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Memory for Drug Related Visual Stimuli in Young Adult, Cocaine Dependent Polydrug Users

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Abstract

Background and Objectives—Implicit (unconscious) and explicit (conscious) memory associations with drugs have been examined primarily using verbal cues. However, drug seeking, drug use behaviors, and relapse in chronic cocaine and other drug users are frequently triggered by viewing substance related visual cues in the environment. We thus examined implicit and explicit memory for drug picture cues to understand the relative extent to which conscious and unconscious memory facilitation of visual drug cues occurs during cocaine dependence.

Methods—Memory for drug related and neutral picture cues was assessed in 14 inpatient cocaine dependent polydrug users and a comparison group of 21 young adults with limited drug experience ($N = 35$). Participants completed picture cue exposure, free recall and recognition tasks to assess explicit memory, and a repetition priming task to assess implicit memory.

Results—Drug cues, compared to neutral cues were better explicitly recalled and implicitly primed, and especially so in the cocaine group. In contrast, neutral cues were better explicitly recognized, and especially in the control group.

Conclusion—Certain forms of explicit and implicit memory for drug cues were enhanced in cocaine users compared to controls when memory was tested a short time following cue exposure. Enhanced unconscious memory processing of drug cues in chronic cocaine users may be a behavioral manifestation of heightened drug cue salience that supports drug seeking and taking. There may be value in expanding intervention techniques to utilize cocaine users' implicit memory system.

INTRODUCTION

Neurobiological models of addiction posit that both explicit (conscious; effortful) and implicit (unconscious; automatic) memory processes play a crucial role in the escalation and persistence of drug abuse.^{1–3} Drug use behaviors can be initiated by purposefully activating explicit memories of previous drug use, or alternatively they can be enabled by particular stimulus configurations in the environment (i.e., stimulus bound) and initiated implicitly in the presence of triggering stimuli without conscious memory of the trigger. During the past

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Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

decade, addiction research has increasingly focused on the role that implicit cognitive processes play in supporting substance use.⁴ Implicit cognition involves automatic processes that can be unrecognized precipitants of many real-life behaviors including substance use.⁵

A promising approach that has been used to assess automatic processing of alcohol and drug related stimuli is the study of implicit memory associations. According to Stacy,⁶ individuals differ in the strength of their associations between outcomes (e.g., relaxation) and behaviors (e.g., substance use) in their memory. For example, in individuals with strong associations between alcohol and an outcome such as relaxation, alcohol use spontaneously comes to mind when the related outcome is used as a prompt. Such implicit memory associations predict alcohol and drug use in college students.⁶ Only a handful of studies have examined implicit memory associations in cocaine users.^{7–10} Szalay and colleagues⁹ used a free association task wherein participants were asked to write associations in response to a given word (e.g., cocaine). They found that college student cocaine users associated cocaine words with positive experiences and feelings, and were more familiar with cocaine names, methods, and effects than college students who did not use cocaine. Wiers et al.¹⁰ examined implicit cocaine-related memory associations in a group of cocaine dependent poly-substance users and control subjects by using word stimuli in an implicit association test (IAT). Cocaine users scored higher on explicit arousal and lower on explicit sedation compared to controls. Furthermore, unlike control subjects, cocaine users demonstrated strong implicit associations between cocaine and positive valence related words and between cocaine and sedation related words, relative to the contrast category of “sports.” In general, past studies suggest that cocaine users, compared to non-cocaine using controls, implicitly and explicitly associated cocaine related verbal information with unique experiential states that were largely positive in nature.

The present study was designed to examine both implicit and explicit memory for drug related (cocaine, club drug, and marijuana) visual cues, compared to neutral visual cues in cocaine dependent polydrug users in treatment and similarly aged young adults who had limited drug experience. The use of visual picture cues in the present study was motivated by the consistent finding that drug and alcohol use behaviors in chronic users are frequently triggered by viewing substance related cues in the environment. For example, according to Grusser et al.,¹¹ stimuli in the environment, such as an image of a favorite alcoholic drink, induces a strong craving for that drink in persons with alcohol dependence. Thus, rather than examining verbal associations of affective states with cocaine use, we directly studied how cocaine and other drug related picture cues were processed in explicit and implicit memory retrieval tasks. Comparing cocaine dependent persons with controls who infrequently used any drug will advance understanding of how frequent cocaine and polydrug use modifies memory processing of drug related visual cues, compared to the level of pictorial drug cue memory processing in controls.

Memory research using alcohol-related cues suggests that encountering stimuli that match previously encoded material relevant to drinking or drug taking (e.g., a bottle of beer, cocaine powder), contributes to an implicit spread of activation between addiction related stimuli and their respective expectancy concepts in the semantic memory network.¹² Goldman has argued that alcohol expectancy concepts (e.g., images, memories of

sensorimotor and affective experiences) are nodes in the semantic memory network and activation of particular nodes occurs in a predictable fashion once the individual encounters a stimulus cue (e.g., a beer bottle) that matches previously encoded material relevant to drinking. These activation patterns in turn influence the onset and pattern of drinking by activating affective systems in the brain.¹

The present study applied this conceptual model to implicit spread of activation in cocaine dependent poly-substance users. Memory for drug-related and neutral visual cues was tested using an implicit repetition priming task, and explicit free recall and recognition memory tasks. To our knowledge, this was the first study to examine both implicit and explicit drug related cognition in cocaine users by utilizing drug related picture cues. In line with previous research,¹⁰ our primary hypothesis was that cocaine users compared to control participants would have enhanced implicit and explicit memory for drug related picture cues. Consistent with prior research demonstrating that cocaine abusers, compared to controls, had impaired recall memory for neutral verbal stimuli,^{13,14} our secondary hypothesis was that the cocaine group would show relatively lower levels of explicit memory for neutral picture cues compared to the control group.

METHODS

Sample

Participants included 14 (three women) cocaine dependent polydrug users, and 21 (14 women) similarly aged young adults with limited drug experience. Participants were selected from those taking part in a larger study of emotion regulation and memory in individuals with different histories of drug exposure. The cocaine group was recruited from consecutive admissions to an inpatient addiction treatment facility following detoxification and acute withdrawal, who met criteria for cocaine dependence. The control group included all participants who had been recruited from sports teams of a large US state university. Inclusion criteria were English as a first language and a minimum age of 18 years of age. Exclusion criteria were a history of serious medical or psychological disorders, loss of consciousness for more than 30 min, and uncorrected hearing or vision problem.

The mean age for the cocaine and control groups was 23.6 years ($SD = 3.8$) and 19.48 years ($SD = 1.12$), respectively. All those in the cocaine group had a DSM-IV-R diagnosis of cocaine dependence confirmed by SCID,¹⁵ nine also met diagnostic criteria for marijuana dependency, four met criteria for marijuana abuse, and all but three had lifetime exposure to club drugs. Of those in the control group, one had used cocaine one or two times in the past year, four had used marijuana in the past year, and an additional six had lifetime marijuana exposure, but not in the past year. None had ever used club-drugs.

Procedures

This study was approved by the Rutgers University Institutional Review Board for the Protection of Human Subjects Involved in Research. All participants provided written informed consent, after which they completed a series of questionnaires, including use of alcohol and other drugs. Participants were then seated in a comfortable chair in front of a TV

screen in a sound-attenuated, dimly lit room to take part in a picture cue exposure phase of the study. Cardiovascular responses were recorded during this phase as a part of another study. During cue exposure, participants viewed blocks of standardized pictures that either were neutral, negative or positive in emotional valence,¹⁶ or alcohol-, polydrug (cocaine and club drugs), or marijuana-related.^{17–19} Based on the IAPS norms¹⁶, the mean $\pm$ SD ratings for the neutral, positive and negative picture cues were 2.99 ± 0.49 , 5.92 ± 0.71 and 6.38 ± 0.49 for arousal, and 4.89 ± 0.40 , 7.27 ± 0.51 , and 2.14 ± 0.46 for valence, respectively.

Each picture cue block included a set of 15 pictures, which was presented twice per block. Presentation order of pictures within sets was randomized. Presentation order of picture cue blocks was counterbalanced across participants. Cues were presented at a frequency of 0.1 Hz (5 s on and 5 s off) with a 30 s inter-block interval. During the 5-s inter-stimulus (off) interval, participants provided liking and arousal ratings of the pictures (Self-Assessment Manikin¹⁶). Memory testing started approximately 10 min after picture cue exposure. The free recall task was always completed first, followed by the recognition memory and implicit repetition priming tasks which were presented in a counterbalanced order. Repetition priming is not contaminated by prior free recall of the same stimulus cues.²⁰ In this study, we only utilized the neutral, and drug picture cues that included the polydrug and marijuana-related picture cues.

Free Recall Task—Participants were given 10 min to verbally recall as many picture cues as possible seen during the exposure phase. In order to be identified as correct, all of the recalled content information had to be accurate and the picture had to be identifiable based on the description.^{21,22} The total number of pictures correctly recalled was calculated for the neutral picture cue block and the drug cue blocks, averaged across the polydrug and marijuana cues.

Recognition Memory Task—Participants viewed 120 picture cues (60 of the presented pictures and 60 new pictures from the same six categories) presented in six blocks. Each block contained 10 previously shown and 10 new pictures from a particular category. Within each block, each picture was presented for 10 s in a random order. Participants pressed mouse buttons to indicate whether or not they had viewed the picture during the exposure phase. Mean accuracy and error rates for the polydrug, marijuana and neutral picture cue blocks were calculated for each participant. Accuracy rates included hit and correct rejection rates. Error rates included false positive and miss response rates. False positives were the number of new picture cues that the participant mistakenly recognized as seen in the exposure phase. Misses were the number of pictures from the exposure phase that the participant failed to recognize. Hit and false positive rates were calculated for each picture category. A signal detection measure of recognition sensitivity (d') was derived from these ratings.²³ Recognition sensitivity is defined as participants' ability to correctly identify an old item as seen during the exposure phase and correctly identify a new item as new. The overall d' value for the drug category was the average of the d' values for the polydrug and marijuana picture cue categories.

Repetition Priming Task—Repetition priming is unconscious facilitation in processing (e.g., a reduction in reaction time [RT]) of previously viewed items compared to non-viewed

items.²⁴ Participants gave picture/non-picture decisions for 360 items presented for 10 s each in random order. These included the 90 studied pictures from the six categories, 90 non-viewed pictures from the same categories, and 180 non-pictures. Non-pictures were created by electronically distorting category-matched pictures that were not used in the experiment. Participants were asked to indicate their picture/non-picture decisions as quickly as possible without many errors by making one of two keyboard responses. Any RT > 3000 ms and incorrect responses were excluded from analysis. Response errors were 3.92%. The amount of priming for the neutral, polydrug and marijuana picture cue blocks was calculated by subtracting the mean RT to previously viewed pictures from the mean RT to non-viewed pictures.²⁵ The amount of priming for drug pictures was the average of the polydrug and marijuana picture cue blocks.

Data Analyses

Three repeated measures analysis of variance (ANOVA) were conducted to examine the effects of cue type (two within-subjects repeated measures: neutral and drug), group (two between-subject conditions: cocaine and control), and their interaction on free recall, recognition, and repetition priming performance. Whether memory for the two picture cue categories was different across the two groups was tested by the within-subject-by-between-subject interaction terms.

RESULTS

A comparison of the mean arousal and liking ratings in response to drug and neutral cues during the exposure phase showed that cocaine and control participants rated neutral cues similarly, however the cocaine group reported they liked the drug cues more and found them more arousing (Table 1).

The repeated measures ANOVA of recall data showed a significant main effect of cue type and group (see Figure 1). Drug picture cues were better recalled than neutral cues; the cocaine group had enhanced recall compared to the control group. There was a trend for an interaction between cue type and group. As can be seen in Figure 1, there was little difference between the two groups' recall of neutral cues ($p = .43$), but the cocaine group showed enhanced recall for drug cues, $t(33) = 2.88$, $p < .01$.

The repeated measures ANOVA of recognition sensitivity showed a significant main effect of cue type, and a trend for group differences (see Figure 2). The mean d' was higher for neutral compared to drug picture cues. Compared to the cocaine group, the control group showed a trend for enhanced recognition sensitivity. The interaction between cue type and group was significant. As illustrated in Figure 2, there was no significant difference between the groups' recognition sensitivity to drug cues, but the control group showed enhanced recognition sensitivity to neutral cues.

The repeated measures ANOVA of amount of repetition priming (see Figure 3) revealed a significant main effect of cue type. The amount of repetition priming of drug-related cues was greater than that of neutral cues. There was no significant group difference. The interaction between cue type and group was significant. There was no difference in amount

of priming for neutral cues between groups, but an enhanced amount of priming for drug cues in the cocaine group.

DISCUSSION

Although chronic verbal memory deficits are often found in cocaine users,²⁶ little is known about memory for picture cues in this population. This is an important question because visual cues in the environment can initiate drug craving and relapse.^{11,27} Further, few experimental paradigms have been used to probe the operation of different types of memory processing of such cues. Examining how picture cues are processed unintentionally is especially important as neurobiological models of addiction have suggested a crucial role of implicit memory processes in supporting substance use,¹⁻³ and drug related cues in the environment appear to induce drug seeking behavior in chronic drug users.^{11,27} To our knowledge, this preliminary study was the first to use picture cues to examine both implicit and explicit drug related cognition in young adults who were cocaine dependent polydrug users, compared to a similarly aged group with limited lifetime exposure to drugs. Consistent with previous studies demonstrating that cocaine users associate cocaine with positive experiences and feelings⁷⁻⁹, the cocaine dependent polydrug users in the current study rated the drug related visual information as more likable than the controls. The cocaine group also found the drug cues more arousing, as Wiers et al.¹⁰ observed for cocaine words. The results of the present study suggest that exposure to drug related visual cues tends to selectively enhance certain forms of implicit and explicit memory for those cues in young adults in treatment for cocaine and other substance use disorders, compared to those with little or no drug taking experience.

Implicit memory processing was facilitated by the drug cues compared to the neutral cues, and the cocaine dependent group showed significantly more memory priming by drug cues than the control group; the cocaine dependent participants showed more than twice the facilitation in processing drug-related cues compared to controls (Figure 3). This study of implicit memory for pictures extends the previous finding that chronic cocaine users had enhanced implicit verbal memory for drug related information.⁷⁻¹⁰ Previous studies have examined implicit cognition in marijuana users by using a picture association task wherein participants had to generate a very first word response to a marijuana picture cue and found that associative memory responses were strongly related to drug use.²⁸⁻³⁰ The present study extends evidence for drug-related memory facilitation in drug users to include another form of implicit memory that has to do with enhanced implicit drug-related memory processing.

Although the concept of implicit cognition is often described generically, it in fact refers to multiple descriptive constructs, and the tasks used to assess implicit information processing vary in characteristics that are dimensional, such as the presence or absence of deliberation and conscious reflection.^{31,32} Within this context, results of past studies, together with those of the present study, provide evidence for implicit cognitive processing in chronic drug users that is distinctive, fast, and positively biased towards verbal and picture drug stimuli across varying extents of participant reflection on the content of the cue. The free association tasks used by Ames et al.,^{28,29} Stacy,³⁰ Szalay et al.,⁷⁻⁹ demonstrated unique drug related implicit cognition when a first word was generated in response to a given word (e.g.,

cocaine)⁷⁻⁹ or drug picture.²⁸⁻³⁰ The IAT as used by Wiers et al¹⁰ involved assessing associations between cocaine, affect, arousal and sedation (e.g., cocaine-pleasant).¹⁰ To varying extents, these tasks required the participant to think about the drug. The repetition priming task used in the present study required participants to make picture/non-picture decisions based on whether the picture contained a “real” (natural appearing) picture or whether it contained distorted forms that would not be encountered in real life, and thus made little demand on participants to think about the drug, per se. This continuum of findings suggests that unique and enhanced properties of implicit processing of drug related information in chronic drug users appear to generalize across a range of implicit processing constructs and tasks. In the present study, we examined facilitated processing of drug cues involving perceptually based repetition or identity priming, that is, the same visual stimulus was used as both prime and target. Research on implicit drug-related cognition can be extended in the future by using an implicit semantic priming paradigm³³ to determine whether processing facilitation extends to the semantic memory network, that is, the conceptual relationship between different drug-related visual cues.

Support for the hypotheses that the cocaine group would have poorer explicit memory for neutral visual cues and better explicit memory for drug cues compared to the control group was mixed. Statistical significance testing suggested that cocaine dependent polysubstance users had better recall across all picture cue categories compared to young adults with limited drug experience. Yet, the medium effect size (but not significant) interaction suggested that this primarily was due to the cocaine group’s enhanced recall of drug cues (Figure 1). This result provides tentative support for the prediction of enhanced explicit free recall memory for drug related picture cues in the cocaine group. The absence of decreased recall performance for the neutral visual cues in the cocaine group may have been related to the picture superiority effect³⁴ in which pictures are better recalled than words due to deep encoding during learning.³⁵⁻³⁷ Thus, it is possible that deep encoding of pictures worked against the likelihood that the cocaine group would show impaired recall for the neutral picture cues, in contrast to verbal memory deficits that have been found in substance abusing individuals compared to controls.^{13,14}

Nonetheless, the cocaine group did not demonstrate the picture superiority effect benefit in the recognition memory task for the neutral cues. In fact, they showed impaired recognition sensitivity for the neutral cues compared to controls. Thus, it is possible that deep encoding of pictures benefited the cocaine group only in a context that required substantial retrieval effort (i.e., the free recall task) compared to a task that required less retrieval effort as in recognition memory. The group by cue interaction effect on recognition memory further showed no significant difference between the groups in terms of explicit recognition sensitivity for drug related picture cues. As can be seen in Figure 2, recognition of drug cues in this study was difficult for both groups. Although not anticipated, we speculate that this may have been due to a potentially higher degree of similarity between “previously viewed” and “new” drug related picture cues, compared to neutral picture cues. That is, IAPS neutral picture cues were drawn from an unrestricted number of categories, while drug related picture cues were by definition related to marijuana, cocaine, and club drugs. Thus, while we attempted to match drug and IAPS cues on a number of dimensions such as complexity

and whether a person appeared in the picture, future research utilizing picture cues should also match the number of categories from which cues are drawn.

Thus, the results of this study should be interpreted within the context of its limitations. As just noted, this paradigm may not have provided a strong test of the hypothesis of superior recognition memory for drug related visual cues in the cocaine group because it was too challenging. In addition, the modestly sized sample did not have sufficient power to demonstrate statistical significance of the medium effect size interaction observed between picture cue type and group in the recall task. We further acknowledge that there was a substantial difference in the distribution of gender between the two groups (21% women in cocaine users, 67% in controls). Future studies would benefit from being sufficiently powered to examine sex differences and interaction effects in memory processing of drug cues in different populations.

CONCLUSION

We found that certain forms of explicit and implicit memory for drug cues were enhanced in cocaine dependent young adults compared to controls when the memory was tested a short time after cue exposure. These findings suggest that drug use may be facilitated through memory processes that occur both consciously and outside of conscious awareness in chronic cocaine and polydrug users. Enhanced unconscious memory processing of drug cues in chronic cocaine users may be a behavioral manifestation of heightened drug cue salience that supports drug seeking and taking. There may be value in studying a broader array of implicit memory processes and exploring the value of manipulating implicit memory processing of visual cues in drug use prevention and intervention programs.

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Figure 1.

This histogram shows mean performance from the repeated measures ANOVA of the effects of picture cue type and group on participants' verbal free recall of the pictures shown during the exposure phase. The cocaine group had significantly enhanced recall compared to the control group, $F(1, 33) = 4.94, p < .05$, partial $\eta^2 = .13$. Drug picture cues were significantly better recalled than neutral cues, $F(1, 33) = 12.20, p = .001$, partial $\eta^2 = .27$. There was a trend for an interaction between cue type and group, $F(1, 33) = 3.05, p < .10$ (partial $\eta^2 = .09$; power = .40). While the two groups were similar in their recall of neutral cues ($p = .43$), the cocaine group showed enhanced recall for drug cues, $t(33) = 2.88, p < .01$.

Figure 2.

This histogram shows mean performance from the repeated measures ANOVA of the effects of picture cue type and group on participants' recognition memory task when they were asked to report whether or not they had viewed the picture during the exposure phase. Recognition sensitivity (d') was significantly higher for neutral compared to drug picture cues, $F(1, 33) = 14.91, p = .00$, partial $\eta^2 = .31$. Compared to the cocaine group, the control group showed a trend for enhanced recognition sensitivity, $F(1, 33) = 3.23, p < .10$, partial $\eta^2 = .09$. The interaction between cue type and group was significant, $F(1, 33) = 8.94, p < .01$, partial $\eta^2 = .21$. The two groups did not differ in recognition sensitivity to drug cues ($p = .56$), but the control group showed enhanced recognition sensitivity to neutral cues, $t(33) = 2.70, p < .05$.

Figure 3.

This histogram shows mean performance from the repeated measures ANOVA of the effects of picture cue type and group on participants' amount of repetition priming. In the repetition priming task, participants made picture/non-picture decisions. The amount of priming represents facilitation of reaction time to cues they had previously seen compared to cues they had not previously seen. Repetition priming of drug-related cues was significantly greater than that of neutral cues, $F(1, 33) = 9.27, p < .01$, partial $\eta^2 = .22$. There was no significant main effect of group, $F(1, 33) = 0.30, p = .59$. The interaction between cue type and group was significant, $F(1, 33) = 4.47, p < .05$, partial $\eta^2 = .12$. The difference between groups in amount of priming for neutral cues was not significant ($p = .45$), but there was a significantly greater amount of drug cue priming in the cocaine group compared to the control group, $t(33) = 2.14, p = .04$.

Table 1

Mean arousal and liking ratings of drug and neutral cues made by cocaine and control participants

	Cocaine (n=14)	Control (n=21)	<i>t</i> statistics (df=33)
Drug Cues			
Arousal	4.65 (2.00)	2.75 (1.41)	3.30*
Liking	5.31 (1.61)	3.92 (0.95)	3.24*
Neutral Cues			
Arousal	2.10 (0.93)	2.42 (0.99)	-0.94
Liking	4.45 (1.08)	4.93 (0.43)	-1.86

Notes. Numbers in parentheses indicate standard deviations

* $p < .01$.