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Individual predictors of the subjective effects of intravenous cocaine

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Abstract

The subjective and reinforcing effects of addictive substances can vary greatly between individuals. This study compared the relative contributions of baseline drug use, craving, stressful life events, and social factors in determining the subjective effects of cocaine in individual participants. Twelve veterans meeting criteria for cocaine dependence were evaluated in a laboratory setting. Self-report of the subjective effects of intravenous cocaine was recorded following single- and double- blind, placebo-controlled injections. Increased positive subjective effects of cocaine, including drug-induced ‘good’ effects and the value of intravenous injections, were most strongly correlated with greater family and social dysfunction measured through the Addiction Severity Index. Social dysfunction was the strongest predictor of cocaine-induced euphoria, accounting for approximately one-half of its variability. Participants who were dissatisfied with their current marital status reported almost no ‘bad’ effects of cocaine but instead reported increased drug-induced ‘high’, euphoria, and injection value. Although further research is required to determine the generalizability of this association, our findings are parallel to recent preclinical results showing that social interaction can attenuate psychostimulant reward. Effects of substance abuse treatment that rely on improved social function may be mediated through changes in the brain’s reinforcement system that modify the rewarding effects of cocaine.

Keywords

Cocaine; Cocaine-related disorders; Intravenous injection; Marriage satisfaction; Social interaction

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1. Introduction

The subjective and reinforcing effects of addictive substances can vary greatly between individuals (Volkow and Swanson, 2003). For example, intravenous administration of cocaine in a laboratory setting causes self-report of 'high' in some healthy volunteers, but dysphoric or crying reactions in other participants who receive the same drug dose (Resnick et al., 1977). Genetic and environmental factors are believed to interact to play an important role in the etiology of substance abuse disorders (Ellenbroek et al., 2005). Stress has been implicated as an important factor in augmenting human drug use, and it can robustly enhance drug-seeking behavior in animal models (Sinha, 2008). However, there is no consensus on which behavioral characteristics in individual subjects are associated with enhanced drug reward.

For treatment of substance abuse disorders, learned and environmental influences that occur later in life may offer the greatest potential for therapeutic intervention. Drug-induced elevations in mood may motivate drug use to offset negative affect (Markou et al., 1998). Greater baseline measures of depression were associated with larger drug-induced increases in craving after smoked cocaine (Sofuoglu et al., 2000), further implicating depressed mood as a contributor to drug use. Expectancies for negative drug effects (such as feeling paranoia or 'burn out' after drug use) are associated with more positive subjective effects of cocaine (Lundahl and Lukas, 2007). This finding may be due to greater experience with cocaine, leading to exposure to higher doses and more negative consequences of drug use. Even so, a recent evaluation failed to find a relationship between years of cocaine use and self-report of liking or 'good' effects after smoked cocaine (Kalapatapu et al., 2012). This result does not support a prominent role for greater levels of dependence or sensitization of positive drug effects that are often implicated as mediators of drug liking. After intravenous injection in dependent subjects, cocaine-induced euphoria was positively correlated with frontal and temporal cortical gray matter volume (Bartzokis et al., 2004). As stimulant abuse has consistently been associated with reductions in brain volume in the cortex and prefrontal areas (Mackey and Paulus, 2013), it has been suggested that chronic drug use may be associated with lower levels of euphoria over time because of this mechanism.

Recent preclinical findings also implicate social interaction as a competing influence on psychostimulant-reinforced behavior (Fritz et al., 2011; Liu et al., 2011). In these studies, pairing with an age-matched rat attenuated cocaine-induced conditioned-place preference. Reductions in reinstatement of place preference produced by social interaction were associated with lower values of cocaine-induced FosB expression in the nucleus accumbens shell and core (El Rawas et al., 2012). Cocaine self-administration and dopamine release can be augmented by exposure to episodic defeat stress, but decreased in animals chronically housed in the vicinity of an aggressive male with a daily defeat encounter (Miczek et al., 2011).

Despite evaluation of many compounds, no medication has been shown to be effective for treatment of cocaine abuse and dependence. We have previously reported that pretreatment with the cholinesterase inhibitor donepezil was ineffective in modifying the positive subjective effects of cocaine in a group of cocaine-dependent veterans (Grasing et al., 2010). The present analysis was conducted to identify alternative factors that might explain the actions of cocaine in these participants. Our initial hypothesis was that baseline measures of stress would be predictive of the positive subjective effects of cocaine. We also assessed cocaine use (including amounts, craving, and dependence), family and social problems, work function, and marital status. In addition, we determined baseline mood, symptoms, and function in other areas.

2. Methods

2.1. Participants and Procedure

A detailed description of participants, dosing, and study measures has previously been reported (Grasing et al., 2010). Briefly, twelve male veteran volunteers meeting Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criterion for cocaine dependence participated in a laboratory-based evaluation of the subjective effects of cocaine after pretreatment with donepezil. A within-subject, placebo-controlled design was utilized. Each of three sessions was conducted using identical procedures. After pretreatment with oral placebo, an initial intravenous session was conducted under single-blind conditions. Two subsequent sessions were then completed following double-blind treatment with oral placebo or 5 mg daily of donepezil. Each session included injections of intravenous placebo, low-dose cocaine, and high-dose cocaine (0.0, 0.18 and 0.36 mg/kg).

We observed significant variability for each subject's response to cocaine administered during different sessions. This is consistent with previous research showing that the subjective responses to cocaine during different laboratory sessions are poorly correlated (Nagoshi et al., 1992). None of the primary or secondary measures differed according to session number. Regression analysis was used to evaluate data pooled from all three sessions for 12 subjects. This is justified because of the limited effects of donepezil, within-subject variability in the subjective effects of cocaine, and the absence of differences across session number. This approach allows response predictors to be identified that would otherwise be obscured.

2.2. Demographic Measures

On entry into the study, we recorded age, race, length of education, and number of children. Cocaine use was specified as the number of days used over the 30 days preceding entry into the trial, duration of use in years, and typical weekly spending in dollars for purchase of drug. Years of lifetime alcohol use and smoking were recorded, with weekly values for cigarettes smoked or standard drinks consumed. Clinical severity of drug use was estimated by recording the number of DSM-IV items that participants responded to as positive for criteria of cocaine abuse, dependence, and withdrawal. The Addiction Severity Index (ASI) was also used to rate substance abuse, alcohol use, medical, employment, legal, family/social, and psychological function. Marital status was assigned a value of 1 for participants who had never married, 2 for those who had separated after a previous marriage, and 3 for those who were currently married. Satisfaction with marital status, whether single, cohabitating, or married was recorded as a categorical response (yes or no), as part of the family-social subscale of the ASI.

2.3. Baseline Craving, Mood, and Stress

During screening, participants rated recent events for distress and life change using the Life Events Inventory (Tennant and Andrews, 1976). Otherwise, additional measures in this category were recorded immediately prior to intravenous sessions. These included the Perceived Stress Scale, which provides a rating of the degree to which recent experiences are appraised as stressful (Cohen and Williamson, 1988). The Minnesota Craving Scale was used to record the intensity, frequency, and duration of psychostimulant craving (Halikas et al., 1991). Mood and affect were assessed using the Profile of Mood States (McNair et al., 1971) and Beck Depression Inventory (Beck et al., 1996), with psychological distress evaluated with the Brief Symptom Inventory (Derogatis and Melisaratos, 1983).

2.4. Dependent Psychometric Measures

For visual analogue scales (VAS), participants used a computer mouse to position a 100 mm scroll bar marked at 0 ('not at all') to 100 ('extremely'). VAS responses were prompted by questions that asked whether 'any', 'stimulated', 'good', or 'bad' effects of the intravenous injections were experienced. Additional questions asked whether subjects experienced drug-induced 'high' or desire to use cocaine (craving).

For the Multiple Choice Questionnaire (MCQ), participants used a computer mouse to make a series of hypothetical choices between receiving a second dose of the test drug they just received or a series of monetary alternatives of increasing value (Jones et al., 1999). Participants typically choose a second hypothetical dose at lower dollar amounts, but prefer monetary alternatives for larger values. The dollar amount at which responding switched from cocaine to money is the *crossover point*, which is a valid index of the reinforcing effect of the test injection.

An additional computer module recorded responding for the Addiction Research Center Inventory (ARCI), which is based on empirically-derived prototypical measures (Martin et al., 1971). Its subscales include 1.) Psychostimulant effects, the Amphetamine (AMP) and Benzedrine (BG) Groups; 2.) Euphoria, the Morphine-Benzedrine Group (MBG), 3.) Sedation, the Pentobarbital-Chlorpromazine-Alcohol Group (PCAG), and 4.) Somatic-dysphoric effects, the lysergic acid diethylamide (LSD) scale.

2.5. Data Analysis

Statistical analyses were performed by Systat Inc. (version 12, Evanston, IL), with results presented as group means $\pm$ standard error. For VAS responding, an average of change from baseline at 3, 6, 10, and 15 minutes after intravenous injections was assessed. Additional dependent measures included results of the MCQ and ARCI questionnaires. All other variables, including determinations of mood, stress, and cocaine pharmacokinetics, were considered to be independent measures. For the primary analysis, simple linear regression was used to compare the degree to which independent variables predicted dependent measures (subjective effects of cocaine). Based on the evaluation of independent variables in 15 broad areas, with dependent measures obtained from three sessions for each participant, $p < 0.001$ was used as the criterion for the significance of regression results (0.05 divided by the product of 15 and 3).

Independent and dependent variables were also evaluated nonparametrically, using Spearman's Rho statistic. A secondary analysis evaluated whether marital satisfaction influenced dependent measures, using analysis of variance (ANOVA) with dose as an additional factor. For VAS responding which was evaluated at multiple time points, repeated measures ANOVA was performed. Post hoc comparisons were accomplished by performing separate ANOVAs using marital satisfaction as a factor, or through Bonferroni t -tests using $p < 0.017$ as a criterion for significance (0.05 divided by three sessions for each participant).

3. Results

3.1. Use of Cocaine, Cigarettes, and Alcohol

Table 1 shows baseline characteristics that were significantly correlated with different subjective effects of cocaine. Data is shown in order of increasing numbers of predicted dependent variables, with the lower rows showing items for which more than one dependent measure was correlated. Otherwise, independent measures are listed according to increasing R^2 values. In general, baseline characteristics were more strongly correlated with effects of high-dose cocaine. No significant correlations were observed for any measure of stress,

symptoms, or mood. For each of the correlations shown in Table 1, Spearman's Rho statistic indicated a significant association, at the level of $p < 0.003$.

Baseline weekly spending for cocaine was positively correlated with the PCAG subscale of the ARCI, which provides a measure of sedation, following high-dose cocaine (see Figure 1, panel A). Also for high-dose cocaine, responding on the ARCI benzedrine group subscale (a measure of psychostimulant effect), was negatively correlated with lifetime cigarette use (panel B). Lifetime alcohol use was positively correlated with the perceived value of low-dose cocaine (panel C).

3.2. Craving Intensity

We observed a wide range in the intensity of craving reported by different subjects prior to cocaine injections. Increased values for this measure were associated with greater drug-induced feelings of stimulation and 'high' recorded by VAS, following injections of low-dose cocaine (Figure 2, panels A and B, respectively). No craving measures were correlated with the subjective effects of high-dose cocaine.

3.3. Marital Status and Family-Social Problems

Self-reported marital status was a strong predictor of the positive effects of high-dose cocaine in individual participants, which included measures of injection value, stimulation, and euphoria (Figure 3). These measures increased linearly for those participants who reported either being separated or currently married, relative to participants who had never been married (panels A, C, and E), and were also positively correlated with greater dysfunction on the ASI subscale for family and social problems (panels B, D, and F). There was a trend for a positive correlation between marital status score and the ASI subscale for family and social problems which did not reach statistical significance ($p < 0.05$). No effects were observed for low-dose cocaine.

To better understand the relationship between social dysfunction and the subjective effects of cocaine, we reviewed individual responses to the ASI subscale for family and social problems. This measure is partially derived from whether respondents report being satisfied with their current marital status, whether single or married. In response to this question, four participants reported being dissatisfied with their current marital status, seven reported being satisfied, with data missing for one additional subject. Of those who were dissatisfied, two individuals reported currently being married, and two reported being separated.

Representative data for cocaine-induced euphoria, the measure for which family-social problems had the greatest predictive value, are shown in Table 2. Note the significant within-subject variability for change in euphoria, measured across three sessions. Most participants reported their marital status as being separated. Of the two subjects who reported being currently married, both were dissatisfied with their current marital status.

For cocaine-induced 'high', repeated measures ANOVA showed significant main effects of marital satisfaction [$F(1,217) = 20.5, p < 0.001$] and cocaine dose [$F(2,434) = 159, p < 0.001$], with a significant interaction between these factors [$F(2,434) = 18.7, p < 0.001$]. With the exception of craving for cocaine, similar repeated measures ANOVA results were obtained for all VAS questions, including 'bad' drug effects. Repeated measures ANOVA also showed significant interactions between satisfaction and cocaine dose for injection value and ARCI subscales for euphoria and somatic-dysphoric effects.

As shown in Figure 4, participants who were dissatisfied with their current marital status reported different effects of intravenous cocaine. Note the qualitatively different patterns for positive and negative effects of cocaine, with dissatisfaction augmenting reports of 'high'

(panels A and C) but decreasing 'bad' drug effects to values of zero at most time points (panels B and D). For the additional measures shown, dissatisfaction magnified the effects of increasing cocaine dose. These included injection value, euphoria, and somatic-dysphoric effects (panels E, F, and G, respectively).

4. Discussion

4.1. Summary of findings

We found that individual mood, stress, and symptom measures were relatively weak predictors of the subjective effects of cocaine administered in a laboratory setting. In contrast, baseline craving intensity along with drug, cigarette, and alcohol use were significant predictors of the effects of cocaine. Unexpectedly, social status measures were the strongest predictors of positive drug effects. Social and family dysfunction measured by the ASI was the best predictor, accounting for approximately one-half of the variability in cocaine-induced euphoria. Participants who were dissatisfied with their current marital status, whether separated or cohabitating, had greater cocaine-induced 'high', with diminished 'bad' effects of cocaine.

4.2. Associations with drug use, craving, and depression

Our findings show a complex interaction of multiple individual factors that modify the subjective effects of cocaine in a human laboratory setting. Increased monetary spending for cocaine by some subjects likely paralleled exposure to greater psychostimulant dose prior to participation in this protocol. Although known for its stimulant actions, we found a positive association between increased prestudy spending for cocaine and the sedating effects of high-dose cocaine (Figure 1, panel A). This seemingly paradoxical association may modify stimulant actions that could have aversive properties. For example, children of alcoholics who experience diminished subjective and physiological actions of alcohol are at increased risk for developing alcoholism (Crabbe et al., 2010). Apparently, the absence of pronounced effects leads to greater use of alcohol in these individuals. If stimulation produced by high-dose cocaine can be offset by sedating actions, this may also promote increased use by some individuals.

In agreement with a report by Kalapatapu et al. (2012) that evaluated smoked cocaine, we did not identify a relationship between years of previous use and positive drug effects after intravenous cocaine. Cocaine, tobacco, and alcohol use disorders commonly occur together (Falk et al., 2006), and enhanced release of dopamine in the nucleus accumbens underlies the reinforcing effects of all three agents (Sulzer, 2011). Accordingly, we found that individuals with greater levels of prestudy alcohol use placed a larger value on injections of low-dose cocaine (Figure 1, panel C). This correlation may reflect an enhanced sensitivity to the reinforcing effects of small doses of cocaine in individuals who chronically consume alcohol. Greater cigarette use was associated with diminished stimulant effects of cocaine (panel B). Use of either cocaine (Adinoff et al., 2010) or tobacco (Teaktong et al., 2004) can cause alterations to the brain's cholinergic system, and our results support a role for smoking in modifying cocaine-induced stimulation.

Craving can be described as an intense desire to use cocaine or other addictive substances (Rosenberg, 2009). We found that individuals with greater intensity of craving at pre-drug baseline reported increased drug-induced 'high' and stimulation after receiving low-dose cocaine (Figure 2). Increased craving predicts relapse in treatment-seeking populations (Paliwal et al., 2008). Our findings indicate that the negative effects of amplified craving on treatment prognosis could be mediated by enhanced positive and reinforcing effects of low-dose cocaine in some individuals. In contrast to earlier findings by Sofuoglu et al. (2000),

greater baseline depression as measured via the Beck Depression Inventory was not associated with larger cocaine-induced increases in craving.

4.3. Associations with social status and function

Measures of social status and function were strongly associated several positive effects of intravenous cocaine (Figure 3). Firstly, family-social dysfunction measured by the ASI was positively correlated with reported stimulation, value, and euphoria following high-dose cocaine (right-hand panels). When divided according to marital status, these measures increased linearly with ratings indicating greater long-term contact with an intimate partner (left-hand panels). This corresponded to values that were lowest for individuals who had never married, intermediate for those who had separated, and greatest for participants who reported being either married or cohabitating. Furthermore, dissatisfaction with current marital status both diminished negative effects of cocaine, and increased several positive effects. These included drug-induced 'high', injection value, and euphoria (Figure 4). Somatic effects and dysphoria also increased in individuals with marital dissatisfaction. These changes indicate that either dose of cocaine had greater effects in individuals who were not satisfied with their marital status, and are likely to produce greater reinforcement in this group.

Increased aggressive behavior has been associated with drug abuse in humans, as well acute or chronic administration of cocaine in animals (Johns et al., 2010). Drug use is frequently a source of conflict for drug-abusing patients and their intimate partners (Fals-Stewart et al., 1999). In one study, male-to-female physical aggression was nearly three-times more likely on days in which cocaine was used (Fals-Stewart et al., 2003). In contrast, marital closeness has been associated with success in avoiding relapse to drug use in treatment-seeking patients (Kosten et al., 1987).

Of those participants in the current study who reported being satisfied with their current marital status, the majority were not cohabitating with a female (5 of 7 individuals, see Table 2). Apparently, intimate partner relationships in most study participants were dominated by interpersonal conflict. If so, this would explain the positive association between previous or current marriage and positive effects of cocaine (left side of Figure 3). Rather than a source of interpersonal closeness, existing or previous marriage appeared to be associated with greater conflict. Greater conflict and dissatisfaction for married participants was associated with increased positive effects of cocaine, with diminished negative effects of cocaine.

Taken together, our findings support a model in which different reinforcers compete with cocaine. Productive work relationships, interpersonal closeness, and sexual intimacy are alternative behaviors to drug use. Importantly, a pattern of failure in these behaviors is correlated with perception of cocaine in a manner that allows it to be more reinforcing. In contrast, greater success with alternative social reinforcers may decrease vulnerability to drug abuse by attenuating the reinforcing actions of cocaine. We speculate that social dysfunction and interpersonal conflict in a home or work setting enhance psychostimulant reinforcement. This may occur because repeated drug use serves as a surrogate or alternative to meaningful social contact, and involves different neurocircuitry. In contrast, positive social interaction in a non-drug setting has an opposite effect, decreasing drug reinforcement as alternative neural pathways are emphasized. As noted above, drug use can be associated with conflict between intimate partners. If so, drug-use and social dysfunction may facilitate each other, resulting in a positive-feedback loop that can produce a downward clinical course for some individuals. An alternative interpretation is that social dysfunction and enhanced positive drug effects are premorbid characteristics that preceded exposure to cocaine.

4.4. Study strengths and limitations

Strengths of the present study include use of a within-subject, blinded, placebo-controlled design, with detailed methods to characterize effects of cocaine. An important limitation is the modest number of participants evaluated. Given that no married participant endorsed positive marital satisfaction, veterans included in this study are not representative of the general population. Nonetheless, our findings are consistent with preclinical findings showing that social interaction made in the absence of drug can attenuate psychostimulant reward. For example, social contact can prevent cocaine-induced conditioned-place preference in rats (Fritz et al., 2011). In prairie voles, which are socially monogamous rodents that form long-term pair bonds after mating, amphetamine-induced conditioned-place preference occurs in sexually-naïve but not pair-bonded males (Liu et al., 2011).

4.5. Implications for treatment and future research

Although many studies have implicated the presence of strong social bonds in decreasing vulnerability to drug abuse (Kosten et al., 1987; Caspers et al., 2005), the underlying mechanisms are poorly understood. Our findings show that intravenous cocaine differs in its positive and negative effects in dependent individuals with different levels of social function. In human cocaine addicts studied after a period of prolonged abstinence, striatal dopamine release is diminished (Volkow et al., 1997). Suckling stimulation in lactating dams and cocaine exposure in virgin females activates the dopamine reward system (Ferris et al., 2005). In contrast, this study showed that lactating dams exposed to cocaine instead of pups showed a suppression of brain activity in the reward system. Pair-bonding experience in prairie voles decreases psychostimulant reward through a D₁ dopamine receptor mediated mechanism (Liu et al., 2011). Future studies should characterize dopamine release in human addicts, with attention to D₁ receptor function and social status.

In summary, social function was a strong predictor of the subjective effects of cocaine in dependent individuals. When divided according to satisfaction with current marital status, dissatisfied individuals reported almost no 'bad' effects of cocaine with increased 'high', euphoria, and injection value. To our knowledge this the first report that the subjective effects of cocaine differ according to social factors in humans. Although further research is required to determine the generalizability of these effects in humans, our findings are parallel to recent preclinical results showing that social interaction can attenuate psychostimulant reward. Steps to improve social and occupational function are often components of treatment for substance abuse disorders. It remains to be determined whether improving function in these areas can diminish the reinforcing properties of cocaine.

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Figure 1.

Baseline individual characteristics that were correlated with a single subjective effect of cocaine. These measures correspond to the first three rows of Table 1. Characteristics recorded prior to intravenous injections of cocaine are shown on the horizontal axes, with dependent measures of cocaine effects plotted on vertical axes. For each of 12 participants, values are shown for cocaine delivered at three different times, at either low or high doses. Dashed lines show the results of simple linear regression, with statistical significance and R values shown in Table 1.

Figure 2.

Subjective effects of cocaine which were correlated with baseline measures of craving intensity, prior to intravenous injections (rows 4 and 5 of Table 1). Data presentation is similar to Figure 1.

Figure 3.

Marital status and family-social problems were correlated with the positive subjective effects of intravenous cocaine (the final rows of Table 1). All participants described themselves as either currently married, separated, or never having been married. Data presentation is again similar to Figure 1.

Figure 4.

Satisfaction with current marital status determines the subjective effects of cocaine. Left-hand graphs show VAS responding for 'high' (panels A and C) and 'bad' drug effects (B and D), with low and high doses of cocaine shown in the lower and upper panels, respectively. A single determination of marital satisfaction was made for each subject during administration of the ASI at the screening phase of the study, as each participant was being enrolled. For each subject, dependent measures (i.e. VAS responding) were included from three different sessions in which intravenous cocaine was administered. * indicates significant differences between participants who responded as either satisfied or dissatisfied with their current marital status, with one, two, or three symbols corresponding to $p < 0.01$, $p < 0.001$, and $p < 0.00001$, respectively.

Table 1

Baseline measures for which linear regression showed significant correlations with the subjective effects of cocaine. L and H indicate low and high doses of cocaine, 0.18 and 0.36 mg/kg per injection, respectively. Stimulant effects are shown for responding by VAS, the ARCI Benzedrine Group (BG), or the ARCI Amphetamine Group (AMP). Sedation and euphoria were measured through the PCAG and MBG groups of the ARCI, respectively. Somatic and dysphoric effects indicate responding for the LSD Group of the ARCI. Injection value was measured by the MCQ. Otherwise, results are shown for different VAS measures.

Independent	Dependent	Dose	R	R ²
Cocaine Spending	Sedation (PCAG)	H	+0.533	0.284 *
Lifetime Cigarette Use	Stimulated (BG)	H	-0.568	0.323 *
Lifetime Alcohol Use	Cocaine Value	L	+0.587	0.344 *
Craving, Intensity	Stimulated (VAS)	L	+0.551	0.303 *
	'High'	L	+0.551	0.304 *
Marital Status (never married, separated, or married / cohabitating)	Somatic / Dysphoria (LSD)	H	+0.528	0.279 *
	Cocaine Value	H	+0.544	0.296 *
	Stimulated (AMP)	H	+0.574	0.330 *
	Euphoria (MBG)	L	+0.649	0.421 **
	Euphoria (MBG)	H	+0.740	0.548 ***
ASI, Family and Social Function	Cocaine Value	H	+0.544	0.282 *
	Stimulated (VAS)	H	+0.537	0.288 *
	Good (VAS)	H	+0.575	0.331 *
	Stimulated (AMP)	H	+0.613	0.375 **
	Euphoria (MBG)	H	+0.691	0.477 ***

* indicates significance of correlation, with one, two, and three symbols indicating $p < 0.001$, $p < 0.0001$, and $p < 0.00001$, respectively.

Table 2

Measures of euphoria in individual participants, for which family-social problems had the greatest predictive value. Values are the same as those graphed in panel E of Figure 3, and were obtained during three different sessions in conducted in each subject. Data is listed in order of increasing ASI family-social score (greater values indicate increased problems). Change in euphoria after 0.36 mg/kg of cocaine was measured by the ARCI, based on comparison with a previous saline injection administered during the same session. Prior to receiving cocaine injections, participants indicated their marital status and whether they were currently living with a female (cohabitating). Satisfaction with current marital status (single, separated, or currently married) was recorded as a yes-no response, with data for one subject not available (NA).

Subject	Family-Social Problems	Marital Status	Cohabitating	Marital Satisfaction	Change in Euphoria, Session Number			
					1	2	3	4
001	0.000	Never Married	No	Yes	3	0	0	-4
010	0.000	Never Married	No	Yes	-11	-18	-6	-6
003	0.000	Separated	No	Yes	-3	0	4	4
006	0.000	Separated	No	Yes	11	10	7	7
009	0.000	Separated	No	Yes	0	0	0	0
012	0.063	Never Married	Yes	Yes	4	-3	-3	-3
002	0.088	Separated	No	NA	5	12	7	7
007	0.200	Separated	No	No	18	25	19	19
008	0.200	Separated	No	No	2	-3	-6	-6
011	0.200	Currently Married	Yes	No	22	27	18	18
004	0.629	Separated	Yes	Yes	28	14	18	18
005	0.833	Currently Married	Yes	No	28	29	20	20