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Self-Reports of Interoceptive Responses During Stress and Drug Cue-Related Experiences in Cocaine- and Alcohol-Dependent Individuals

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Abstract

Cocaine dependence is associated with neuroadaptations in stress and reward pathways that could alter stress and drug-related experiences and associated interoceptive sensations and result in enhanced craving states. Subjective interoceptive emotional and physiological responses experienced in stressful and drug cue situations were examined in abstinent cocaine-dependent individuals. Fifty-six treatment engaged cocaine-dependent patients with comorbid alcohol abuse or dependence were interviewed to identify personal stressful, drug cue, and neutral situations using a scene construction questionnaire (SCQ) that includes an emotional and physiological response checklist. Using this checklist, subjects identified emotional and bodily sensations that they recently experienced in the stress- and drug-related scenarios. Kappa coefficients indicated fair to moderate but significant degree of concordance in heart ($p < .01$), perspiration ($p < .05$), stomach ($p < .05$), and blood flow ($p < .01$) sensations for both stress and drug cue scenarios, while the McNemar change test indicated differential endorsement of interoceptive responses in stress and drug cue situations for breathing ($p < .05$), stomach ($p < .05$), tension ($p < .05$), and chest ($p < .05$) sensations, and for sad ($p < .01$), anger ($p < .01$), and excitement ($p < .01$) responses. Increased heartbeat and tension, tears, and anger urges were most commonly endorsed in the stress scenarios (between 50% and 79%), whereas butterflies in stomach, increased heartbeat and tension, jittery, restless, and warm excitement (53%–73%) were the most frequently endorsed sensations in the drug cue-related experiences. These self-reported sensations comprise both general arousal and specific interoceptive responses pertaining to stress or drug cue-related experiences in cocaine dependence, with potential value in guiding treatments targeting craving reduction.

Keywords

cocaine dependence; stress and drug cues; interoceptive responses; drug craving

Chronic cocaine abuse is associated with increased anxiety, irritability, restlessness, and drug craving during early cocaine withdrawal and abstinence and altered emotional, autonomic, and biophysiological responses to stress and drug cue exposure (Fox et al., 2008;

Sinha, 2007; Sinha et al., 2003). This increased stress- and cue-related reactivity is also associated with increased relapse susceptibility and treatment retention in substance abuse (Back et al., 2009; Daughters et al., 2009; Sinha, 2007; Sinha et al., 2006). To date, however, the potential effects of stress-related alterations on the experience of interoceptive bodily sensations in cocaine dependence have not been investigated. Interoceptive sensations provide a sense of the physiological condition of the body (Craig, 2003) and are thought to represent internal signals initially generated within the autonomic and homeostatic centers of the body and subsequently processed subjectively within the emotional limbic and cortical systems of the brain (Craig, 2002).

These “bodily” feelings may be related to homeostatic changes in temperature, pain, visceral sensations, hunger, and thirst (Craig, 2004) and could be significant markers of treatment outcome in substance abusers for several reasons. First, growing evidence documents chronic cocaine abuse related dysregulation of emotional, autonomic, Hypothalamic-pituitary-adrenal axis (HPA), and neural systems in response to stress and cue exposure in both laboratory animals and humans (Mantsch et al., 2008; Sinha et al., 2003). Of note, this dysfunctional response to stress and cue may reflect allostatic changes in hedonic set-point (Koob & le Moal, 2009) associated with increased cocaine craving, and risk of dependence in humans (Back et al., 2006; Fox et al., 2008; Sinha et al., 2006; Sinha et al., 2003) and cocaine self-administration in laboratory animals (Ahmed, Kenny, Koob & Markou, 2002; Ahmed & Koob, 1998; Wheeler et al., 2008). Because studies have shown that such allostatic and somatic changes are often accompanied by self-reported internal cues, including bodily sensations, thoughts, memories, and positive or negative mood states (Sinha et al., 2003), subjective measures of internal bodily state could provide sensitive indices of altered stress and cue-related experiences in addictions.

Second, markers of internal “bodily” states may additionally help discriminate between emotional and autonomic response to stress exposure compared with cue exposure. For example, prior research has shown that while both healthy and cocaine-dependent women respond to stress exposure with increased sadness and anxiety compared with men (Chaplin et al., 2008; Earle et al., 1999), males demonstrate a significantly greater cardiovascular and HPA sensitivity to cue compared with women (Fox et al., 2008). Similarly, in alcohol-dependent individuals, although response to both stress and cue results in increased negative emotions such as sadness and anger, emotional dissociations have also been documented. While stress exposure has been associated with an increase in blood pressure and craving, cue exposure is predominantly related to a more appetitive state characterized by increased cortisol, anxiety, fear, and craving (Fox et al., 2007). Most important to note, studies have shown that the major categories of emotions such as sadness, fear, anger, and joy show a differential pattern of neural, cardiovascular, and hemodynamic changes (Montoya et al., 2005; Prkachin et al., 1999; Phan et al., 2004; Sinha, Lovallo, & Parsons, 1992).

Because both emotional similarities and differences have been observed in response to laboratory-induced stress and cue exposure across emotional, autonomic, and biophysiological domains, such findings raise the question of whether self-reports of changes in internal state reflect these similarities and differences in substance abusers. If so, they may represent sensitive and discriminative markers of stress- and cue-related arousal that may be available to target in development of new treatments aimed to decrease stress and cue reactivity associated with chronic substance abuse. The present study therefore aims to examine substance dependent individuals’ self-reports of interoceptive sensations endorsed while describing stressful and drug cue related situations, to assess similarities (concordance) and differences in the interoceptive sensations during stress- and drug cue-related experiences. We hypothesize that some sensations will reflect general arousal and be

reported equally in stress and drug cue scenarios while other discriminatory sensations will be reported either during stress or drug cue scenarios.

Method

Participants

Fifty-six recently abstinent, treatment-seeking cocaine dependent participants with comorbid alcohol abuse or dependence, aged 21–50, were recruited from advertisements placed in area newspapers and flyers placed in community locations. Current cocaine dependence and comorbid alcohol abuse or dependence was ascertained using the Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)* (SCID-I; First, Spitzer, Gibbon, & Williams, 1995), as well as documented cocaine-positive urine screen at the time of enrollment. Subjects were excluded if they met criteria for dependence on any other substance, excluding nicotine and alcohol. As such, all participants were seeking treatment for cocaine dependence and identified cocaine as their primary drug of choice. Exclusion criteria included any psychotic disorder, mental retardation, medication for medical or psychiatric problems, and need for alcohol detoxification. Upon admission to the unit, all subjects completed a physical examination, including electrocardiography and laboratory tests of renal, hepatic, pancreatic, hematopoietic, and thyroid functions to ensure that subjects were in good physical health. Following a complete description of the study, written informed consent was obtained and the study was approved by the Human Investigation Committee of the Yale University School of Medicine.

Procedure

After screening and interviewing for study eligibility, participants were admitted for a 3-week inpatient stay on the Clinical Neuroscience Research Unit (CNRU) at the Connecticut Mental Health Center. The CNRU is a locked inpatient treatment and research unit with no access to alcohol or drugs and limited and monitored access to visitors. Urine and breathalyzer testing was also conducted every 3 days to ensure drug abstinence. During the inpatient stay, subjects participated in standard relapse prevention drug counseling and study sessions for completion of assessments/interviews. All study procedures were conducted following 2 weeks of inpatient treatment to account for the influence of acute withdrawal symptomatology on interoceptive state.

Measurement of Interoceptive Sensations

In the second week of the inpatient stay, subjects participated in a script development interview session, during which recent stressful and drug cue-related experiences were elicited using a scene development questionnaire (SCQ; Miller et al., 1987) and further adapted for our studies (Sinha, 2001b; Sinha et al., 1992). All scripts were subsequently used as part of a larger laboratory based study to assess the biophysiological mechanisms underlying the stress- and cue-related craving state in cocaine-dependent individuals (Sinha et al., 2003). The SCQ was developed by Lang and his colleagues to elicit specific emotion and anxiety situations that were used to generate scripts for guided imagery in laboratory experiments (Cook, Melamed, Cuthbert, McNeil, & Lang, 1988; McNeil, Vrana, Melamed, Cuthbert, & Lang, 1993; Miller et al., 1987; Lang et al., 1998; Lang et al., 2006). This scene development procedure has been successfully used in our group's previous work on emotions, stress, and drug-related situations (Sinha et al., 1992; Sinha & Parsons, 1996; 2003; see description in Sinha, 2009). Using the SCQ, the subject identified a recent stressful experience from the past year that was experienced as "most stressful." Subjects were also asked to rate the subjective distress experienced in the situation being described on a 10-point Likert scale, anchored at "1 = *not at all stressful*" and "10 = *the most stress*

they have felt recently in their life.” Only situations rated as 8 or above were accepted for further description. Stress was specifically defined for subjects as, “situations that made you sad, mad or upset and in which, at that moment, you felt as if you could not do much to change it.” Commonly identified stressful situations included conflicts with significant others, child custody issues, being evicted, and being fired. Stressful situations relating to drug use, such as being arrested for drug possession, were not allowed. In addition, stressful situations identified as traumatic and involving reexperiencing of trauma related anxiety symptoms were excluded.

A drug-related experience was also developed by having subjects identify a recent situation that included explicit drug-related cues and increased anticipation or craving for cocaine and led to subsequent cocaine use. Examples of drug-related situations described by subjects are having extra money available, special occasions, running into dealers or friends who use, or receiving a paycheck. Drug-related situations that are associated with negative affect or psychological distress were not accepted. In eliciting drug cue-related situations, the focus is on the “wanting” and anticipatory drug craving experience that resulted in drug use and not on the experience after use. Drug-related situations were defined to the subject as “a situation where you really wanted to use drugs and get high, you were around the drug and you ended up using the drug.”

Subjects verbally expressed the situations and the interviewer recorded the scene descriptions. For each situation that was described, the subject then completed the checklist of interoceptive sensations of the SCQ by selecting the specific mood and physiological bodily feelings they experienced in the situation being described. The SCQ checklist includes a list of 67 bodily sensations describing changes in heart, chest breathing, perspiration, muscle tension, stomach, anxiety/fear, sadness/depressed, anger feelings and urges, and excitement (see list on Table 2).

Statistical Analysis

To examine the similarities and differences in interoceptive responses endorsed for the stress and drug cue situations, we first assessed the number of individuals that endorsed each of the interoceptive responses on the SCQ checklist for stress and drug cue scenarios. Because a high degree of agreement could potentially occur because of a sensation not being endorsed in either condition, and our primary interest was to identify interoceptive responses specific to or common to the stress and the drug cue experiences, sensations that were endorsed by less than 10% of the subjects in each condition were eliminated from the analysis. The *kappa coefficient of agreement* was used to determine whether the concordance in frequency of sensations endorsed in the stress condition and drug cue condition was statistically greater than chance (Cohen, 1960; Landis & Koch, 1977). In addition, the nonparametric *McNemar change test* was employed to examine whether a sensation was likely to be endorsed to a greater extent under one condition compared with the other condition. The McNemar test is a function of only the cell frequencies that show disagreement (i.e., reporting the sensation for one condition but not the other); thus, it is possible for a sensation to have a significant kappa and a significant McNemar value. This would indicate that there was significant agreement between conditions, but for the subjects who endorsed the sensation in only one of the two conditions, it was significantly higher for one condition compared to the other condition.

Results

Table 1 reports the demographic and drug use characteristics of the sample. Of the 56 subjects in the study, the majority was male (68%), and the ethnic breakdown was 30% Caucasian, 54% African American, and the remaining Hispanic or other. On average,

subjects held a high school degree (mean = 12.4 years of education), had a mean age of 37 years ($SD = 6.5$), and typically were not married (21% currently married).

The mean reported years of cocaine use was 9 ($SD = 6.3$), over 50% used daily, and the average weekly cost was \$222. All participants additionally met either alcohol dependence or abuse criteria, with a mean weekly consumption of 17 drinks ($SD = 24.6$). In addition, 38% of the subjects met the criteria for lifetime marijuana dependence, and 5% met lifetime criteria for opioid dependence.

Table 2 shows the percentage of subjects who endorsed each sensation under the stress and drug cue conditions and the McNemar change test and the kappa coefficient of agreement. Of the original 67 bodily sensations listed on the SCQ, six were endorsed by less than 10% of the sample under both the stress and drug cue condition and were excluded from further analysis (not included in Table 2). These were “heart stops,” “heartbeats slower,” “pants/grasping for breath,” “physically less responsive,” “sweat oozes out,” and “eyes twitch.” The majority of remaining sensations were grouped according to physiological and emotional domains, including changes in heart rate, chest, breathing, stomach, perspiration, feelings of muscle tension, anxiety/fear, sadness/depressed, anger feelings, and urges and excitement. Four sensations did not fit with these domains and were considered separately in the “other” category. Subjects were considered to endorse a domain if they endorsed at least one of the sensations that comprised the domain.

As shown in Table 2, the domains pertaining to changes in heart ($p < .01$), sweat/perspiration ($p < .05$), stomach ($p < .05$), and anger ($p < .001$) sensations showed a significantly similar endorsement under the stress and drug cue conditions. In particular, the heart sensation of “heartbeats faster” was reported by over 50% of the subjects in both conditions. In addition, the additional sensations that were endorsed in both conditions at a significant higher agreement rate were heart races, shallow breathing, heavy feeling in stomach, tension in back, flushed face, whole body shaking, jittery, gritting teeth, blood rushes to head, feel hot all over, palms are clammy, heaviness in chest, and lump in throat.

The McNemar test was significant for the domain of breathing ($p = .02$), stomach ($p < .05$), tension ($p < .04$), sadness ($p < .001$), anger ($p < .001$), chest ($p = .025$), and excitement ($p < .001$), but only in the domains of breathing, tension, sadness/depressed, chest and excitement were there no corresponding kappa significance for agreement. These differences in domains and agreement across domains in the two conditions arise from different sensations within each domain that were more likely to be endorsed in one condition than the other. For example, butterflies and cramps in stomach (73% and 45%, respectively) were endorsed more frequently in the drug cue condition, but heavy feeling in stomach and stomach in a knot were endorsed at similar rates in both stress and drug cue conditions, although at a frequency less than 50%. Also the sensation of tension all over was endorsed similarly in both groups at over 60%, but tightness in face and tension in forehead received above 50% and more frequent endorsement in the stress condition relative to the drug cue condition. Sad and depressed sensations were highly distinct for the stress condition (82% vs. 46%), while excitement sensations was distinct in endorsement for the drug cue condition (79% vs. 39%).

Table 3 presents specific sensations that were endorsed by 50% or more subjects in both stress and drug cue conditions, and those that were endorsed by 50% or more subjects in only one of the two conditions. Increased heart rate, tension, tears, and anger urges were the most commonly endorsed sensations in the stress scenarios (between 50% and 63%), while butterflies in stomach, increased heartbeat, tension, jittery, restlessness, and warm

excitement (55%–73%) were the most frequently endorsed sensations in the drug cue-related experiences.

Discussion

This study examined self-reports of interoceptive sensations provided by cocaine-dependent individuals with co-morbid alcohol abuse/dependence during their description of specific stress and drug cue-related experiences. We hypothesized that while sensations pertaining to general arousal would be reported in both types of experiences, certain sensations would be specific to either stress- or drug cue-related experiences. The findings generally support the hypothesis and indicate that there was a fair to moderate level of concordance in interoceptive sensations endorsed in the stress- and drug-related scenarios, but there were some distinct interoceptive responses for the stress- and drug-related experiences, as well.

Similarities and agreement in interoceptive response to stress and drug cues included increases in heart responses (e.g., heartbeat faster, heart races), tension (tension in back, tension all over) sweat/perspiration (palms clammy), stomach or gastrointestinal sensations (heavy feeling in stomach), and blood flow sensations (flushed face, feeling hot all over). These sensations represent a general arousal state resulting from autonomic activation (Tsigos & Chrousos, 2002) and show high concordance with the physiological and neuroendocrine responses observed in the same individuals following exposure to their guided imagery scripts during a subsequent laboratory study (Sinha et al., 2003). Responses in that laboratory study included significantly enhanced cardiovascular output, increased Adrenocorticotrophic Hormone (ACTH), cortisol, norepinephrine, epinephrine, as well as increased craving. The consistency in the self-reported interoceptive sensations reported here and the previously reported laboratory autonomic, neuroendocrine, and subjective responses suggests that self-reports of interoceptive sensations could serve to identify biophysiological changes associated with the stress- and cue-related craving states in substance abusers (Fox et al., 2008; Sinha et al., 2006).

Because cocaine dependence has been conceptualized as a chronic stressor leading to a “shift” in hedonic set-point (Ahmed & Koob, 1998, 1999; Koob & Le Moal, 2009), it may not be surprising that some similar interoceptive sensations are identified in both the stress- and drug-cue related conditions. For example, prior studies have shown that, in cocaine-dependent and in alcohol-dependent individuals, stress and cue exposure are both associated with increases in negative affect and anxiety. Conversely, in healthy controls, cue exposure is typically a positive state, highlighting potential changes in hedonic homeostasis and motivational drive in substance abusers (Fox et al., 2008; Sinha et al., 2009). This is reflected in the current study by similar reported experiences of increased heart rate, tension, perspiration, visceral, and vagal sensations following both conditions. Other possibilities for similarities in certain subjective interoceptive sensations may be related to the fact that feelings relating to all physiological internal states within the entire body are thought to be engendered in a common homeostatic afferent system, modulated by the hypothalamus and right insula (Craig, 2003). The latter of which is documented as being involved in generating emotional awareness and subjective emotional motivation states (Craig, 2002, 2004).

Current findings also indicate that certain sensations were more frequently endorsed in the stress condition relative to the drug cue condition and vice versa. Sensations endorsed by more than 50% of the subjects included increased heartbeat, tension, tears and anger urges for the stress scenarios (between 50% and 79%), while butterflies in stomach, increased heartbeat, increased tension, feelings of being jittery and restless as well as warm excitement (53%–73%) were most commonly endorsed in the drug cue-related experiences (Table 3). While the stress scenarios include increased negative emotionality along with sensations

associated with autonomic arousal during negative emotions (Smith & Siebert, 1984), the drug-related experiences seemed to reflect a combination of both the euphoric and anxiogenic experiences induced by the acute effects of cocaine (Rademacher et al., 2000). While feelings of excitement, feel like singing, inner warm glow, warm excitement, and a sense of being more alive are consistent with cocaine-related euphoria, increased stomach sensations, tension, jittery, and restlessness, are associated with highly aroused and anxiety states. The high endorsement of these euphoric sensations in the drug cue situation, combined with the overlapping sensations reported in the stress situations, suggests an upregulated general arousal system in response to drug cue experiences that includes the primary components of the peripheral stress pathways, namely the HPA and sympathetic nervous system. This suggests that self-reports of interoceptive sensations during drug cue experiences include measures of stress arousal representative of a shift in hedonic set-point toward negative reinforcement processes. This may reflect a homeostatic dysregulation in stress and reward pathways, often observed in substanceabusing humans (Koob & Kreek, 2007) and laboratory animals (Koob, 2006; Mantsch et al., 2000, 2003). However, it is important to note that future research warrants comparisons with healthy controls to thoroughly ascertain interoceptive responses that represent potential homeostatic changes during stress and cue experiences.

Cocaine craving questionnaires, substance use treatment approaches, and research studies on craving have historically focused on cognitive aspects of craving and cognitive models of relapse prevention, including a focus on primarily external cues to drug use (i.e., people, places, and things) (Drummond, Tiffany, Glautier, & Remington, 1995; Littleton, 1995; Ooteman, Koeter, Vserheul, Schippers, & van den Brink, 2006; Szegedi, Lorch, Scheurich, Ruppe, & Hautzinger, 2000). However, the importance of targeting internal biophysiological cues in treatment, in addition to identifying external cues, has long been understood in the treatment of panic disorder (Marshall et al., 2008; Otto, Powers, & Fischmann, 2005). Similarly, current findings suggest that by extending treatment and research to target internal aspects of craving states associated with stress and drug-related stimuli, including those physiological aspects that are known to be associated with relapse, we may be able to develop treatments to increase resiliency to relapse cues. Moreover, the use of interoceptive measures to identify similarities and specificity within the craving state is particularly germane because discrepancies are commonly documented between self-report assessments of craving and biological data. As such, this information can be of value both in the development of craving questionnaires and in the establishment of treatments to target craving reduction.

The potential efficacy of using self-reports of interoceptive sensations to identify stress and cue-related responses associated with the craving state also lends support to the theory that homeostatic emotions such as craving may be experiential components of conditioned autonomic arousal responses (Gray & Critchley, 2007). In support of this, neuroimaging studies have identified the anterior insula as being an important substrate in the feedback of interoceptive sensations by playing a critical role in the representation of viscerosensory information as well as affective behavior (Craig, 2005). These studies have included lesion research where feelings of nicotine craving and urges to smoke have been associated with the interoceptive functions of the anterior insula (Naqvi et al., 2007). Of note, these studies all suggest that increased craving may be attributable to a disruption in the ability to represent and respond to interoceptive signals generated by external cues (Craig, 2002; Critchley, 2005) such as stress and drug cue experiences. Furthermore, identifying interoceptive sensations associated with the stress- and cue-related responses may potentially serve to highlight internal bodily markers, which underlie the pathology of stress-induced and cue-induced craving and addiction.

In addition, greater understanding of interoceptive responses to drug-related and stressful states may lead to pharmacological and behavioral treatments targeting regulation of physical responses or restoration of homeostasis, which may in turn break the behavioral cycle of addictive behaviors. If stress and drug cue situations evoke many similar self-reported physiological sensations, it follows that both would elicit a drug use response, and hence the high rates of relapse susceptibility associated with these situations (see Sinha, 2007, for review). This suggests that an important aspect of addiction treatment may be to break the behavioral associations between physiological sensations and habitual behaviors through treatments aimed at deconditioning or decreasing sensitivity to these interoceptive cues and enhance regulation of physiological and interoceptive responses in stressful and drug related situations. This view is consistent with recent attempts that target heightened anxiety, drug withdrawal symptoms, and negative reinforcement/negative affect reduction as a focus of addiction treatment (Tull, Schulzinger, Schmidt, Zvolensky, & Lejuez, 2007; Zvolensky et al., 2005; Zvolensky, Gonzalez, Bonn-Miller, Bernstein, & Goodwin 2008). Similarly, exposure techniques to address heightened interoceptive sensations in stress and drug cue states and biofeedback strategies to teach subjects to identify and reduce physiological symptoms of drug craving and stress could be of potential utility. Mindfulness meditation may also be a useful skill in regulation of stress and cravings and has some initial evidence indicating decreases in alcohol, marijuana, and cocaine use (Bowen et al., 2006).

This study is limited by the use of subjective reports of past physiological sensations. It is possible that subjects' memories of stressful and drug cue situations may be altered over time and the physiological symptoms experienced may differ from those reported. However, the consistency of these results with previous laboratory studies using objective physiological measurements in cocaine dependent and alcohol addicted patients, compared to healthy volunteers (Fox et al., 2007, 2008; in press; Sinha et al., 2009; 2003) suggests this to be an unlikely possibility. More importantly, the self-reported interoceptive sensations in the current study suggest that these responses may be elicited easily from patients in a clinical setting and available for manipulation in treatments to improve stress regulation and decrease associated drug cravings in addiction treatment.

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Table 1

Demographics: Characteristics of Subjects in Sample

Subject variable	Cocaine-dependent subjects (<i>N</i> = 56)
Caucasian	30%
African American	54%
Hispanic/other	16%
Age ^a	37.20 (6.46)
Male	67.90%
Years of education ^a	12.38 (1.67)
Currently married	21.40%
Days of cocaine use in past 30 ^a	16.18 (9.46)
Average amount of cocaine use per week ^a	\$222.45 (332.89)
Lifetime years of regular cocaine use ^a	9.00 (6.26)

^aValues represent means and *SDs*.

Table 2

Percentage Who Experienced the Sensations for Each Condition (n=56)

Sensations	Stress (%)	Drug (%)	Both (%)	McNemar	Kappa
Heart	91.1	80.4	76.8	3.60	.288**
Heart beats faster	78.6	64.3	55.4	3.56	.232*
Heart pounds	50.0	33.9	21.4	3.52	.179
Heart skips a beat	10.7	12.5	3.6	0.11	.217
Heart quickness	30.4	44.6	17.9	2.91	.180
Heart races	48.2	35.7	23.2	2.33	.242*
Breathing	78.6	60.7	51.8	5.00*	.186
Breaths faster	60.7	46.4	32.1	2.67	.156
Breaths slower	16.1	3.6	1.8	5.44*	.131
Gasping for air	12.5	3.6	0.0	2.78	-.059
Shallow breathing	7.1	14.3	3.6	2.00	.263*
Labored breathing	16.1	12.5	3.6	0.33	.127
Stomach	71.4	87.5	66.1	5.40*	.211*
Cramps in stomach	25.0	44.6	14.3	5.26*	.132
Stomach is in a knot	48.2	48.2	28.6	0.00	.213
Butterflies in stomach	42.9	73.2	33.9	10.70**	.096
Heavy feeling in my stomach	26.8	25.0	7.1	0.05	.023*
Tension	91.1	76.8	69.6	4.00*	-.021
Tightness in face	55.4	19.6	14.3	15.38***	.128
Feel tense all over	67.9	62.5	42.9	0.36	.020
Tension in back	28.6	17.9	10.7	2.57	.310**
Tension in arms	17.9	14.3	1.8	0.25	-.057
Flushed face	23.2	17.9	8.9	0.69	.292**
Tension in the forehead	53.6	21.4	10.7	10.80**	-.030
Head pounds	32.1	10.7	5.4	8.00**	.106
Fear/Anxious	73.2	78.6	57.1	0.43	-.021

Sensations	Stress (%)	Drug (%)	Both (%)	McNemar	Kappa
Whole body shakes	21.4	16.1	7.1	0.69	.242 *
Jittery	39.3	53.6	26.8	2.91	.226 *
Hands trembling	30.4	25.0	8.9	0.43	.067
Feel restless	37.5	53.6	23.2	3.24	.123
Sad/Depressed	82.1	46.4	41.1	15.38 ***	.112
Eyes water	39.3	7.1	3.6	14.73 ***	.038
Feelings seem dulled	14.3	8.9	1.8	0.82	.049
Feeling choked up	41.1	21.4	12.5	5.76 *	.165
Feel like crying	51.8	1.8	0.0	26.13 ***	-.036
Feeling empty, drained, hollow	46.4	3.6	3.6	24.00 ***	.082
Deep intense pain sensation	16.1	3.6	0.0	4.45 *	-.062
Hurts to be alive	25.0	0.0	0.0		
Tears come to my eyes	50.0	8.9	3.6	18.24 ***	-.036
Anger	87.5	66.1	64.3	10.29 **	.341 **
Want to smash something	55.4	1.8	1.8	30.00 ***	.029
Clenched jaw	44.6	23.2	12.5	6.00 *	.091
Grit my teeth	55.4	23.2	17.9	13.50 ***	.189 *
Clenched fist	35.7	12.5	5.4	8.05 **	.046
Eyes burn	16.1	1.8	0.0	6.40 *	-.033
Want to scream or strike someone	62.5	3.6	1.8	31.11 ***	-.015
Blood rushes to my head	28.6	16.1	10.7	3.77	.345 **
Sweat	67.9	62.5	48.2	0.47	.255 *
Sweat pours out	30.4	19.6	3.6	1.50	-.126
Feel hot all over	41.1	25.0	19.6	5.40 *	.412 **
Palms are clammy	25.0	37.5	17.9	3.27	.388 **
Feel sweaty	32.1	26.8	10.7	0.43	.101
Beads of perspiration	17.9	8.9	0.0	1.67	-.135
Chest	35.7	17.9	8.9	5.00 *	.125

Sensations	Stress (%)	Drug (%)	Both (%)	McNemar	Kappa
Sinking feeling in my chest	26.8	8.9	3.6	6.25 *	.076
Constriction in the chest	10.7	8.9	1.8	0.11	.094
Heaviness in the chest	19.6	10.7	5.4	2.27	.249 *
Excitement	39.3	78.6	32.1	16.13 ***	.046
Feel like singing	1.8	23.2	0.0	10.29 **	-.034
General sense of release	14.3	23.2	3.6	1.47	.017
Sense of lightness, buoyancy and upsurge of the body	7.1	21.4	1.8	4.57 *	.020
Sharpening of senses	3.6	17.9	1.8	6.40 *	.114
Inner warm, glowing radiant sensation	5.5	34.6	3.6	14.22 ***	.097
Lessening of tension	0.0	12.5	0.0		
Warm excitement	12.5	55.4	8.9	20.57 ***	.074
Sense of being more alive	8.9	30.4	5.4	9.00 **	.156
Want to hold time; capture the moment	7.1	25.0	0.0	5.56 *	-.125
Feel like smiling or laughing	5.4	26.8	1.8	9.00 **	.024
Other					
Nauseous	12.5	21.4	5.4	1.92	.188
Feel warm	21.4	19.6	7.1	.07	.180
Lump in my throat	26.8	21.4	10.7	0.60	.271 *
Feel strong inside	21.4	26.8	8.9	0.53	.174

* $p < .05$.

** $p < .01$.

*** $p < .001$.

Table 3

Sensations Occurring in More Than 50% of the Participants in Each or Both of the Stress (s) and Drug Cue (d) Conditions

Similar	Stress	Drug cue
Heart beats faster (s = 79%, d = 64%)	Heart pounds (s = 50%, d = 34%)	Jittery (d = 54%, s = 39%)
Feel tense all over (s = 68%, d = 63%)	Breaths faster (s = 61%, d = 46%)	Restless (d = 54%, s = 38%)
	Tightness in face (s = 55%, d = 20%)	Butterflies in stomach (d = 73%, s = 43%)
	Tension in forehead (s = 54%, d = 21%)	Warm excitement (d = 55%, s = 13%)
	Tears come to my eyes (s = 50%, d = 9%)	
	Grit teeth (s = 55%, d = 23%)	
	Want to smash something (s = 55%, d = 2%)	
	Want to scream/strike someone (s = 63%, d = 4%)	
	Feel like crying (s = 52%, d = 2%)	