002). These findings suggest that, through a process of associative learning, previously neutral stimuli acquire incentive-motivational properties following repeated pairing with drug consumption. Cue reactivity, therefore, is a conditioned response that occurs as a result of learned association between the cue and drug intake (Drummond, 2000). Thus, conditioned stimuli play a critical role in sustaining ongoing drug-seeking behavior and relapse after periods of abstinence (Childress et al., 1988; O'Brien et al., 1998; Sinha et al., 2000; Stewart, 2003).

Most studies have assessed cue reactivity among alcohol, cocaine or nicotine dependent individuals (Drobes, 2002; Niaura et al., 1988; Reynolds & Monti, 2012) and several studies have examined heroin dependent individuals (Childress et al., 1986a,b; Daglish et al., 2001; Sell et al., 2000; Franken et al., 1999; Powell et al., 1990). To our knowledge, there have not been any studies examining cue reactivity among individuals with PO dependence. This critical gap in the literature is likely due to the fact that no drug cue paradigm for POs has been developed.

The development of a drug cue paradigm specific to PO dependent individuals is essential in order to facilitate research aimed at identifying factors that predict relapse and testing novel relapse prevention interventions. Therefore, the goal of this study was to assess the ability of a newly developed PO drug cue paradigm to elicit: (1) subjective responses (e.g., craving, stress, negative emotion); (2) physiological reactions (heart rate, blood pressure, skin conductance); and (3) neuroendocrine changes (cortisol) in PO-dependent participants as compared to healthy control participants. We hypothesized that PO-dependent participants would demonstrate greater cue-induced increases in subjective, physiological and neuroendocrine responses compared to control participants.

2. Methods

2.1. Participants

Participants were non-treatment seeking, PO dependent individuals ($n = 20$) and healthy control participants who did not have PO or any other substance use disorders ($n = 17$). PO dependence was defined as meeting current (i.e., past 6 months) Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV; American Psychiatric Association, 2000) criteria for substance dependence on opioid analgesics (e.g., oxycodone, hydrocodone). Newspaper and other media advertisements were the primary source of recruitment. Participants were recruited as part of a larger study on the relationship between stress, drug cues, and the hypothalamic-pituitary-adrenal (HPA) axis.

Potential participants were initially screened by telephone and individuals meeting preliminary eligibility criteria came into the office for a clinical assessment and a history and physical examination. Exclusion criteria included: pregnancy or nursing; BMI > 39; major medical problems (e.g., diabetes, HIV, Addison's or Cushing's disease) or comorbid psychiatric conditions (e.g., current major depressive disorder or post-traumatic stress disorder, current or history of bipolar affective disorder or psychotic disorder) that could effect the HPA axis; use of methadone or other opioid replacement therapies in the past three months; use of antihypertensive medications, beta-blockers, synthetic glucocorticoid therapy, or treatment with other agents that may interfere with stress response in the past month; or DSM-IV criteria for substance dependence (except caffeine or nicotine) within the past 60 days. Individuals who met criteria for abuse of other substances had to identify POs as their primary drug of choice. Controls were excluded if they met DSM-IV criteria for current or history of substance dependence (except caffeine or nicotine). Participants were informed about all study procedures. IRB-approved written informed consent was obtained before any study procedures occurred. Eligible participants (both PO and healthy controls) were scheduled for a one-night hospital stay at a large southeastern university medical center and testing was completed the next morning.