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Stimulus–response learning in long-term cocaine users: Acquired equivalence and probabilistic category learning[☆]

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Abstract

Objective: The purpose of this study was to examine stimulus–response (S–R) learning in active cocaine users.

Participants and methods: Twenty-two cocaine-dependent participants (20 males and 2 females) and 21 non-drug using control participants (19 males and 2 females) who were similar in age and education were administered two computerized learning tasks. The Acquired Equivalence task initially requires learning of simple antecedent–consequent discriminations, but later requires generalization of this learning when the stimuli are presented in novel recombinations. The Weather Prediction task requires the prediction of a dichotomous outcome based on different stimuli combinations when the stimuli predict the outcome only probabilistically.

Results: On the Acquired Equivalence task, cocaine users made significantly more errors than control participants when required to learn new discriminations while maintaining previously learned discriminations, but performed similarly to controls when required to generalize this learning. No group differences were seen on the Weather Prediction task.

Conclusions: Cocaine users' learning of stimulus discriminations under conflicting response demands was impaired, but their ability to generalize this learning once they achieved criterion was intact. This performance pattern is consistent with other laboratory studies of long-term cocaine users that demonstrated that established learning interfered with new learning on incremental learning tasks, relative to healthy controls, and may reflect altered dopamine transmission in the basal ganglia of long-term cocaine users.

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1. Introduction

Recent theories regarding the development and maintenance of substance abuse and dependence have emphasized the relevance of learning and memory functions (e.g., Everitt and Robbins, 2005; Garavan and Stout, 2005). Most investigations of learning and memory in cocaine users have focused on declarative memory, which refers to the conscious acquisition, retention and recall of information and events. A meta-analysis (Jovanovski et al., 2005) revealed mild to moderately impaired performance on tests of declarative verbal memory and visual memory among cocaine users compared to non-drug using controls. However, stimulus–response (S–R) learning, which refers to the incremental learning of responses to stimuli, has been unexplored in cocaine users.

A central component of S–R learning is the ability to learn from feedback. As such, deficits in S–R learning have the potential to interfere with the ability to respond to the changing consequences of behavior. For example, so-called "habit" learning is one form of S–R learning, whereby learned responses in laboratory animals become resistant to extinction even when the reinforcer that maintained responding to the stimuli has been devalued (see Packard and Knowlton, 2002); in other words, the stimulus comes to elicit the response directly, with no intervening "expectancy" of the outcome (e.g., Miles et al., 2003). Cocaine-dependent individuals report that they continue to take cocaine despite receiving negative consequences

in social, emotional and physical realms. Thus, S–R learning has been hypothesized to be relevant to the understanding of repeated drug-seeking and taking in humans, particularly highly experienced users (Everitt and Robbins, 2005). Laboratory assessment of S–R learning in long-term cocaine users may therefore provide insight into the cognitive functions associated with long-term cocaine use.

Data collected in both laboratory animals and humans indicate that S–R learning is mediated primarily by dopaminergic mechanisms in the basal ganglia, with some contributions from medial-temporal lobe pathways (for a review, see Packard and Knowlton, 2002). Studies conducted in humans also suggest that dopaminergic function in the basal ganglia, particularly the striatum, is altered in long-term cocaine users (Martinez et al., 2004; Volkow et al., 1990, 1997). For example, a PET imaging study (Volkow et al., 1990) found that experienced cocaine users exhibited decreased availability of dopamine D2 receptors in the striatum relative to healthy controls, within 1 week of most recent reported cocaine use. Thus, long-term cocaine users exhibited a decrease in dopaminergic function in the primary brain area that mediates S–R learning, during early reported abstinence from cocaine. Correspondingly, long-term cocaine users may also exhibit disruptions in S–R learning within a similar time frame.

Two types of S–R learning that may be relevant to cocaine abuse are equivalence learning and probabilistic category learning. Equivalence learning refers to the phenomenon that when two superficially distinct stimuli are associated with the same response, these stimuli come to be regarded as equivalent. Thus, subsequent learning about one stimulus tends to transfer to the other stimulus in the absence of direct training (Myers et al., 2003). Probabilistic category learning refers to the prediction of a dichotomous outcome based on different stimulus compounds, when the discrete stimuli within the compound are each only a partially accurate predictor of the outcome (Gluck et al., 2002). Thus, both forms of S–R learning are based on incremental feedback but involve distinct learning functions, which have been operationalized in two computerized tasks (the Acquired Equivalence task; Myers et al., 2003; the Weather Prediction task; Knowlton et al., 1996).

Assessment of long-term cocaine users' performance on these S–R learning tasks may help characterize the way such individuals respond to complex feedback, and how they generalize learning across categories of stimuli. Importantly, performance on different phases of each of these tasks has been independently associated with basal ganglia and medial-temporal lobe functioning via cross-sectional methodology (Knowlton et al., 1996; Myers et al., 2003) and fMRI techniques (Poldrack et al., 1999), re-emphasizing the association of S–R learning with circuitry centered on these brain regions. Therefore, examination of long-term cocaine users' performance on these tasks may also yield insight into the cognitive implications of dopaminergic alteration in the basal ganglia that has been previously reported in neurobiological studies of cocaine users. To our knowledge, no studies of performance on these tasks have been conducted in long-term cocaine users. Hence, the purpose of the current study was to examine the S–R learning

abilities of long-term cocaine users compared to healthy controls via their performance on the Acquired Equivalence and Weather Prediction tasks.

2. Methods

2.1. Participants

All participants were recruited by local newspaper, Internet and flier advertisements. They were all native English speakers, screened for color blindness or hearing impairment, and able to view a computer monitor at a comfortable distance. Participants were excluded if they reported any history of head injury or neurological or medical illness that could interfere with brain function (including HIV/AIDS), and all participants reported that they were not taking psychoactive medications. All participants signed a consent form that was approved by the respective Institutional Review Boards (New York State Psychiatric Institute or Rutgers University), completed their participation within 1 week of screening and were compensated for their time.

2.1.1. Cocaine users. Twenty-two active cocaine smokers who met DSM-IV criteria for current cocaine dependence and were not seeking treatment participated in this outpatient study. All cocaine users reported that cocaine was their substance of choice, and that they used cocaine for a minimum of 2 days per week. All cocaine users tested positive for cocaine on urine toxicology tests during screening as well as on the day of testing. Seventeen cocaine users (77.3%) reported current alcohol use, and seven cocaine users (31.8%) reported current marijuana use (confirmed by urine toxicology). Self-reported substance use characteristics for the cocaine users are presented in Table 1.

Potential cocaine-using participants were excluded from participation in the current study if they reported current use of any psychoactive substance besides cocaine, marijuana, alcohol, nicotine or caffeine, which was verified by urine toxicology tests during screening and before testing. As assessed by the Structured Clinical Interview for DSM-IV (First et al., 1995), administered by trained doctoral level clinical psychologists, no cocaine users met DSM-IV criteria for abuse/dependence for any other substance besides cocaine (nicotine or caffeine use disorders were not assessed) nor for any other Axis I psychiatric disorder. All cocaine users were instructed not to use any psychoactive substance on the morning of testing, except regular caffeine and nicotine; consistent with this requirement, no cocaine user reported such use when queried. Prior to testing, all cocaine users passed an alcohol breathalyzer test, and spent 30–45 min completing urine toxicology tests and self-report instruments. Additionally, no behavioral signs of intoxication were noted by the experimenter. Thus, it is unlikely that any cocaine user was intoxicated during testing.

2.1.2. Control participants. Twenty-one non-drug using control participants participated in this study. All potential control participants were screened

Table 1
Self-reported substance use of the cocaine users

	Mean	S.D.
Cocaine		
Days of use/week	4.8	1.9
$ spent/week	323.0	225.7
Years of regular use	21.0	4.9
Most recent use (hours prior to testing)	44.9	40.0
Most recent use ($)	101.6	64.5
Marijuana		
Days of use/week	1.0	2.1
$ spent/week	7.8	17.3
Alcohol		
Days of use/week	2.6	2.2
SDUs[a]/week	13.9	13.9

[a] Standard drink units (i.e., 12-oz beer, 4.5-oz wine, 1.25-oz liquor).

Table 2
Demographic characteristics and depressive symptoms

	Cocaine-dependent		Controls		Test value	*p* value[a]
Age						
Years	$M = 39.3$	S.D. = 3.5	$M = 38.9$	S.D. = 6.6	$t = -0.26$	0.79
Sex						
Male	90.9%	$n = 20$	90.5%	$n = 19$	Fisher's exact = 1.0[b]	
Female	9.1%	$n = 2$	9.5%	$n = 2$		
Race						
Black	**90.5%**	**$n = 19$**	**47.6%**	**$n = 10$**	**$x^2 = 9.02$[c]**	**0.003**
Hispanic	4.8%	$n = 1$	9.5%	$n = 2$		
White	4.8%	$n = 1$	42.9%	$n = 9$		
Education completed						
Years	$M = 12.4$	S.D. = 1.7	$M = 13.3$	S.D. = 1.8	$t = 1.61$	0.12
Depressive symptoms						
BDI-II total score	$M = 8.8$	S.D. = 6.6	$M = 5.3$	S.D. = 4.4	$t = -1.8$	0.08

[a] Bold indicates significant group difference ($p < 0.05$).
[b] Comparison based on male vs. not male.
[c] Comparison based on Black vs. not Black.

for the presence of psychiatric disorders and lifetime or current drug or alcohol abuse, and were excluded if there was evidence of these disorders. Additionally, no control participant reported any past or current use of illicit drugs, and all control participants reported infrequent current alcohol use.

Demographic characteristics and depressive symptoms for both groups are presented in Table 2. There were no group differences on any demographic variable except race (there were more Black participants in the cocaine-dependent group). Notably, there was no group difference in depressive symptoms as assessed by the Beck Depression Inventory (BDI-II; Beck et al., 1996), and the BDI-II scores for both groups were below the clinically accepted "mild" threshold (Beck et al., 1996).

2.2. Measures

The Acquired Equivalence and Weather Prediction tasks were described in detail in Myers et al. (2003) and Knowlton et al. (1994), respectively, and are presented briefly here. The tasks were run on Macintosh PowerBook 520c/1400cs or iMac computers with color screens, using software programmed in the Super-Card language. Testing took place in a quiet room, with the participant seated in front of the computer at a comfortable viewing distance (approximately 18 in.). Two keys were labeled "LEFT" and "RIGHT", which the participant could press to record a response.

2.2.1. Acquired Equivalence task. Four drawings of faces (man, woman, girl, boy) served as the antecedent stimuli. The boy and woman had yellow hair while the girl and man had brown hair. Thus, each antecedent had three obvious, binary-valued features: (1) age (adult vs. child), (2) gender (male vs. female) and (3) hair color (blond vs. brown); each antecedent shared exactly one feature with each other antecedent. For each participant, the four face drawings were randomly assigned to be antecedents A1, A2, B1, and B2. The consequents were four drawings of a fish colored red, orange, pink and purple. For each participant the colored fish were randomly assigned to be the consequents X1, X2, Y1, Y2. The antecedents and consequents all appeared about 1 in. tall on the computer screen.

At the start of the experiment, the following instructions appeared on the screen: "Welcome to the experiment. You will see drawings of people who each have some pet fish. Different people have different kinds of fish. Your job is to learn which kinds of fish each person has. At first, you will have to guess." The experimenter also read these instructions aloud to the participant and then clicked the computer mouse button to begin the acquisition phase. On each trial, the screen showed an antecedent (face) and two consequents (fish) along with the prompt: "Which fish does this person have? Use the LEFT or RIGHT key to choose" (Fig. 1A). The participant responded by pressing one of the two labeled keys. The selected consequent (fish) was circled, and corrective feedback was given (Fig. 1B). In the case of an incorrect response, an alert beep also sounded.

There were three stages of acquisition, each with increasing numbers of trial types as shown in Table 3. During acquisition stage 1 (shaping), two distinct
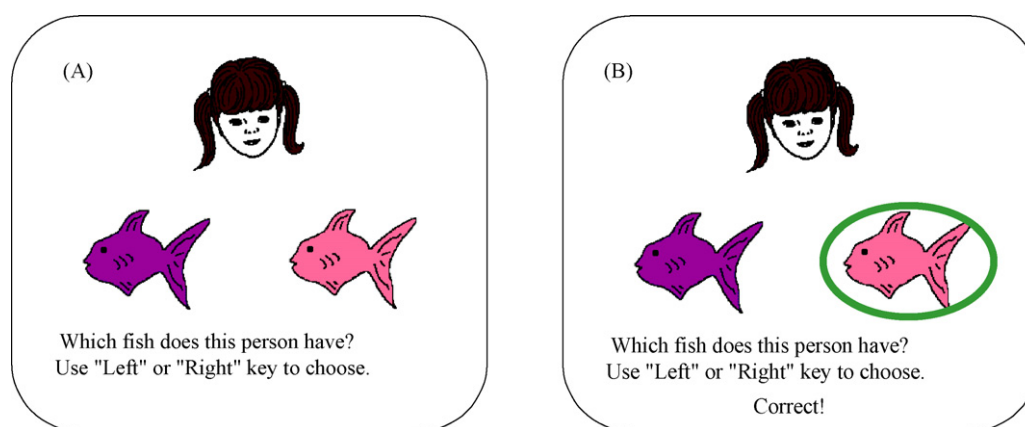

Fig. 1. Acquired equivalence stimuli.

Table 3
Acquired equivalence paradigm (Myers et al., 2003)

Acquisition stage 1 (shaping)	Acquisition stage 2 (equivalence training)	Acquisition stage 3 (novel consequents)	Transfer phase[a] (equivalence testing)
A1 → X1	A1 → X1 A2 → X1	A1 → X1 A2 → X1 A1 → X2	A2 → X2 or Y2?
B1 → Y1	B1 → Y1 B2 → Y1	B1 → Y1 B2 → Y1 B1 → Y2	B2 → X2 or Y2?

[a] Note that the transfer phase interleaved trials with the previously learned information as well as the novel pairs.

antecedents were each associated with a different consequent. During acquisition stage 2 (equivalence training), two novel and distinct antecedents were each associated with an initial consequent from acquisition stage 1, while initial shaping continued. During acquisition stage 3 (novel consequents), the initial antecedents from acquisition stage 1 were each associated with a novel and distinct consequent, while shaping and equivalence training continued. Since the consequents could appear in either the left or right position under the antecedent, there were 4 trial types in acquisition stage 1, 8 in acquisition stage 2, and 12 in acquisition stage 3. Each stage consisted of a maximum of eight blocks, each consisting of one instance of each trial type in random order.

Acquisition stages 1 and 2 terminated early if the participant reached criterion performance of eight consecutive correct responses; acquisition stage 3 terminated early if the participant reached criterion performance of 12 consecutive correct responses. The start of a new training stage was not signaled to the participant. At the conclusion of acquisition stage 3, the following instructions appeared: "Good! In this part of the experiment, you will need to remember what you have learned so far. You will NOT be shown the correct answers. At the end of the experiment, the computer will tell you how many you got right. Good luck!"

The transfer phase followed (see Table 3). On each trial, the screen showed one face and two fishes; the fish chosen by the participant was circled, but no corrective feedback was given. During this phase, participants were presented with the novel antecedents from acquisition stage 2 and were required to pair them with one of the two novel consequents from acquisition stage 3. Selection of the appropriate consequents indicated that equivalence had formed between the initial antecedents from acquisition stage 1 and the novel antecedents from acquisition stage 2. There were 16 types of trials: all 6 trial types from the acquisition phase plus the 2 new test trial types (A2 → X2 or Y2, and B2 → X2 or Y2). Each new trial type was presented twice, once with X2 on the left and once with X2 on the right under the antecedent, yielding four total types of test trials. Trial order was random for each participant. On each trial, the computer recorded the antecedent and consequents shown, as well as the desired and actual responses. The primary dependent measure for acquisition stages 1–3 was errors to criterion, and the primary dependent measures for the transfer phase were total errors made on novel and on previously learned pairs.

2.2.2. Weather Prediction task.

The Weather Prediction task (Knowlton et al., 1994) was administered using the modified probabilities of Gluck et al. (2002). The instructions stated that the participant was to learn to predict the weather ("sun" or "rain") based on four tarot cards, that on each trial between one and three cards would be dealt, and that the participant should enter a prediction by pressing the "sun" or "rain" key. After the participant responded, the correct answer was shown in the form of a sun or a rain cloud icon, which appeared above the stimuli. If the participant's response was correct, a score bar would increase and a smiley face would appear; otherwise, the score bar would decrease and a frowning face would appear. The stimuli remained on the screen until the participant responded or for 5 s maximum; if the participant did not respond within 2 s, a prompt appeared: "answer now."

All possible combinations of one, two or three cards were used. Each card was associated with each outcome with a fixed probability: $P(\text{"sun"}|\text{card 1}) = 0.8$, $P(\text{"sun"}|\text{card 2}) = 0.6$, $P(\text{"sun"}|\text{card 3}) = 0.4$, $P(\text{"sun"}|\text{card 4}) = 0.2$. Thus, card 1 was associated with sun on 80% of the trials on which it appeared and with rain on 20% of the trials on which it appeared. Similarly, cards 2, 3, and 4 were associated with sun on 60, 40, and 20% of trials, respectively. These probabilities were used to generate a series of 200 trials in which the outcomes sun and rain appeared equally often (Gluck et al., 2002). These trials were presented in a random but fixed order for all participants. Cards could appear in any spatial order on the screen. The primary dependent measure was percent optimal responding (choosing the outcome that was most associated with the particular stimulus configuration over the course of the task).

2.2.3. Stroop Color-Word task.

This task is a measure of response inhibition that requires the participant to focus on a target feature of a written stimulus while simultaneously inhibiting response to a distracting feature of the same stimulus (Golden, 1978), and was administered to assess the potential contributions of attentional/executive functions to learning performance. There were three conditions, presented in the following order: (1) Word, (2) Color, and (3) Color-Word. The Word condition required the participant to read the names of three colors (Red, Green and Blue) as quickly as possible. The Color condition required the participant to name the ink color of strings of Xs (Red, Green and Blue) as quickly as possible. The Color-Word condition (conflict condition) required the participant to name the color of the ink that the names of colors were written in, when the ink color and color-names were mismatched, as quickly as possible. For each condition, there were 100 items divided equally into five columns. Each condition was presented on a separate laminated 8.5 in. × 11 in. card. Participants were required by the experimenter to successfully complete each item before moving on the next one. The dependent measure for each condition was the number of items completed in 45 s.

2.3. Data analyses

2.3.1. Acquired Equivalence task.

First, individual data were examined to assess participants' rate of task completion. Since transfer phase data were meaningless in participants who did not adequately learn the original stimulus relations, only data from participants who completed acquisition stage 3 within 96 trials were analyzed. Second, initial learning (errors to criterion) was examined by a mixed (group × stage) repeated-measures Analysis of Variance (ANOVA) on acquisition stages 1–3. Transfer of learning (total errors) was examined by a mixed (group × discrimination type) repeated-measures ANOVA on the transfer phase.

2.3.2. Weather Prediction task.

First, individual data were examined to insure that participants completed all 200 trials. Next, responses for each trial were examined for optimal responding. Group differences on mean percent of optimal responses were assessed with 2 mixed (group × block) repeated-measures ANOVAs on the first 50 trials (5 blocks of 10 trials) and all 200 trials (4 blocks of 50 trials).

2.3.3. Stroop task.

Group differences in word-reading, color-naming, and color-naming (conflict) performance were assessed with a mixed (group × condition) repeated-measures ANOVA.

All differences were considered significant at $p < 0.05$, unless otherwise noted.

3. Results

3.1. Acquired Equivalence task

Four cocaine users and three control participants were considered non-completers and were excluded from further analysis; the ratio of solvers to non-solvers did not differ significantly between groups ($r^2 = 0.17$, $p > 0.50$).

Fig. 2 shows the performance data from acquisition stages 1–3 (upper panel) and the transfer phase (lower panel). There was no overall difference between cocaine users and control participants in errors made during acquisition stages 1–3, but there was a within-subjects effect of stage ($F_{2,66} = 7.02$, $p < 0.01$) and a group–stage interaction ($F_{2,66} = 9.42$, $p < 0.001$). Post hoc pairwise comparisons ($\alpha = 0.02$) revealed that cocaine users made about six more errors, on average, than control participants on acquisition stage 3 ($p < 0.02$), when novel consequents for the initial antecedents were introduced. No group differences were found on the transfer phase, indicating that cocaine users generalized new learning about the initial antecedents to the novel antecedents at an equivalent level to control participants. There was a significant effect of type of transfer, with all participants performing better during the transfer phase on the old (acquisition stage 1) discriminations than on the new (transfer

Fig. 3. Weather Prediction task performance by group; percent of optimal responses as a function of blocks of trials on the Weather Prediction task in cocaine users and controls; each error bar represents one S.E.M.

phase) discriminations ($F_{1,40} = 2.77$, $p < 0.001$); there was no group–type interaction. Thus, cocaine users and control participants retained their initial learning at equivalent levels.

3.2. Weather Prediction task

One control participant failed to respond on nearly half of the trials; his data were discarded from subsequent analysis. No group differences were seen for the first 50 trials (examined as five 10-trial blocks). A significant effect of block ($F_{4,116} = 3.45$, $p < 0.05$), but no group–block interaction, was seen. Performance over all 200 trials, examined as four 50-trial blocks, is shown in Fig. 3.

Similar to the first 50 trials, no group differences were seen for all 200 trials. A significant effect of block ($F_{3,87} = 18.11$, $p < 0.001$), but no group–block interaction, was seen. Thus, cocaine users chose the optimal response per trial, and improved their optimal responding over time, at rates equivalent to control participants.

3.3. Stroop task

Stroop performance data are presented in Table 4. No group differences were seen for performance on any Stroop condition, including the conflict condition, indicating that cocaine users and control participants experienced equivalent interference on the Stroop task.

4. Discussion

This study found that long-term cocaine users who met diagnostic criteria for cocaine dependence made more errors during
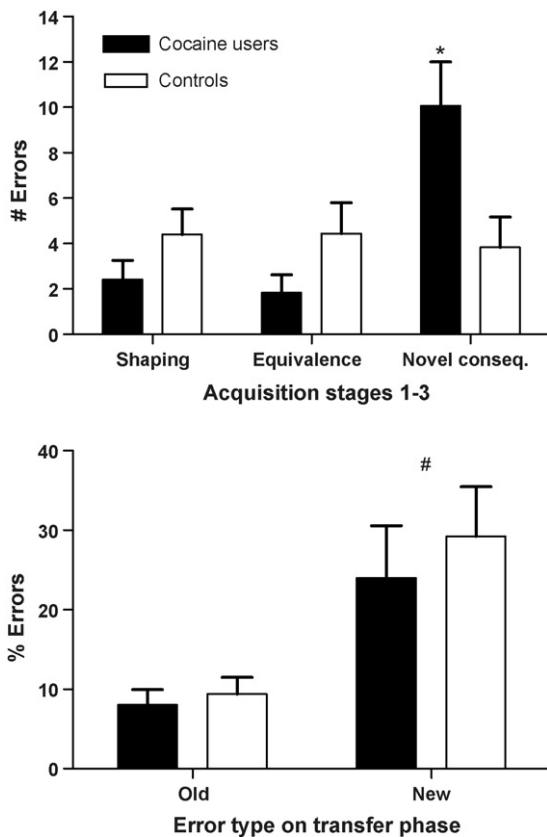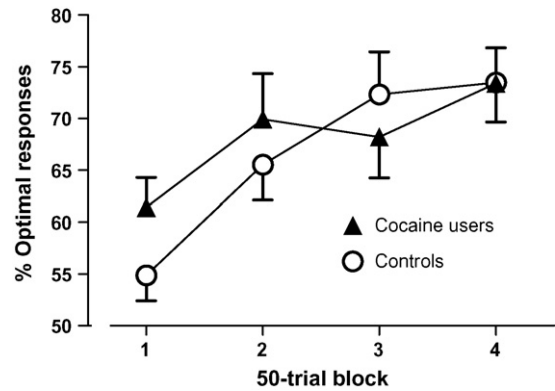

Fig. 2. Acquired equivalence performance by group; number of errors during acquisition (top panel) and transfer (lower panel) phases of the Acquired Equivalence task in cocaine users and controls; each error bar represents one S.E.M.; *indicates a between-group difference; #indicates an overall within-group difference; $p < 0.05$.

Table 4
Stroop performance (# items completed)

Condition	Cocaine users		Controls	
	Mean	S.D.	Mean	S.D.
Words	94.7	18.8	90.4	15.2
Colors	71.5	8.2	73.9	12.1
Color-Words	38.5	8.6	39.9	18.4

the novel consequents stage of the Acquired Equivalence task than healthy controls with similar age, education and depressive symptom levels. Specifically, the performance of the cocaine users was impaired when they were required to pair initial antecedents with *novel* consequents while maintaining the previously learned antecedent–consequent relations. However, the cocaine users and control participants made an equivalent number of errors when relatively simple relations between antecedent and consequent stimuli were being learned (shaping and equivalence training). The performance of the cocaine users was also not impaired when they were required to generalize new learning about the initial antecedents to novel antecedents in the absence of direct training. No group differences were seen on the Weather Prediction task, where participants were required to learn to optimally predict an outcome based on the probabilistic relationship between the predictor stimuli and the outcome.

Neurobiological interpretation of these results may be aided by examining the performance patterns of participants with clearly defined neuropathology. In a previous study (Myers et al., 2003), the Acquired Equivalence task was administered to participants with Parkinson's disease, a degenerative disorder that decreases dopamine transmission in the basal ganglia, and to non-demented participants with atrophy in the hippocampus. Parkinson's patients on their normal dopaminergic medication were impaired on all three stages of the acquisition phase (but not the transfer phase) of the Acquired Equivalence task, whereas the participants with hippocampal atrophy were impaired on the transfer phase (but not the acquisition phase), relative to healthy controls. Given the pathophysiology of the two clinical samples, this finding suggested that learning of the initial discriminations was mediated by dopaminergic mechanisms in the basal ganglia, while learning transfer was mediated by medial-temporal lobe pathways, specifically involving the hippocampus. Within the context of this double dissociation, the cocaine users' impaired performance during one of the stages of acquisition (but not during learning transfer) may be consistent with alteration in basal ganglia (but not hippocampal) function in long-term cocaine users who have used cocaine recently.

Convergent evidence for altered basal ganglia function in cocaine users includes findings of decreased D2 receptor availability in the striatum (Martinez et al., 2004; Volkow et al., 1990, 1997), and increased hand tremor of a type indicating basal ganglia involvement (Bauer, 1996), in cocaine-abusing individuals, relative to healthy controls. The cognitive and neural specificity of the current finding is further supported by the lack of group differences on Stroop task performance, as Stroop performance has been previously found to be correlated with the level of resting glucose metabolism in the orbitofrontal gyrus but not the basal ganglia, in cocaine-dependent participants whose Stroop performance was not impaired relative to healthy controls (Goldstein et al., 2001). Thus, the current study documented a specific S–R learning decrement in long-term active cocaine users that, interpreted within the context of previous findings in non-drug-abusing neurologic participants (Myers et al., 2003), may be tied to dopaminergic alteration in the basal ganglia. This interpretation is speculative since no neurobio-

logical measures were administered in the current study, and is further limited by the observation that the cocaine users' impairment was restricted to only one stage of acquisition, whereas the Parkinson's patients (Myers et al., 2003) exhibited impairment across the entire acquisition phase.

Only one other study has directly examined both basal ganglia- and medial-temporal lobe-based learning in cocaine abusers (van Gorp et al., 1999); this study used a motoric procedural learning task and two declarative learning tasks to measure these respective learning systems. Results indicated that within 72 h of their most recent cocaine use (confirmed by urine toxicology), cocaine users exhibited faster learning of motor tracking (Pursuit Rotor task; Spreen and Strauss, 1991), weaker performance on a visual learning test (Rey-Osterreith Complex Figure task; Spreen and Strauss, 1991), and similar performance on a verbal learning task (California Verbal Learning Test; Delis et al., 1987), relative to age-matched healthy control participants. These results suggested that the cocaine abusers were more proficient at motoric procedural learning, mediated by the basal ganglia, but less proficient at visual declarative learning, mediated by the medial-temporal lobe, than the control participants.

These previous results appear to contrast with the current findings from the Acquired Equivalence task. The discrepancy between results may be related to the distinct types of learning assessed in these two studies (e.g., S–R learning vs. motor skill learning), as well as van Gorp et al.'s (1999) use of topographically and structurally different tasks (i.e., procedural and declarative learning tasks) to probe the two discrete learning systems. Participants in the study of van Gorp et al. (1999) also reported abstinence from alcohol for the 6 months prior to testing, whereas the participants in the current study reported current light alcohol use, and it is unknown how comparable the cocaine users from the two studies were in terms of self-reported amount and frequency of cocaine used, since these variables were quantified differently in the two studies.

Unexpectedly, no differences were seen between cocaine users and controls in the current study on the Weather Prediction task, a measure of probabilistic category learning. Previous studies have found that Parkinson's patients performed worse than healthy controls on the Weather Prediction task (Knowlton et al., 1996; Shohamy et al., 2004), and that in healthy participants, performance early in this task was associated with fMRI activation in the medial-temporal lobe, whereas performance later in the task was associated with activation in the basal ganglia (Poldrack et al., 1999). Based on these findings and the Acquired Equivalence task results from the current study, it would have been predicted that the cocaine users would have performed less well on the Weather Prediction task overall than controls, with group differences most apparent in the later stages of task performance. However, the groups performed equivalently, indicating that performance on the Acquired Equivalence and Weather Prediction tasks is dissociated in long-term cocaine users. This finding, along with the specific nature of the cocaine users' performance impairment on the Acquired Equivalence task, further underscores important differences in the S–R learning abilities of Parkinson's patients and long-term cocaine users. As such, the

nature of S–R learning in cocaine users and its neural substrates requires further clarification.

The cocaine users' difficulty in learning stimulus discriminations on the Acquired Equivalence task was specifically restricted to new learning in the presence of established learning. This pattern is consistent with other laboratory studies of incremental learning in long-term cocaine users, with diverse paradigms such as go/no-go tasks (Fillmore and Rush, 2006) and non-probabilistic category learning tasks (Beatty et al., 1995), which found that established learning interfered with new learning relative to healthy controls. Collectively, these findings are consistent with the hypothesis that repeated drug-taking in the presence of negative consequences may reflect difficulties in responding to feedback in experienced users (Garavan and Stout, 2005), and suggest that this may be related to interference from established learning. It should be noted that since there were no tangible consequences for responses on these tasks in the studies cited (e.g., monetary earnings or losses for performance), nor in the current study, the degree to which performance on incremental learning tasks in these studies modeled the naturalistic behavior of cocaine users is unclear. However, cocaine users' performance on these types of tasks may provide insight into the cognitive functions that are related to repeated cocaine-taking.

There are several limitations to the current study. Since this was an outpatient study, the amount and proximity of most recent cocaine and other drug use could only be estimated by self-report. However, all of the cocaine-dependent participants tested positive for cocaine on urine toxicology tests on the day of cognitive testing, corroborating participants' report that, on average, cocaine had been most recently used about 2 days prior to testing. It has been noted that the performance of cocaine users on the Iowa Gambling task (Bechara et al., 1994), another choice task requiring incremental learning, may improve with increasing abstinence (Bartzokis et al., 2000). Thus, the current results are best seen as an indication of S–R learning abilities in active, not abstinent, cocaine users. Additionally, our exclusive use of a non-drug using control group did not allow us to account for the performance effects of marijuana and alcohol use, substances that were reported to be used by the cocaine-dependent group. Except for broad demographic characteristics, the study design also did not allow us to account for various premorbid factors that may have influenced performance. Therefore, the specific association between S–R learning and cocaine use remains the subject of future research.

Conflict of interest

All authors declare that they have no conflicts of interest.

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