Behavioural Processes 115 (2015) 169–180

Contents lists available at ScienceDirect

Behavioural Processes

journal homepage: www.elsevier.com/locate/behavproc

Configurations of the interoceptive discriminative stimulus effects of ethanol and nicotine with two different exteroceptive contexts in rats: Extinction & recovery

Joseph R. Troisi II*, Elizabeth M. Craig

Saint Anselm College, Manchester, NH, USA

ARTICLE INFO

Article history:
Received 8 October 2014
Received in revised form 2 April 2015
Accepted 15 April 2015
Available online 17 April 2015

Keywords:
Configural learning
Drug discrimination
Ethanol
Extinction
Interoception
Nicotine
Rats
Relapse
Renewal

ABSTRACT

Interoceptive states interact with exteroceptive contexts in modulating operant behavior, which is maintained by its consequences. Evaluating discriminative stimulus control by overlapping interoceptive and exteroceptive configurations (gestalts) and the contribution of each modality may be clinically important for understanding aspects of relapsing behavior (e.g., drug abuse). With rats, the current investigation used a completely counterbalanced one-manipulandum operant drug discrimination procedure that established discriminative stimulus control between nicotine (0.3 mg/kg) in one exteroceptive context and EtOH (1.0 g/kg) in a differing exteroceptive context. One combined interoceptive–exteroceptive condition occasioned sessions of food reinforcement (S^D) and the other counterbalanced condition occasioned sessions of non-reinforcement (S^Δ). Each stimulus modality contributed to discriminative control, but to lesser extents than the combined intero–exteroceptive compound configurations (Experiments 1 & 2). In Experiment 1, responding was extinguished in the interoceptive stimulus conditions alone in a neutral exteroceptive context, but then renewed by reconfiguring the drugs with the exteroceptive contexts, and reversed in the opposing exteroceptive contexts. In Experiment 2, responding was extinguished in the interoceptive and exteroceptive contexts separately. Reconfiguration of the full intero–exteroceptive compound configurations did not promote recovery. These results suggest that interoceptive and exteroceptive discriminative control can be methodologically configured in modulating operant behavior during acquisition, extinction, and recovery of behavior; however, configuring interoceptive and exteroceptive discriminative stimuli do not appear to function as *unique cues* that differ from each stimulus modality alone. Clinical implications are discussed.

1. Introduction

Drug-seeking and taking behavior is modulated by an interaction among interoceptive states (e.g., affect, stress, thirst, hunger, fatigue, or other drug effects; see Paulus et al., 2009; Verdejo-Garcia et al., 2012) and exteroceptive contextual stimuli (e.g., drug paraphernalia, bars, social cues) present at the time of drug self-administration (Bouton et al., 2012b; Hogarth and Troisi, 2015 in press; Kirby et al., 1997; Troisi, 2013c, 2014; Troisi et al., 2012).

One experimental method for manipulating interoceptive states is offered by the *drug discrimination* paradigm (Gauvin et al., 1989; Lubinski and Thompson, 1987, 1993; Troisi et al., 2012), in which organisms are trained to respond differentially under the influence of specific drug states (e.g., drug vs. no-drug, or drug A vs. drug B). Drug discrimination methodology may be useful for simulating stimulus control functions that govern the manner in which other interoceptive states evoke drug seeking behavior (Hogarth and Troisi, 2015; Troisi, 2003b, 2006, 2011, 2013, 2014; Troisi and Akins, 2004 and see Beardsley et al., 1992). In view of this theoretical perspective, this laboratory has used ethanol and nicotine as two distinct interoceptive discriminative states that occasion sessions of food reinforcement (S^D) or non-reinforcement (S^Δ) in rats. Accordingly, on some sessions, responding is reinforced following pre-session administration of the S^D drug condition (e.g., EtOH) but not on intermixed sessions conducted with the counterbalanced S^Δ drug condition (e.g., nicotine or non-drug). Discriminative control is established within 18–24 sessions (see Troisi, 2013b; c.f., Besheer et al., 2012).

* Corresponding author at: Department of Psychology, Saint Anselm College, 100 Saint Anselm Drive, Manchester, NH 03102 USA. Tel.: +1 603 641 7198.
E-mail address: jtroisi@anselm.edu (J.R. Troisi II).

http://dx.doi.org/10.1016/j.beproc.2015.04.007
0376-6357/

Ethanol and nicotine function effectively as interoceptive operant S^Ds and S^Δs (see Troisi et al., 2013; p 899 for a brief summary). Consistent with the exteroceptive conditioning literature with lights and tones, several stimulus control functions with these drugs have been reported including (but not limited to) *extinction*, *inhibition*, and *recovery* (see Troisi 2003a,b; Troisi 2003a,b; see Troisi, 2006; Troisi et al., 2010, 2012 for several other examples). This laboratory recently reported evidence of *configural* and *elemental learning* (see Kehoe and Gormezano, 1980) with the discriminative stimulus effects of a nicotine (N) plus EtOH (E) (NE) compound; extinction training with the N and E elements did not generalize back when the NE compound was tested following such extinction (Troisi et al., 2013b). Thus, although the N and E elements contributed to the stimulus control by NE compound configuration, the compound was perceived as a unique cue that differed from the N and E elements.

The potential interactive *configurations* among interoceptive and exteroceptive elemental sensory stimuli (i.e., sensory gestalts) may be important for designing effective drug abuse treatment programs that utilize behavioral extinction (Hogarth and Troisi, 2015; Kirby et al., 1997; Troisi, 2013c) – an important methodological manipulation of the present investigation. However, there is a paucity in the number of studies that have evaluated interoceptive discriminative stimulus control by drug states combined with the discriminative stimulus functions of exteroceptive contextual stimuli (e.g., Colpaert et al., 1978; and see Järbe et al., 1989 for review; McMillan et al., 1989; Overton, 1988; Troisi, 2003a) – hence, one critical rationale for the present investigation. Duncan et al. (1979) compared tactile/visual exteroceptive discrimination to ethanol/saline discrimination and found stronger control by exteroceptive contextual cues compared to interoceptive states. The combination of the exteroceptive stimuli with ethanol for one group performed no better than the group that only received the exteroceptive discrimination training. They suggested that the interoceptive ethanol and exteroceptive tactile or visual stimuli did not summate when compounded together in sustaining discriminative control (c.f., Cohn and Weiss, 2007; Kearns and Weiss, 2005). Furthermore, during reversal training, the exteroceptive light and tactile cues continued to evoke greater discriminative control than the interoceptive ethanol/non-drug cues. Overall, it appeared that the exteroceptive stimuli *overshadowed* the 800 mg/kg dose of ethanol, which alone has been shown to promote discriminative control (Barry and Krimer, 1977; Barry, 1991; Troisi, 2003a). It is likely that a higher dose of EtOH (e.g., 1.0 g/kg used in the present study) might have promoted stronger control and undermined such overshadowing produced by the exteroceptive stimuli as later reported by Järbe et al. (1989) with chlordiazepoxide and pentobarbital.

The limited number of studies just mentioned reported interactions among interoceptive drug states and exteroceptive contextual stimuli in rats trained with drug vs. non-drug discriminations – not drug vs. drug in differing exteroceptive contexts. This is an important distinction between the present investigation and those noted above. Prior to actual drug discrimination training, rats have extensive histories in the non-drug interoceptive state, which is likely correlated with other events (e.g., food provisions, water, minor stressors, light dark cycles, environmental sounds, odors, etc.). By contrast, establishing discriminative control with two distinct drugs renders two novel interoceptive conditions that can be more effectively used to carry out conditioning within two different exteroceptive contexts, which are devoid of the potential confound of experience in the non-drug state. The present experiments employed similar configural methodology used by Troisi et al. (2013) by carrying out sessions of extinction and reacquisition of stimulus control to evaluate the contributions of the interocepctive and exteroceptive elements to the full intero–exteroceptive compound configurations. This is another important distinction between the present investigation and previous work by Duncan et al. (1979) and the work described by Järbe et al. (1989).

Consequently, the present investigation sought to establish discriminative stimulus control between EtOH in one exteroceptive context and nicotine in a differing exteroceptive context. The configuration of one interoceptive drug state with one exteroceptive context functioned as the intero–exteroceptive S^D condition, and the counterbalanced configuration of the other drug with the differing but counterbalanced exteroceptive context functioned as the intero–exteroceptive S^Δ condition. Stated differently, the rats were trained to respond differentially among two different counterbalanced intero–exteroceptive configural compounds. The discriminative stimulus contributions of the interoceptive and exteroceptive elements comprising the two configurations were evaluated: (1) following initial acquisition of discrimination training, (2) following extinction of responding with the interoceptive drug states alone, (3) following extinction of responding with the exteroceptive and interoceptive elements presented individually (Experiment 2), (4) following reversal of the interoceptive stimulus roles (Experiment 1), and (5) following reconfiguration of the interoceptive and exteroceptive elements after extinction (Experiments 1 and 2). In both experiments, the interoceptive drug elements were tested in a neutral exteroceptive context to determine if the drug elements alone promoted discriminative stimulus control independently from the exteroceptive contexts in which stimulus control was originally established. In a similar manner, the two exteroceptive contexts were tested without the drugs (i.e., with saline) to determine the extent to which they alone contributed to the overall discriminative stimulus control independent from the drugs with which discriminative control was established (Experiment 1). In Experiment 1, discriminative control with the drug states was extinguished in the neutral context (i.e., devoid of drug discrimination training) and was then tested later in the original exteroceptive training contexts, which were spared extinction training. In Experiment 2, responding in the exteroceptive contexts (with saline) and the interoceptive contexts (in neutral context) was extinguished separately – but was then reconfigured and tested as the full intero–exteroceptive contexts.

2. Experiment 1

Duncan et al. (1979) previously demonstrated that tactile-visual exteroceptive contexts promoted stronger discriminative stimulus control than the 800 mg/kg dose of EtOH. By contrast, Järbe et al. (1989) reported that exteroceptive contextual stimuli combined with interoceptive drug states promoted blocking, overshadowing, and conditional control. Neither report made use of extended extinction training to evaluate stimulus control by the drugs or the external contexts. Extinction training is useful for dissecting functional roles of compound stimuli (e.g., White and Stolerman, 1996). In this experiment, nose-poking was reinforced by food delivery during S^D sessions but not reinforced during S^Δ sessions. Experiment 1 used 1.0 g/kg of EtOH in either of two counterbalanced exteroceptive contexts (dim room plus white noise or strobe light plus tone) as S^D for some animals and was counterbalanced by administrations of 0.3 mg/kg of nicotine in the other of these two counterbalanced exteroceptive contexts as S^Δ. Other animals received the opposite and counterbalanced drugs and exteroceptive contexts. Initially, discriminative control by the two differing intero–exteroceptive S^D and S^Δ conditions was established; tests with each stimulus mode alone were later conducted to evaluate each mode's discriminative stimulus contribution. It was predicted that the exteroceptive contexts and the interoceptive drug conditions presented/administered alone would sustain