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# Differential sensitivity to learning from positive and negative outcomes in cocaine users

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ABSTRACT

*Background:* Altered sensitivity to positive and negative outcomes may be linked to the maladaptive choices characteristic of substance use disorders. Few studies have determined the distinct roles that positive and negative outcomes play in stimulus-response learning in cocaine users. The purpose of the present study was to investigate sensitivity to learning from positive and negative outcomes on a probabilistic learning task in cocaine users employing human laboratory and crowdsourcing techniques.
*Methods:* Individuals who reported cocaine use were recruited for a laboratory study (Experiment 1) or an online study on Amazon.com's Mechanical Turk (mTurk) (Experiment 2). All participants completed a feedback-based probabilistic learning task in which images were classified into categories (A versus B). Positive and negative outcomes were provided in a probabilistic manner on separate trials. Proportion of optimal responses and response times were recorded.
*Results:* Active cocaine users were less sensitive to learning from positive relative to negative outcomes. These effects were consistent across image type and session in the laboratory sample. Similarly, reduced sensitivity to learning from positive outcomes was observed in cocaine users on mTurk. Control participants did not show suboptimal performance following positive or negative outcomes.
*Conclusions:* This study extends the limited research on feedback-based learning in drug users by demonstrating reduced sensitivity to positive outcomes in cocaine users recruited in the human laboratory and online. Future studies on the clinical significance and mechanisms underlying this bias are needed to understand its relevance as a target for intervention development.


## 1. Introduction

Associative, stimulus-response learning contributes to drug-taking behavior (Di Chiara, 1999; Everitt and Robbins, 2005). A critical component of stimulus-response learning is the type of event (i.e., positive or negative) used to maintain behavior. Distorted sensitivity to positive and negative outcomes can contribute to maladaptive choice and is an underlying theme of past and present diagnostic criteria for substance use disorders (American Psychiatric Association, 2000, 2013). For example, decreased sensitivity to positive outcomes may lead to the devaluation of non-drug reinforcers in the environment, resulting in the allocation of behavior away from prosocial alternatives (e.g., interpersonal relationships). Conversely, decreased sensitivity to negative outcomes may render the negative consequences of drug use (e.g., losing friends) ineffective for decreasing drug-seeking behavior.

Many neuropsychological measures used in addiction research are limited in their capacity to dissociate the relative influence of positive and negative outcomes on learning. For example, in the Iowa Gambling Task, participants learn to select cards from four decks based on simultaneous gains and losses associated with each deck (Bechara et al., 1994). Repeated testing using these measures is problematic given that practice effects are observed once the correct strategy to optimize performance has been learned. An alternative to these measures is the feedback-based probabilistic learning task (Bodi et al., 2009). In this task, positive and negative outcome trials, also referred to as "reward/reinforcement" and

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"punishment" trials, are intermixed to determine the relative sensitivity to these consequences. During positive outcome trials, correct responses are reinforced by point gain, whereas in negative outcome trials incorrect responses are punished by point loss. The alternative response in each trial (i.e., an incorrect response on a positive outcome trial or correct response on a negative outcome trial) has no programmed consequence.

The feedback-based probabilistic learning task has previously been used to evaluate changes in learning that may underlie degenerative and psychiatric conditions, including Parkinson's disease, post-traumatic stress disorder, schizophrenia, opioid use disorder, and major depressive disorder (Bodi et al., 2009; Herzallah et al., 2013; Myers et al., 2013, 2016; Somlai et al., 2011). Non-medicated Parkinson's patients show a decreased sensitivity to positive, but not negative, outcomes relative to controls (Bodi et al., 2009; Piray et al., 2014). This impairment is reversed following treatment with dopaminergic drugs, which suggests that decrements in learning from positive outcomes may be associated with alterations in dopaminergic signaling. In individuals with schizophrenia, another condition characterized by alterations in dopaminergic tone, more severe negative symptoms are associated with decreased performance on positive outcome trials (Somlai et al., 2011). These findings suggest that altered performance may reflect the underlying pathology, specifically changes in dopaminergic functioning, in these respective conditions.

Investigating differences in learning from positive and negative outcomes in cocaine users is grounded in the hypothesized neurobiological and behavioral consequences of chronic cocaine use. Chronic use results in the downregulation of dopamine $D_2$ receptors and a hypodopaminergic state that together result in decreased sensitivity to reinforcement (Goldstein et al., 2010; Volkow et al., 1996). Dopaminergic signaling plays a critical role in basic learning processes, with preclinical evidence suggesting a preferential function for dopamine activation in learning from positive feedback (e.g., Beninger, 1983; Stolyarova et al., 2014). Cocaine users display impairments in probabilistic categorical learning compared to controls and alcohol/marijuana users (Vadhan et al., 2014). However, such impairments have not been consistently observed (Lane et al., 2014; Vadhan et al., 2008) and these prior studies have not dissociated the influence of positive and negative outcomes.

The overall purpose of the present study was to evaluate learning from positive and negative outcomes in cocaine users. In Experiment 1, a sample of cocaine users was recruited for a laboratory study in which probabilistic learning from positive and negative outcomes was measured. Participants completed two variations of the probabilistic learning task in which categorized stimuli were either abstract or cocaine-related. Each task variation was completed during two separate laboratory visits to determine whether performance was stable over time and to detect potential practice effects. In Experiment 2, a sample of individuals with and without a history of self-reported cocaine use was recruited using online crowdsourcing techniques. The goals of Experiment 2 included investigating the specificity of outcomes from Experiment 1 and comparing findings from laboratory and online samples.

## 2. Methods and materials: experiment 1

### 2.1. Participants

Participants (n = 21) were recruited during screening for studies conducted at the University of Kentucky. All participants reported recent cocaine use verified with a benzoylecgonine positive urine specimen. Participants with a current prescription for a centrally acting medication or dependence on any drug that could produce significant withdrawal symptoms (e.g., alcohol, opioids, benzodiazepines) were excluded. Screening procedures have been described in detail elsewhere (e.g., Stoops et al., 2010). Briefly, participants completed a battery of questionnaires, including a self-reported drug use history and the sensation-seeking and impulsivity subscales of the Zuckerman-Kuhlman Personality Questionnaire (ZKPQ; Zuckerman et al., 1993). All participants met diagnostic criteria for cocaine abuse or dependence according to a computerized version of the Structured Clinical Interview for the DSM-IV-TR (American Psychiatric Association, 2000). Participants gave sober, written informed consent prior to their enrollment.

### 2.2. Procedures

Participants completed two test sessions separated by 2–13 days. One participant did not return for Session 2 and was not included in data analysis. Participants had to pass a field sobriety test and provide an expired air specimen that was negative for alcohol. The University of Kentucky Institutional Review Board (IRB) approved the protocol and the informed consent document.

### 2.3. Probabilistic learning task

Participants completed a feedback-based probabilistic learning task administered using E-prime software (Psychology Software Tools, Pittsburgh, PA) on a PC computer (Bodi et al., 2009; Fig. 1). During each trial, participants viewed one of four images and were asked to indicate whether an image belonged to Category A or B. Two images (one image for positive outcome trials, one image for negative outcome trials) belonged to Category A with 80% probability and the other two images belonged to Category B with 80% probability. During a positive outcome trial, if a participant selected correctly, 25 points were awarded and positive visual feedback provided (i.e., a smiling face); if the participant selected the image category incorrectly, there was no scheduled consequence. During a negative outcome trial, if a participant selected incorrectly, 25 points were deducted and negative visual feedback provided (i.e., a frowning face); if the participant selected the image category correctly, there was no scheduled consequence.

Participants first completed four practice trials during which they were instructed to press specific keys to observe all possible outcomes. After completing the practice trials, participants received 500 points and were told that the goal of the task was to win as many points as possible. The task consisted of 160 trials. The primary dependent measures were the proportion of optimal response (i.e., the choice most often associated with a correct response) and response time.

Two variations of the probabilistic learning task were used. In the first version, abstract images were presented similar to previous studies (Bodi et al., 2009). In the second version, cocaine-related images were used. Cocaine-related stimuli were images of the drug (e.g., crack rocks) and/or drug paraphernalia (e.g., crack pipes) and were selected from a set of images used in other cognitive-behavioral tasks in our laboratory (Strickland et al., in press). Half of the images depicted smoked cocaine and half of the images depicted intranasal cocaine. The order of completion for the two tasks was randomized across participants. All images were randomly assigned to feedback conditions for each participant and unique images were used in each session. Each participant completed both task variations during each of the two separate laboratory visits.

### 2.4. Data analysis

Statistical analyses were performed in SPSS Statistics version 22 (IBM Corporation, Armonk, NY) with a type I error rate of .05. Proportion optimal choice and response time were analyzed using separate $2 \times 2 \times 2 \times 2$ repeated-measures analyses of variance (ANOVAs) with Outcome (Positive versus Negative), Session (Session 1 versus Session 2), Stimulus Type (Abstract versus Cocaine-Related), and Task Order (Cocaine versus Abstract First) as within-subjects factors. Models not including Task Order were also examined given the possibility for model over-parameterization. The correlation between proportion optimal choice and response time on positive and negative trials was analyzed using Pearson bivariate correlations. The relationships between impulsivity and sensation-seeking scores from the ZKPQ and task performance were also assessed using bivariate correlations. Effect sizes were calculated as Cohen's $d$ for repeated measures ($d_z$) or partial eta-squared ($\eta_p^2$) for ANOVA outcomes.

## 3. Results: experiment 1

### 3.1. Sample characteristics

Demographic information and self-reported cocaine use are presented in Table 1. All participants reported past month cocaine use and provided a benzoylecgonine positive urine specimen during one (10%) or both (90%) sessions.

### 3.2. Probabilistic learning task

Fig. 2 displays proportion optimal choice by Outcome and Stimulus Type for Session 1 (left) and Session 2 (right). A four-way repeated-measures ANOVA revealed a significant main effect