

Enhanced Choice for Viewing Cocaine Pictures in Cocaine Addiction

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Background: Individuals with cocaine use disorder (CUD) chose cocaine over nondrug rewards. In two newly designed laboratory tasks with pictures, we document this modified choice outside of a cocaine administration paradigm.

Methods: Choice for viewing cocaine, pleasant, unpleasant, or neutral pictures—under explicit contingencies (choice made between two fully visible side-by-side images) and under more implicit contingencies (selections made between pictures hidden under flipped-over cards)—was examined in 20 CUD and 20 matched healthy control subjects. Subjects also provided self-reported ratings of each picture's pleasantness and arousal.

Results: Under both contingencies, CUD subjects chose to view more cocaine pictures than control subjects, group differences that were not fully explained by the self-reported picture ratings. Furthermore, whereas CUD subjects' choice for viewing cocaine pictures exceeded choice for viewing unpleasant pictures (but did not exceed choice for viewing pleasant pictures, in contrast to their self-reported ratings), healthy control subjects avoided viewing cocaine pictures as frequently as, or even more than, unpleasant pictures. Finally, CUD subjects with the most cocaine viewing selections, even when directly compared with selections of the pleasant pictures, also reported the most frequent recent cocaine use.

Conclusions: Enhanced drug-related choice in cocaine addiction can be demonstrated even for nonpharmacologic (pictorial) stimuli. This choice, which is modulated by alternative stimuli, partly transcends self-reports (possibly indicative of a disconnect in cocaine addiction between self-reports and objective behavior) to provide an objective marker of addiction severity. Neuroimaging studies are needed to establish the neural underpinnings of such enhanced cocaine-related choice.

Key Words: Choice behavior, cocaine addiction, craving, IAPS pictures reward, neuropsychology, salience, unconscious motivation

Cocaine-addicted individuals pursue cocaine and cocaine-related stimuli over nondrug-related goals (1). The underlying mechanism may involve reduced striatal dopamine D2 receptor availability (2–5) and altered function in dopaminergically innervated corticolimbic areas that mediate processing of reward salience (6–8), such as the orbitofrontal cortex (9–11). In support of this suggested neurobiological mechanism, research in drug-addicted individuals has indeed demonstrated reduced activation of corticolimbic brain areas when viewing erotic compared with cocaine stimuli (12), as well as a unique pattern of neurocognitive changes including attentional bias toward drug-related stimuli (13–16).

This altered valuation of rewards in drug addiction is especially evident in studies that juxtapose choice for drug against choice for competing reinforcers. For example, previously drug-exposed animals choose cocaine over novelty (17), adequate maternal behavior (18), and even food (19–21). Parallel human studies similarly show that drug-addicted individuals routinely choose cocaine over money (22–24).

A neuropsychological task using pictures could provide an

opportunity for similarly testing choice for drug-related compared with competing stimuli outside of an acute drug administration paradigm, therefore suitable for use even when direct drug administration is not feasible or ethical (e.g., in abstaining or treatment-seeking drug-addicted individuals). Following the perspective that drug-related stimuli become increasingly “wanted” in drug addiction (25), drug-related choice in drug addiction should extend to such nonpharmacologic drug-related reinforcers (stimuli that increase behavior). Because drug-related choice may not be fully accessible to conscious awareness (26), as indeed supported by a disconnect between subjective and objective markers of behavior in drug addiction (11,27,28), such behavioral choice may not be fully captured with self-reported ratings.

In this study, we report on two newly developed choice tasks that used four types of pictures (cocaine, pleasant, unpleasant, and neutral) to probe choice behavior for nonpharmacologic stimuli in drug addiction. Subjects also provided self-reported ratings of each picture's pleasantness and arousal. The following hypotheses guided our study: 1) overall choice for cocaine picture viewing will be higher for individuals with cocaine use disorders (CUD) than for healthy control subjects; 2) these group differences in cocaine picture choice will not be fully explained by the self-reported ratings; and 3) within the CUD group, heightened choice for drug-related stimuli, especially when compared with choice for other positively valued stimuli (i.e., pleasant pictures), will relate to indexes of cocaine addiction severity.

Methods and Materials

Subjects

Subjects were recruited through advertisements in local newspapers, word of mouth, and local treatment facilities (see demographics in Table 1). Subjects met the following criteria, as

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Table 1. Demographic Characteristics and Drug Use by Study Subjects

	Cocaine Subjects (n = 20)	Control Subjects (n = 20)
Sex (Male/Female)	19/1	17/3
Ethnicity (African American/Caucasian/Other)	11/4/5	9/10/1
History of Cigarette Smoking (Current or Past/ Never) ^a	18/2	4/16
Daily frequency of smoking (for current users; n = 16)	5.6 ± 5.3	10.0 ± .0
Hours since last cigarette (for current users; n = 16)	11.6 ± 15.1	3.0 ± .0
Education (Years)	12.6 ± 1.4	13.6 ± 1.9
Age (Years)	45.1 ± 9.3	42.4 ± 5.3
Socioeconomic Status (51)	29.3 ± 11.1	31.7 ± 10.7
Nonverbal Intellectual Functioning: Wechsler Abbreviated Scale of Intelligence: MATRIX Reasoning Scaled Score (52)	10.3 ± 5.1	11.3 ± 2.5
Self-Reported State Depression (53) ^b	7.9 ± 6.9	1.7 ± 2.9
Age at Onset of Cocaine Use (Years)	27.7 ± 5.8	—
Duration of Use (Years)	15.5 ± 7.5	—
Frequency of Use (Days/Week): Past 30 Days	3.0 ± 2.9	—
Current Use in \$ per Use (Min–Max, Median): Past 30 Days	0–60, 25	—
Duration of Current Abstinence (Days) (Min–Max, Median)	0–1825, 5	—
Total Score on the Cocaine Selective Severity Assessment Scale (Measure of Withdrawal Symptoms) (Range: 0–126) (54)	15.4 ± 7.7	—
Severity of Dependence Scale (Range: 0–15) (55)	6.3 ± 4.2	—
Cocaine Craving Questionnaire (Range: 0–45) (56)	14.5 ± 2.7	—

Note: Numbers are M ± SD. Subjects were matched on sex, age, intellectual functioning, education, and socioeconomic status.

^a $\chi^2 = 19.8, p < .001$.

^bMann–Whitney (U) $Z = -3.4, p < .01$.

ensured by initial screening by telephone and subsequent on-site medical and neurological evaluation: 1) absence of head trauma with loss of consciousness, 2) absence of current neurological or medical disease that required hospitalization or regular monitoring (subjects were free of any medications), and 3) except for cocaine in the CUD, negative urine screens for all other drugs or their metabolites. Of an initial pool that included 23 CUD and 22 control subjects, this study used 20 CUD and 20 matched healthy control subjects (see Table 1 for matched demographic variables). Subjects were right-handed native English speakers.

On the basis of a comprehensive diagnostic interview (see Supplement 1 online for a complete listing of interview components), all CUD met DSM-IV criteria for current cocaine dependence ($n = 18$) or cocaine dependence in full sustained remission ($n = 2$). Among those meeting current dependence criteria, urine screen results confirmed the presence of cocaine in nine CUD subjects (the other CUD subjects were in active treatment in which cocaine use is prohibited [$n = 6$] or had not used cocaine within 72 hours of the study [$n = 3$]). Urine screens for all other drugs were negative (the control subjects tested negative for all drugs, including cocaine; see Table 1 for drug use variables in all CUD subjects). Comorbid diagnoses within CUD included current marijuana abuse ($n = 1$), alcohol use disorder in full sustained remission ($n = 7$), and major depression disorder (current $n = 1$; in full sustained remission $n = 1$). Given the high degree of lifetime overlap between cocaine addiction and de-

pression, especially among those seeking treatment (29), we retained subjects with comorbid major depression, which increases generalizability of our findings. Nevertheless, we accounted for the possibility that comorbid depression could account for our findings as explained below (see also Supplement 1 online). Subjects received full information about the research and provided written consent in accordance with the local institutional review board.

Stimuli

Both tasks used 90 pictures selected from the International Affective Picture System (IAPS) (30); of these, 30 depicted pleasant scenes (e.g., smiling faces, nude images), 30 depicted neutral scenes (e.g., neutral faces, household objects), and 30 depicted unpleasant scenes (e.g., sad faces, violent images). Additionally, we created a fourth picture category that included 30 images of cocaine and individuals preparing, using, or simulating use of cocaine (e.g., snorting or smoking), collected from freely available online sources and adapted (as still images) from a cocaine video used previously in our laboratory (31). Cocaine pictures were matched to the IAPS pictures on size and ratio of human to nonhuman content.

Picture Ratings

Before completing the two choice tasks, subjects underwent recordings of event-related potentials while passively viewing each of these pictures for 2000 msec (these results will be reported separately). Subjects then rated each picture on pleasantness (“rate how pleasant or unpleasant you felt about this picture”) and arousal (“rate how strong of an emotional response you had to this picture”). Subjects responded using a computerized version of the Self-Assessment Manikin (SAM) (32). For these ratings, subjects chose the numbers 1 through 9 that appeared below the SAM characters (1 = *unhappy/no response manikins*; 9 = *happy/high visceral response manikins*).

Explicit Task

In the explicit choice task, subjects chose between two simultaneously presented (side-by-side) picture types (Figure 1) by continued button pressing. Image categories included the cocaine, pleasant, unpleasant, or neutral pictures described earlier or images of a blank (black) screen (inclusion of blank screens allowed for comparisons between the respective pictorial stimuli and nonstimuli). To ensure that each trial contained unique pictures, only 28 of 30 pictures from each category could be included; two pictures from each of the four picture categories were randomly excluded (the same blank screen was presented 28 times). On each trial, one picture was pseudorandomly paired with another picture from any of the other four picture categories/screens [28 pictures/screens × 5 categories = 140/2 (pictures per screen) = 70 unique trials]. The side (left vs. right) of presentation also varied pseudorandomly: each picture category appeared on each side of the screen 14 times to protect against perseverative responding (e.g., repeatedly choosing pictures from one side). Pressing the button corresponding to the image on the left enlarged this picture to fit the entire screen; pressing the button corresponding to the image on the right enlarged this picture instead (toggling between pictures was allowed). Continued button pressing allowed the chosen picture to remain on the screen for the entire trial duration of 5000 msec; upon nonresponse for 500 msec, the side-by-side images reappeared for the trial duration. We summed the number of button presses (across the 70 trials) per picture category. Scores on this task



Figure 1. Experimental paradigm for the explicit task. The explicit task included training and one block, consisting of 70 trials. Two sample trials (**A and B**) are displayed. At trial onset, two side-by-side images appeared (this default screen remained for the 5000-msec duration unless subjects executed a response). Continuous button pressing enlarged the corresponding image, as shown in both examples (A: right picture; B: left picture, both indicated by red box), for the 5000-msec trial duration; no response (for 500 msec) after initial response returned the side-by-side display. Each trial onset was preceded by a 1500-msec fixation cross to separate trials (not depicted in figure). Note: Due to concerns about maintaining novelty of IAPS images, a “pleasant” IAPS image has been replaced with a “pleasant” image from SJM’s personal collection.

therefore reflect how much subjects worked for each picture type, modeled after previous research in which healthy control subjects button pressed/worked for viewing beautiful compared with nonbeautiful faces (33).

Implicit Task

In the implicit choice task, subjects selected one of four flipped-over cards by a single button press; upon selection, the picture was uncovered to fit the entire screen and passively viewed for 2000 msec (Figure 2). Subjects could then select again from the same deck or switch to another deck. Each deck contained 30 pictures, which, unbeknownst to the subjects, were pseudorandomly sorted according to the following two constraints (except for these two constraints, pictures occurred in a completely random order within a deck): 1) there were no picture repetitions between the four decks and 2) each deck contained 26 pictures (87%) of one picture category (e.g., cocaine), two pictures (7%) of another category (e.g., pleasant), and one picture (3%) of each of the remaining two categories (e.g., unpleasant, neutral; this task did not use blank screens). Following the Iowa Gambling Task (34), these percentages were selected to reduce awareness of deck identity, while allowing for preference to be established. Similar to the Wisconsin Card Sorting Task (WCST) (35,36), a run terminated when subjects selected from a particular deck eight times. In contrast to the WCST, these eight selections could be nonconsecutive (because there were no “correct” or “incorrect” choices, imposing a rule of eight consecutive selections from a particular deck could have decreased interest in the task). Subjects completed four such runs. To further reduce awareness of deck identity and to

overcome the potential impact on results of perseverative responding (e.g., repeatedly choosing from the same deck across the runs), the dominant picture categories were pseudorandomized across the decks between runs (i.e., the deck location of the four picture categories did not repeat across the runs). Because there was no significant effect of run or interaction with diagnosis (CUD, control) [$F(3,36) < 2.2, p > .05$], we summed the total number of cards selected per picture category across the four runs.

Statistical Analyses

The explicit task used a 5 (picture type: pleasant, unpleasant, neutral, cocaine, blank) \times 2 (diagnosis: CUD, control) mixed analysis of variance (ANOVA). The implicit task used a 4 (picture type: pleasant, unpleasant, neutral, cocaine) \times 2 (diagnosis: CUD, control) mixed ANOVA. Both ANOVAs were followed by analyses of covariance (ANCOVA) with total button presses across trials (explicit task) or number of picture selections across runs (implicit task) as covariates to control for individual differences in response frequency. Two 4 (picture type: pleasant, unpleasant, neutral, cocaine) \times 2 (diagnosis: CUD, control) mixed ANOVAs examined differences in self-reported pleasantness and arousal ratings. The Greenhouse-Geisser correction was used if the assumption of sphericity was not met. Significant interactions were followed by paired (within-group) and independent (between-group) parametric *t* tests (choice task variables and self-report ratings were normally distributed). Depression and cigarette smoking status, which differed between the groups (Table 1), were covaried in subsequent ANCOVAs if these measures were significantly associated with the choice task variables or

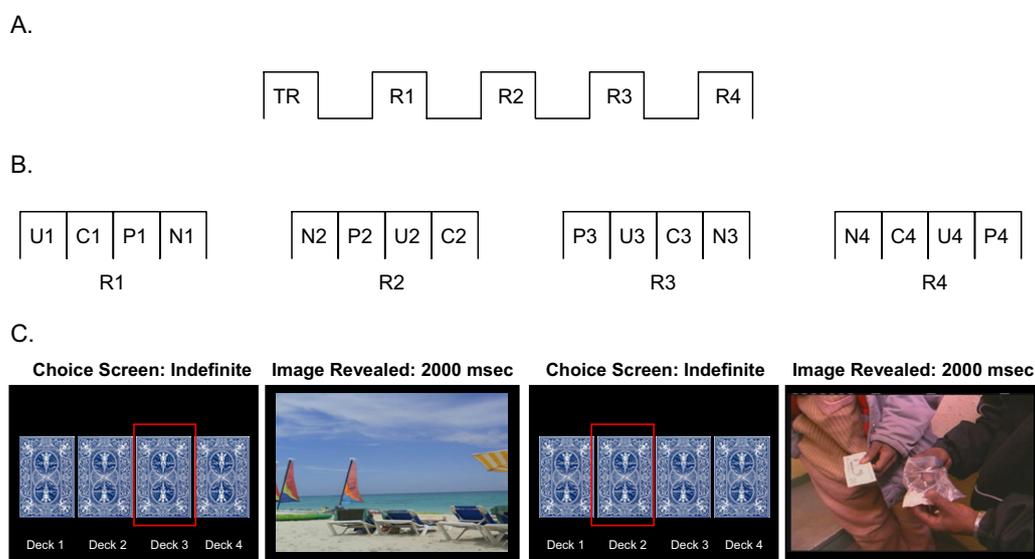


Figure 2. Experimental paradigm for the implicit task. **(A)** Overall design, consisting of training (TR) and four runs (R). **(B)** Breakdown of deck identity across the runs: each run contained four decks that comprised mostly (87%) cocaine (C), pleasant (P), unpleasant (U), or neutral (N) pictures. Deck location did not repeat across the runs. **(C)** Sample trials: in each trial within a run, subjects had to choose one of four flipped-over cards; a run terminated after eight total choices from the same deck (maximum of 29 selections). Subjects pressed one of four buttons corresponding to their chosen deck. After the image appeared for 2000 msec, the choice screen reappeared, and subjects made another selection. Here in two sample trials, decks 3 and 2 are selected, respectively, indicated by the red box. The choice screen remained until a selection was made. Note: Due to concerns about maintaining novelty of IAPS images, a “pleasant” IAPS image has been replaced with a “pleasant” image from SJM’s personal collection.

self-report ratings (37). Associations with depression (which was not normally distributed) were examined with nonparametric Spearman correlations. The dichotomous smoking status was inspected with independent *t* tests. In all ANOVAs and follow-up comparisons, $p < .05$ was considered significant.

To establish between-task reliability, we performed between-task partial correlations (r); in these analyses, we controlled for the total number of button presses/selections. To establish validity of our tasks, we performed partial correlations between the two cocaine choice scores and 1) self-report picture ratings and 2) drug use variables listed in Table 1. Spearman correlations were used for drug use variables (which were not normally distributed). In all correlational analyses, $p < .01$ was considered significant to protect against Type I error (after satisfying this initial criterion, we retained significant correlations if they achieved a significance level of $p < .05$ when accounting for depression or smoking, if necessary).

Results

Picture Ratings

Pleasantness. Results of the mixed ANOVA revealed main effects of picture type [pleasant > neutral > cocaine > unpleasant; $F(1,9,68.7) = 83.4, p < .001$] and diagnosis [CUD > control; $F(1,37) = 20.6, p < .001$]. An interaction between picture type and diagnosis showed that picture type ratings differed as a function of drug addiction [$F(1,9,68.7) = 8.6, p < .01$] (Figure 3A). This interaction was explained by the CUD group’s higher ratings of pleasant pictures [$t(37) = 2.1, p < .05$] and especially higher ratings of cocaine pictures [$t(30.7) = 4.2, p < .001$], but no differences between the groups in ratings of unpleasant or neutral pictures [$t(37) < 1.7, p > .09$]. Interestingly, CUD provided higher ratings for pleasant pictures than cocaine pictures [$t(19) = 2.9, p < .01$], consistent with the picture type main effect. CUD subjects also provided higher ratings for cocaine

pictures than for unpleasant pictures [$t(19) = 5.1, p < .001$] but not neutral pictures [$t(19) = .5, p > .6$]. In contrast, healthy control subjects provided higher ratings for neutral than cocaine pictures [$t(19) = 7.3, p < .001$], but their ratings for cocaine and unpleasant pictures did not differ [$t(18) = .4, p > .6$]. The picture type \times diagnosis interaction remained significant after accounting for depression but not for cigarette smoking history ($p > .2$); this was not unexpected based on the almost parallel distribution between the study groups with cigarette smoking history. In support of this idea, entering as covariates number of cigarettes currently smoked or time since last cigarette did not attenuate this interaction ($p < .001$).

Arousal. Results of the mixed ANOVA revealed main effects of picture type [pleasant > all other categories; $F(2,0,74.9) = 7.3, p < .01$] and diagnosis [CUD > control; $F(1,37) = 8.3, p < .01$]. The interaction was also significant [$F(2,0,74.9) = 4.0, p < .05$; Figure 3B], driven by the CUD group’s higher arousal ratings only for the cocaine pictures [$t(37) = 3.4, p < .01$]; other group differences were not significant [$t(37) < 2.0, p > .06$]. Further, CUD provided arousal ratings that were higher for cocaine than unpleasant pictures [$t(19) = 2.1, p < .05$], whereas this pattern was reversed in healthy control subjects who rated cocaine pictures as less arousing than unpleasant pictures [$t(18) = 3.7, p < .01$]. The interaction again remained significant when controlling for depression but not cigarette smoking history. However, the interaction remained significant when entering as covariates number of cigarettes currently smoked or time since last cigarette ($p < .05$).

Explicit Task

Results of the mixed two-way ANOVA revealed a main effect of picture type (pleasant > all other picture categories), indicating more button presses for pleasant pictures in all subjects [$F(2,9,111.0) = 20.1, p < .001$]. There was no main effect of diagnosis [$F(1,38) = .0, p > .9$]. Importantly, the picture type \times

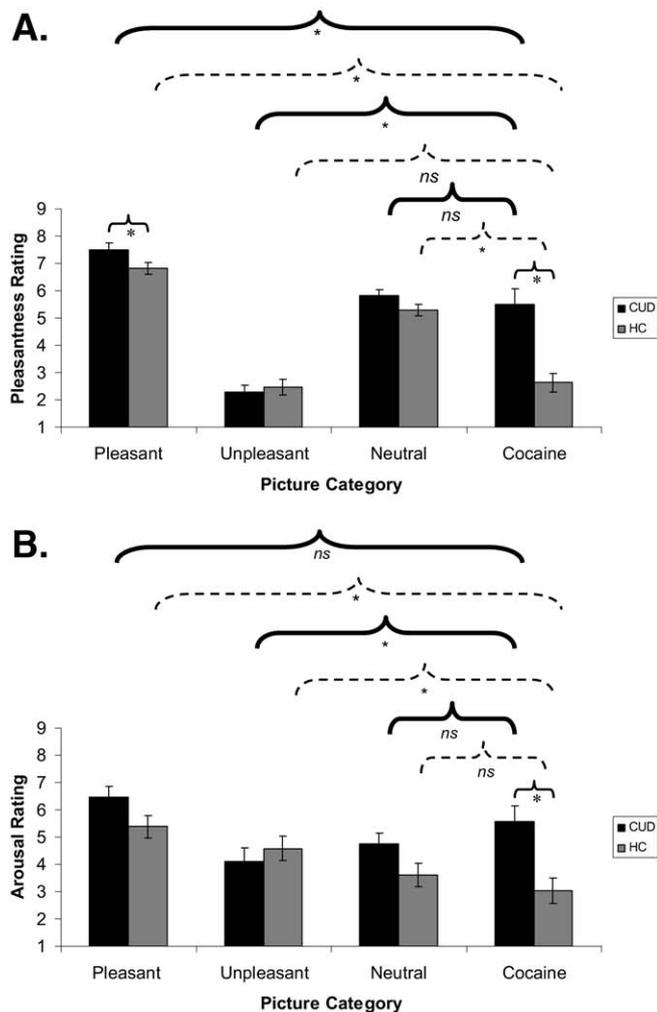


Figure 3. Results of the picture ratings for (A) pleasantness and (B) arousal for each of the four picture types (pleasant, unpleasant, neutral, and cocaine) for individuals with cocaine use disorders (CUD; $n = 20$), compared with healthy comparison subjects (HC; $n = 19$; one control subject did not complete picture ratings because of keypad malfunction). For both (A) and (B), error bars represent standard error of the mean. Between-group comparisons are indicated by light, solid lines; within-group comparisons for CUD are indicated by heavy, solid lines; and within-group comparisons for HC are indicated by broken lines; $*p < .05$; all comparisons shown directly pertain to our a priori hypotheses. Table 1 in Supplement 1 presents all significant comparisons (including comparisons not displayed in Figure 3), as well as means and standard errors for both picture ratings.

diagnosis interaction reached significance [$F(2.9,111.0) = 6.4, p < .01$; Figure 4A], driven by group differences in button pressing for the cocaine pictures [CUD > control; $t(21.1) = 2.9, p < .01$]. Further, CUD button pressed more for cocaine pictures than for unpleasant and blank pictures [$t(19) > 2.2, p < .05$]; a similar trend was observed for neutral pictures [$t(19) = 1.4, p > .1$] but not for pleasant pictures [$t(19) = -1.8, p > .08$]. This pattern was reversed in the healthy control subjects, who button pressed for cocaine pictures significantly less than for all other picture categories [$t(19) > 3.2, p < .01$] except for unpleasant pictures [$t(19) = .7, p > .4$], similar to their pleasantness ratings. This interaction remained significant after accounting for depression and total button presses ($p < .01$) but became attenuated with smoking history as a covariate ($p > .1$). Nevertheless, covarying for cigarettes smoked per day and time since last cigarette did not

attenuate this interaction ($p < .01$), again indicating that the effect of cigarette smoking history may be attributable to its correspondence with diagnosis.

Implicit Task

Results of the mixed two-way ANOVA similarly revealed a main effect of picture type (pleasant > all other categories), indicating increased selection of pleasant pictures in all subjects [$F(2.3,85.9) = 15.8, p < .001$] and no main effect of diagnosis [$F(1,38) = .0, p > .9$]. The picture type \times diagnosis interaction reached significance [$F(2.3,85.9) = 16.5, p < .001$; Figure 4B]. Follow-up tests indicated that this interaction was again driven

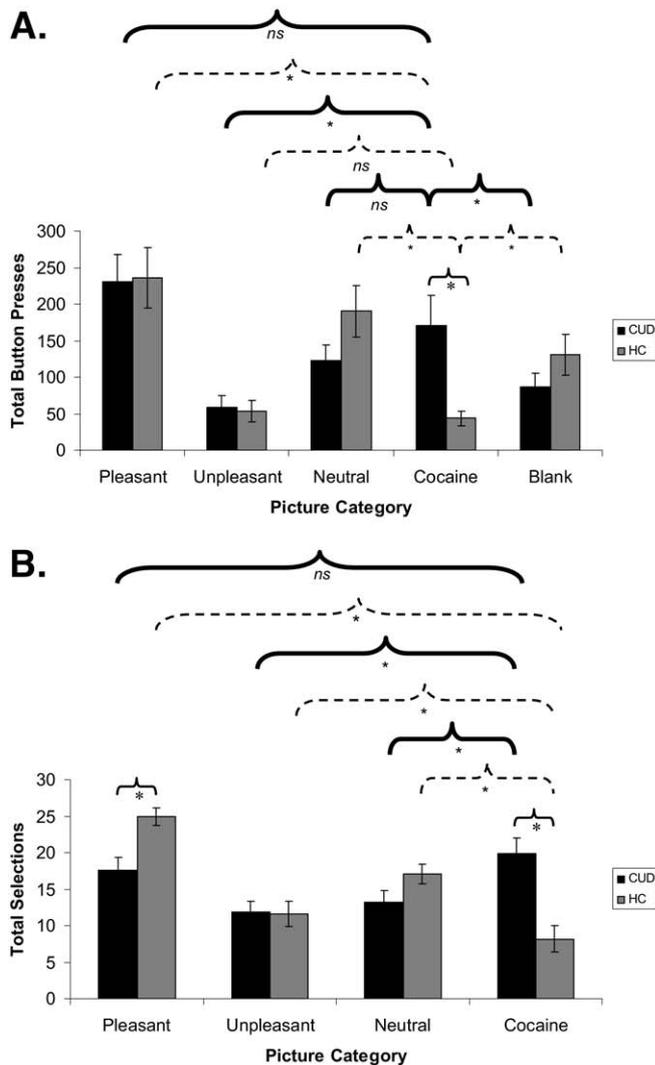


Figure 4. (A) Results of the “explicit” task, showing total button presses for each of the five picture categories (pleasant, unpleasant, neutral, cocaine, and blank) for individuals with cocaine use disorders (CUD; $n = 20$), compared with healthy comparison subjects (HC; $n = 20$). (B) Results of the “implicit” task, showing total picture selections for each of the four picture categories for the same two subject groups. For both (A) and (B), error bars represent standard error of the mean. Between-group comparisons are indicated by light, solid lines; within-group comparisons for CUD are indicated by heavy, solid lines; and within-group comparisons for HC are indicated by broken lines; $*p < .05$; all comparisons shown directly pertain to our a priori hypotheses. Table 1 in Supplement 1 presents all significant comparisons (including comparisons not displayed in Figure 4), as well as means and standard errors for both choice tasks.

by differences between the groups in selection of cocaine pictures [CUD > control; $t(38) = 4.1, p < .001$] and (unique to this implicit task) by differences between the groups in selection of positive pictures [CUD < control; $t(33.5) = 3.5, p < .01$]. This time, the enhanced selection of cocaine pictures in CUD was greater than selection of all other picture categories, reaching significance for the unpleasant [$t(19) = 3.0, p < .01$] and neutral pictures [$t(19) = 2.2, p < .05$]. Conversely, in healthy control subjects, cocaine picture selection was significantly lower than all other picture categories including unpleasant pictures [$t(19) > 3.0, p < .01$]. This interaction remained significant after controlling for all covariates ($p < .05$).

Task Intercorrelations and Correlations with Self-Reported Ratings

Correlation analyses indicated good between-task agreement for cocaine choice in CUD ($pr = .71, p < .01$). Further, in the CUD, both total cocaine button presses and total cocaine selections correlated with both cocaine picture ratings, yielding four significant correlations (cocaine button presses: $pr = .61$ and $pr = .68, p < .01$, for pleasantness and arousal ratings, respectively; cocaine selections: $pr = .74$ and $pr = .80, p < .001$, for pleasantness and arousal ratings, respectively). Together, these correlations highlight our tasks' reliability and validity in probing choice for cocaine pictures in CUD.

Given these correlations and following our second a priori hypothesis, we repeated the two-task ANOVAs using each of the self-reported ratings as a separate covariate; we also controlled for total button presses/selections as appropriate. The picture type \times diagnosis interaction was still detected when controlling for pleasantness (implicit task only: $p < .05$) and arousal (implicit task: $p < .01$; and a similar trend for the explicit task: $p < .06$), indicating that enhanced cocaine-related choice in the CUD compared with control subjects was not fully explained by these self-reports, as best demonstrated with the implicit task.

Spearman Correlations with Drug Use Variables

Total cocaine selections (implicit task) positively correlated with frequency of cocaine use in the month preceding this study ($pr = .59, p < .01$; Figure 5A). Following our third a priori hypothesis, we calculated a change score that subtracted pleasant selections from cocaine selections. This change score also correlated with frequency of cocaine use in the previous month ($pr = .62, p < .01$; Figure 5B). This latter correlation indicates that the higher the choice to view cocaine pictures over hedonically positive pictures, the more severe the current drug use. Other correlations with the drug use variables listed in Table 1 were not significant.

Discussion

In this study, we compared cocaine-addicted individuals and healthy control subjects on choice for viewing pictures of cocaine and standardized pleasant, unpleasant, and neutral pictures, exploring objective cocaine-related choice as a potential marker of addiction severity. We also tested whether choice for viewing cocaine pictures could be fully explained by self-reported ratings of pleasantness and arousal of these stimuli, exploring the novel hypothesis of compromised insight into behavior in drug addiction.

Consistent with our first a priori hypothesis, CUD subjects chose cocaine pictures more than healthy control subjects did. This finding demonstrates drug-related choice in cocaine addiction even for nonpharmacologic (pictorial) stimuli and is consis-

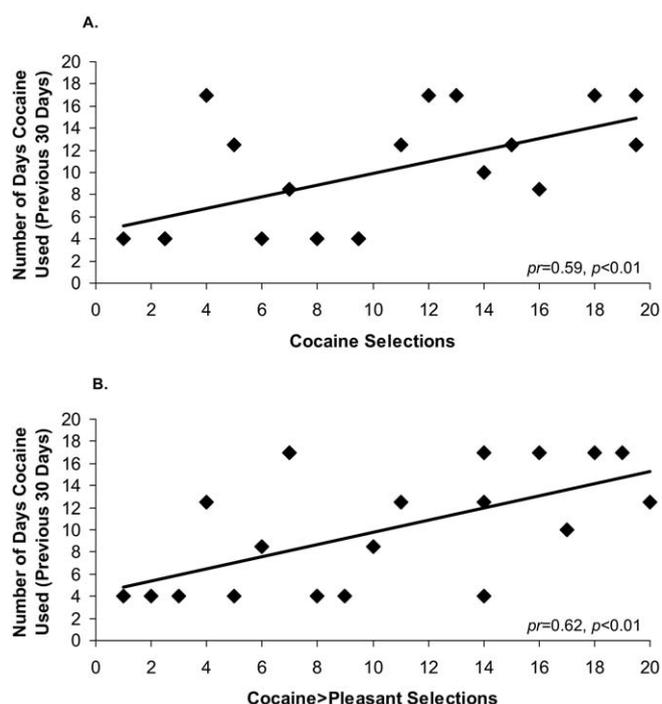


Figure 5. Scatterplots in the individuals with cocaine use disorders (CUD; $n = 20$), showing associations between cocaine selection and drug use variables on the implicit task: (A) correlations between cocaine selection and number of cocaine use days in the past 30 days and (B) cocaine > pleasant selection and number of cocaine use days in the past 30 days. Because these analyses used Spearman correlations, all scores and drug use scores are presented as ranks.

tent with research showing that cocaine-related stimuli have attention-biasing properties in CUD subjects (13–16). Other contributing factors to this choice in CUD may have included enhanced interest, affinity, motivation, salience, or familiarity with these particular drug stimuli. Nevertheless, in our study drug-related choice in CUD cannot be attributed to motor perseveration (in both tasks, location of the cocaine pictures was pseudorandomly varied) or overall increased button pressing/selection (no group main effect emerged in either task, and results remained significant in subsequent ANCOVAs that controlled for total button press/selection).

Consistent with our second a priori hypothesis, this enhanced drug-related choice in the CUD was not completely explained by their self-reported ratings. Moreover, CUD subjects' self-reported ratings were incongruent with their choice behavior, as indicated by discrepancies between picture ratings (cocaine < pleasant) and objective choice as assessed in both tasks (cocaine = pleasant). Together, such results suggest a disconnect in drug addiction between self-reports (as measures of conscious awareness) and objective markers of behavior, as possibly indicative of impaired awareness of internal drives (11,27,28) or of cognitive-behavioral performance (38,39). Such impaired awareness may potentially underlie the evasive nature of using self-reported craving to predict relapse in drug addiction (40) and highlights the potential utility of our choice tasks as objective markers of individualized clinical outcomes.

Finally, results of both tasks showed that cocaine-related choice in CUD surpassed unpleasant, but not pleasant, picture choice. These findings suggest that drug seeking in CUD (as approximated here with cocaine picture choice) may be higher

in the presence of aversive stimuli, but not in the presence of alternative pleasant stimuli, consistent with both human and animal studies (41–48). This interpretation is also consistent with the significant correlations in this study between choice for viewing cocaine pictures, even when directly compared with selections of reportedly more pleasant pictures, and frequency of actual cocaine use. Therefore, behavior on this task may be an indirect marker of actual drug-choice behavior, as remains to be tested in future studies.

Limitations of this study include the following: 1) previous viewing and rating of the same cocaine pictures may have precipitated cue-induced craving in CUD subjects (49). Counterbalancing picture ratings and picture choice tasks should be implemented in future studies. 2) Unexpectedly, healthy control subjects selected fewer cocaine than unpleasant pictures in the implicit task. A completely masked task would eliminate the possible confounding influence of socially desirable responding and other demand characteristics that may have partially driven this finding. Similarly, for CUD, the discrepancy between pleasantness ratings and task performance could have also reflected socially desirable self-reporting. 3) Habituation could have resulted from viewing the same blank screen throughout. However, control subjects pressed for these blank screens over the unpleasant or cocaine pictures, suggesting habituation did not significantly affect our results and further highlights control subjects' aversion to such pictures. 4) Our CUD group was heterogeneous because it included both active users and treatment seekers. Larger CUD samples can ascertain whether the current results differ as a function of active cocaine use (e.g., 50).

In summary, two newly developed tasks examined choice for viewing cocaine pictures compared with pleasant, unpleasant, and neutral pictures. The CUD subjects selected more, and worked more for, cocaine pictures than did healthy control subjects, results that were not fully driven by (or subject to the pitfalls of) self-report. Results also revealed that drug picture choice did not differ from pleasant picture choice but was enhanced when compared to unpleasant picture choice, possibly indicative of modulation of actual drug choice by other pleasant or aversive stimuli in drug-addicted individuals. Further studies are needed to uncover the neural substrates that underlie this drug-biased choice in CUD and whether cue-reactive states enhance such choice over pleasant stimuli (1), especially in individuals with more severe drug use. Overall, such disadvantageously enhanced drug choice could provide a marker of the neurocognitive dysfunction that characterizes drug addiction.

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