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The Subjective Effects of Cocaine: Relationship to Years of Cocaine Use and Current Age

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Abstract

Background—Little is known about whether the duration of cocaine use or an individual's age may influence the acute effects of cocaine, patterns of use, and specific treatment needs.

Objectives—This *post hoc* analysis determined whether the duration of cocaine use or current age influenced the acute subjective response to cocaine. Data from four smoked cocaine self-administration laboratory studies were combined and analyzed to determine whether the subjective effects of a 25-mg smoked cocaine dose varied as a function of years of cocaine use or current age.

Methods—Thirty-six nontreatment-seeking healthy cocaine users (ages 32–49) were admitted to studies lasting from 12 to 105 days. Participants rated the subjective effects of each cocaine dose from 0 to 100 by completing a computerized self-report visual analogue scale (VAS). The main outcome measures were the change in VAS ratings between a baseline placebo dose and the first 25-mg dose of smoked cocaine.

Results—No significant relationship was found between the subjective effects of cocaine and years of cocaine use (mean 20.9, range 5–30) or current age (mean 41.1, range 32–49).

Conclusion—Among long-term cocaine users between the ages of 32 and 49, the acute subjective effects of cocaine did not vary as a function of years of cocaine use or current age.

Scientific Significance—These data fail to support the incentive sensitization theory for addiction by Robinson and Berridge, as cocaine “liking” and “wanting” remained the same regardless of age or years of cocaine use.

Keywords

long-term use; years of use; subjective effects; smoked cocaine; human

INTRODUCTION

Evidence suggests that substance abuse, in general (1), and cocaine abuse, in particular, are becoming more prevalent in older adults (2). However, little is known about whether the duration of cocaine use or an individual's age may influence the acute effects of cocaine, patterns of use, and specific treatment needs (3). Human laboratory studies of cocaine

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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 the article.

administration can provide data on differences in subjective effects of cocaine among long-term/older and short-term/younger cocaine users. To date, limited data are available.

Some studies suggest an association between the subjective effects of cocaine and years of cocaine use or age. It has been reported that age-related decreases in levels of cocaine-induced euphoria correlate with regional brain volume reductions (4,5). In a study of intranasal cocaine self-administration, the number of episodes of cocaine use in one's lifetime was positively correlated with anxiety after cocaine administration (6). One study of intravenous cocaine administration comparing occasional cocaine users with cocaine- and opioid-dependent individuals found that long-term cocaine use was associated with tolerance to positive subjective effects, such as "high" and "euphoria" (7). In addition, greater paranoia was found in older participants (34 years old) compared with younger participants in a study of smoked cocaine (8).

However, other studies have found no association between the subjective effects of cocaine and years of cocaine use or age (9–11). Only limited evidence to support long-term tolerance to cocaine's reinforcing effects has been found in human laboratory studies (9). The duration of cocaine use did not impact ratings of "feeling high" or "desire cocaine" in one study (10), and years of cocaine use and current age did not correlate with self-rated "high" in another study (11).

To contribute empirical data to the limited literature on this topic, we conducted a *post hoc* analysis of the subjective effects of cocaine from four laboratory studies in which participants self-administered smoked cocaine. The aim of this analysis was to determine whether the acute subjective effects of a single administration of smoked cocaine (25 mg) varied as a function of years of cocaine use or current age among a sample of long-term cocaine users. Based on the limited but disparate literature, we hypothesized that the subjective effects of cocaine would decrease as years of cocaine use and current age increased.

METHODS

Screening Procedures and Measures

Nontreatment-seeking individuals (ages 32–49) who reported smoking cocaine were recruited and underwent screening to ensure that they were psychiatrically and physically healthy, as described in detail elsewhere (12). All studies were approved by the New York State Psychiatric Institute's Institutional Review Board.

Participants provided informed consent specific for the study they entered. Four published smoked cocaine self-administration laboratory studies (conducted between 2003 and 2010) (12–16) were included in this analysis. If the study involved medication administration, only data from the placebo medication condition were used for the current analysis. Participants were admitted to combined inpatient/outpatient and inpatient studies lasting from 12 to 105 days. In these studies, participants were allowed to self-administer repeated doses of smoked cocaine (0, 6, 12, 25, and/or 50 mg per dose) on multiple occasions. Maximum possible exposure to cocaine in each study ranged from 486 mg/week to 1598 mg/week. The data given herein only included the first administration of active cocaine (25 mg) within the session compared with baseline placebo administration.

After each dose of cocaine, participants rated their mood and drug-related effects from 0 to 100 using a computerized self-report visual analogue scale (VAS, 25 items). Five clusters of VAS ratings have been previously identified with factor analysis (17). Altogether, 20 of the 25 ratings were grouped into five independent clusters (16): (1) "good drug effect" consisted

of three items (high, good drug effect, stimulated); (2) “bad drug effect” consisted of seven items (bad drug effect, anxious, confused, depressed, irritable, sedated, tired); (3) “self-esteem” consisted of five items (social, self-confident, focused, alert, talkative); (4) “drug rating” consisted of three items related to the cocaine dose (drug quality, drug potency, drug liking); and (5) “calm” consisted of two items (calm, able to concentrate). One VAS rating asked about current hunger, labeled “I feel hungry”. The final three ratings were used to operationalize drug craving; these were labeled “I Want” “...Cocaine”, “...Alcohol”, and “...Tobacco.” A final question asked “How much would you pay for the dose you just received?” (range \$0–\$25).

Statistical Analysis

The main outcome measures were the change in VAS ratings between a baseline placebo dose and a 25-mg dose of smoked cocaine. Note that this 25-mg cocaine dose was the first active dose of cocaine given in the sessions included in this analysis; change from baseline when placebo was smoked was chosen to subtract out the cocaine expectancy of a placebo response and to account for any individual differences in ratings. In some studies, additional doses of cocaine were smoked in the session after the initial 25-mg dose, but the effects of these additional doses were not analyzed because the timing of their administration varied among studies. The first 25-mg cocaine dose was given noncontingently across studies, and the timing between the two sets of VAS ratings and other conditions were the same across studies. We analyzed the first 20 VAS ratings by clusters (described above) and individually analyzed the remaining five VAS ratings.

Based on our experience with dose–response relationships of smoked cocaine in the laboratory (18–22), we only analyzed the intermediate strength 25-mg dose, in order to avoid floor and ceiling effects associated with subjective responses to smaller (6 and 12 mg) and greater (50 mg) doses, respectively.

Data from 36 participants who completed the first multiple 25-mg smoked cocaine dosing sessions in each study were used. Altogether, 9 out of the 10 female participants were part of a study that included menstrual cycle measures. As the subjective effects of cocaine can vary as a function of the menstrual cycle phase (17), VAS ratings only from the follicular phase session were used for this analysis. Regarding the coding of other substance use, alcohol use was converted into standard drinks, and one tobacco cigar was coded as three cigarettes (based on the “cigarillo” type of cigar (23)).

All analyses were conducted using SPSS version 18 (Chicago, IL). For continuous variables, normality was assessed using Kolmogorov–Smirnov and Shapiro–Wilk tests. Simple regression model was used to assess whether years of cocaine use or current age predicted a difference in participants’ VAS ratings. *P*-values <.01 were considered significant for the analysis of the 20 VAS ratings by clusters and for the remaining five individual VAS ratings; a conservative *p*-value cut-off of .01 was used to correct the number of analyses being conducted. For each continuous variable and for the residuals in the simple regression model, *z*-scores were assessed for outliers; values with a *z*-score >3.29 or <−3.29 were adjusted to the next highest value. Adjusted results did not differ from original data; so, original results are presented. Correlational analyses assessed the relationship between demographics and current age, as well as years of cocaine use.

RESULTS

Table 1 presents the baseline demographics, diagnoses, and past-month substance use. Most participants were African-American males in their forties, single, unemployed, and high-

school educated. Nearly 70% of participants were diagnosed with cocaine dependence. Years of education and age were positively correlated (Pearson's $r = .34$, $p = .045$).

No significant relationship was found between any of the 25 subjective effects of cocaine and years of cocaine use or current age. As an example, Figure 1 presents regression plots for the "good drug effect" cluster as related to years of cocaine use and current age; change scores from baseline placebo are presented to depict the absence of a relationship. As another example, Figure 2 presents regression plots for "drug liking" as related to years of cocaine use and current age; actual scores after the first 25-mg smoked cocaine dose are presented to depict the absence of a relationship.

Restricting the analyses to the 26 men did not affect any outcomes; the sample of women ($n = 10$) was too small to permit statistical analyses of females alone.

DISCUSSION

There was no relationship between the acute subjective effects of cocaine and years of cocaine use or current age in this sample of long-term cocaine users. There was no increase or decrease in good or bad drug effects with increasing years of cocaine use or current age.

Although the participants in this analysis were not in a treatment setting, these data have clinical relevance. For example, because cocaine continues to result in pleasurable subjective effects as age increases, the motivation to stop cocaine use may not decrease for cocaine users as they grow older. Rather than assuming that cocaine use will remit as age increases and underdiagnosing substance abuse in older adult populations (24–29), clinical treatment providers may need to continue screening for cocaine use in cocaine users as they grow older and, if present, discuss the risk–benefit ratio of continued cocaine use in later life. In addition, as cocaine's subjective effects appear to be unaltered by age or years of cocaine use, these data suggest that increasing rates of cocaine abuse in older populations may be mediated by the same factors relevant to younger initiates to cocaine use.

These data fail to support the incentive sensitization theory for addiction by Robinson and Berridge (30), suggesting that sensitization develops to drug "wanting" but not drug "liking." In our data, cocaine "liking" and "wanting" remained the same, regardless of age or years of cocaine use. Perhaps sensitization, if it occurs in humans, is more apparent in the early initiation of cocaine use and no longer evident following years of continued cocaine abuse.

These analyses have several strengths. First, we analyzed an intermediate strength dose of cocaine to allow differentiation of either increases or decreases of subjective effects of cocaine. Second, we were able to analyze a wide range of subjective effects based on 25 VAS ratings; we combined these items into five clusters to reduce the number of multiple comparisons. Third, we used change scores as the outcome measures to subtract out the cocaine expectancy of a placebo response and to account for any individual differences in ratings.

These analyses also have limitations. First, the studies were not specifically designed to assess the aim of this *post hoc* analysis. Second, the demographics of our sample were not diverse, with respect to sex, work status, marital status, education, and race, which may have influenced the results. Third, participants used cocaine for an average of 21 years; changes in cocaine's effects may be more evident in recent initiates. Finally, because our research group does not administer cocaine to individuals over the age of 50, our findings do not address the subjective effects of a 25-mg cocaine dose for individuals older than 50.

Laboratory studies in which cocaine is administered to nontreatment-seeking research volunteers above age 50 could improve research about cocaine use in a growing population of aging cocaine users. Such studies provide valuable behavioral and performance data for understanding the neurobiology of drug abuse (31). However, caution is required in considering the administration of cocaine to aging substance abusers, given their existing greater risk for medical morbidity and mortality (32).

CONCLUSION

In this group of long-term cocaine users between the ages of 32 and 49, the acute subjective effects of cocaine did not vary as a function of years of cocaine use or current age. With appropriate safety measures, laboratory studies in which cocaine is administered to nontreatment-seeking research volunteers above age 50 may provide further insight about cocaine use in a growing population of aging cocaine users (33–36).

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FIGURE 1.

“Good drug effect” cluster (change scores): mean of changes in VAS ratings between a baseline placebo dose and the first 25-mg dose of smoked cocaine.

Note: The y-axis represents change scores from a visual analogue scale (VAS), in which participants rated a range of subjective effects from 0 to 100 mm.

FIGURE 2.

“Drug liking” (actual scores): VAS ratings after the first 25-mg dose of smoked cocaine.

Note: The y-axis represents a visual analogue scale (VAS) in which participants rated a range of subjective effects from 0 to 100 mm.

TABLE 1

Baseline demographics, diagnoses, and past-month substance use.

Age (mean years, SD) ¹	41.06 (3.57), range 32–49, <i>n</i> = 36
Education (mean years, SD)	12.69 (1.80), <i>n</i> = 36
Sex ²	
Male	26
Female	10
Race ²	
AA ³	31
Non-AA	5
Work status ²	
Unemployed	26
Employed	10
Marital status ²	
Single/never married	30
All other	6
Current axis I ^{2,4} substance diagnoses	
Cocaine dependence	25
Lifetime axis I ^{2,4} substance diagnoses	
Cocaine dependence	22
Cocaine abuse	3
Alcohol dependence	7
Alcohol abuse	7
Cannabis dependence	5
Cannabis abuse	7
Total years of cocaine use ⁵	20.86 (5.69), range 5–30, <i>n</i> = 36
Cocaine – \$/week ^{5,6}	469.02 (395.94), <i>n</i> = 33
Alcohol – No. of standard drinks/day ^{5,7}	3.28 (2.68), <i>n</i> = 20
Marijuana – \$/week ^{5,7}	24.47 (24.62), <i>n</i> = 17
Tobacco – No. of cigarettes/day ^{5,7}	9.54 (6.14), <i>n</i> = 26

¹SD, standard deviation.²Frequencies are reported.³AA, African-American.⁴Based on the Structured Clinical Interview for DSM-IV-TR Axis I disorders.⁵Raw mean (SD); past-month use.⁶*n* = 33 due to three missing data points.⁷*n*'s represent individuals currently using.