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Anhedonia and Amotivation in Psychiatric Outpatients with Fully Remitted Stimulant Use Disorder

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Abstract

This study evaluated whether psychiatric outpatients with a past stimulant use disorder in full remission for ≥ 2 months (STIM+, n = 204) and those with no history of stimulant use disorder (STIM −, n = 2070) differed in the prevalence of current anhedonia and amotivation. Results showed that a significantly greater proportion of STIM+ participants reported anhedonia and amotivation than STIM− participants. The relation between stimulant use disorder history and anhedonia remained robust after controlling for other relevant clinical and demographic factors. These findings suggest that anhedonia may be a preexisting risk factor or protracted effect of stimulant misuse.

INTRODUCTION

The misuse of psychostimulant drugs—methamphetamines/amphetamines and crack/cocaine—is associated with the co-occurrence of depressive symptoms.[1–5] Characterization of the type and time course of depressive symptoms in relation to stimulant use may inform the development of more targeted treatments for stimulant use disorders. Studies suggest that dysphoria, irritability, and somatic/vegetative symptoms are common within the context of a stimulant use episode and during short-term abstinence.[1–5] These symptoms tend to resolve to subclinical levels over more extended periods of abstinence.[1–6] Other depressive symptoms, such as anhedonia (ie, inability to experience pleasure) and amotivation (ie, reduced drive to perform activities), however, may persist over longer periods of remission.[3,6] In addition, there is some evidence to suggest that anhedonia and amotivation may actually predate stimulant use.[7,8]

Relatively few studies have examined anhedonia and amotivation during extended periods of stimulant abstinence. Gawin and Kleber[3] longitudinally examined symptoms across acute and protracted abstinence phases in cocaine abusers. They found that among individuals who did not relapse, anhedonia did not resolve for one to ten weeks following cessation; however, these results were not compared to a control group of non-abusers. Kalechstein and colleagues[6]

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assessed anhedonia and amotivation using the apathy subscale of the Neuropsychiatric Inventory among cocaine-dependent subjects and non-abusing control subjects. Subjects (N = 11) in this study were abstinent from cocaine for five days and were free from other psychiatric comorbidity. They found that the cocaine-dependent subjects demonstrated elevated levels of anhedonia and amotivation compared to the control group. These effects were not accounted for by differences in overall depressive symptoms. These findings highlight the potential clinical relevance of anhedonia and amotivation in stimulant use disorders. However, it remains unclear whether these findings generalize to the greater population of stimulant abusers, who usually demonstrate considerable psychiatric comorbidity.[9,10]

In addition, it is unknown whether anhedonia and amotivation are present during continuous remission (ie, periods greater than one week). This is notable because anhedonia and amotivation may be preexisting clinical features of stimulant misuse. This notion is supported by human laboratory drug administration studies, which have found that baseline levels of anhedonia and amotivation predict the subjective "high" from acute amphetamine intoxication in nonabusers[7,8] and acute cocaine intoxication in abusers.[11,12] These findings suggest that individuals with anhedonia and amotivation are more sensitive to the reinforcing properties of stimulant drugs. As a result, these symptoms may prospectively increase the future risk of stimulant use episodes through two mechanisms:

- anhedonic/amotivated drug-naïive individuals may be more vulnerable to developing a stimulant use disorder after an initial exposure to the drug; and
- anhedonic/amotivated stimulant abusers who have quit may be more prone to a full relapse after an initial slip.

The current study sought to overcome limitations of existing studies (eg, limited generalizablity due to small sample sizes and lack of psychiatric comorbidity, brief duration of stimulant use remission) by evaluating the association between stimulant use disorders and anhedonia and amotivation in a large sample of treatment-seeking psychiatric outpatients. Using data from a pretreatment baseline psychiatric evaluation, we compared current anhedonic and amotivational symptoms in individuals with a past stimulant use disorder (STIM+; n = 204) to those with no history of stimulant use disorder (STIM−; n = 2070). STIM+ subjects were in full remission for at least two months, allowing us to evaluate whether anhedonia and amotivation are elevated during an extended period of abstinence. In addition, the current study's sample had substantial psychiatric comorbidity, suggesting enhanced generalization to the general population of stimulant abusers. We hypothesized that the prevalence of current anhedonia and amotivation would be greater in STIM+ than STIM− patients, and that these differences would not be accounted for by overall clinical severity or other diagnostic or demographic characteristics. We also hypothesized that differences between STIM+ and STIM − group would be greater for anhedonia and amotivation than current depressed mood, given that previous studies have found that negative mood generally remits after short periods of stimulant abstinence.[1–6]

METHODS

Subjects

Participants were recruited from the Rhode Island Hospital Department of Psychiatry's outpatient practice as part of the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project.[13] In an initial telephone screen, patients were invited to participate in an in-depth, face-to-face diagnostic evaluation prior to meeting with their treating clinician (psychiatrist, psychologist, or social worker). The current report is based on data from a pretreatment assessment of 2274 participants who completed the diagnostic evaluation. Based on previous studies that have found that amphetamine and cocaine abusers do not differ in

depressive symptoms[14] and can be combined into a general category,[15] we used a stimulant use disorder category to classify individuals who abused or were dependent on amphetamines, cocaine, or both substances. Two hundred and four (9.0%) patients in this sample had a past history of a stimulant use disorder in full remission for at least two months (amphetamine use disorder only, $n = 28$; cocaine use disorder only, $n = 147$; both substance use disorders, $n = 29$). That is, results from structured clinical interviews indicated that these patients did not meet any DSM-IV criteria for stimulant abuse or dependence for at least two months prior to the evaluation. No other information on the extent of substance use beyond information about DSM-IV diagnoses was collected. In addition, patients were not asked whether they received any treatment prior to or during the period of remission. Those diagnosed with stimulant use disorders that were either current or in partial remission ($n = 26$) were excluded from the sample because we were solely interested in anhedonia and amotivation occurring outside the context of a stimulant use disorder episode. The Rhode Island Hospital institutional review board approved the research protocol, and all participants provided informed written consent.

Assessment

Patients were interviewed using the Structured Clinical Interview for DSM-IV (SCID)[16] to diagnose current and past psychiatric disorders based on DSM-IV definitions. Clinical Global Impression–Severity (CGI-S)[17] ratings were also obtained for each patient by the diagnostic rater. Regardless of ratings on the depressed mood or loss of interest or pleasure criteria, all participants were administered the entire SCID Current Depressive Episode module, which rated all individual current depressive symptoms according to DSM-IV definitions. Depressed mood was considered present if participants reported depressed mood most of day, nearly every day, for at least two weeks. Additional symptoms assessing anhedonia and amotivation were rated according to the same framework used for major depressive disorder criteria in the SCID.[18] Anhedonia was considered present if participants reported markedly diminished interest or pleasure in several activities for most of the day, nearly every day, for at least two weeks. The anhedonia symptom used in the present report assesses diminished interest or pleasure in several activities, which contrasts with the DSM-IV anhedonia criteria requiring diminished interest or pleasure in all or almost all activities. The former was used because it should be a more sensitive indicator. Amotivation was considered present if participants reported a markedly diminished drive to perform usual activities, nearly every day, for at least two weeks. Interviewers explicitly distinguished amotivation from anhedonia, such that if patients initially endorsed amotivation, they were additionally queried: “I’m not talking about enjoyment in activities, but instead your drive to do them. Which things did you lose motivation to do? Was it nearly every day?”[18] Diagnostic interviewers were Ph.D.-level psychologists or college graduate research assistants who had undergone extensive training, as described elsewhere.[19]

Interrater reliability estimates for each of these symptoms were obtained for 48 subjects by multiple diagnostic raters. The reliability estimates (Kappa [K] values) for each symptom indicated excellent reliability: anhedonia ($K = .91$); amotivation ($K = .87$); and depressed mood ($K = .91$). The interrater reliability of psychiatric diagnoses in the MIDAS sample was adequate and has been reported previously.[19]

Statistical Analyses

The primary analytic approach involved comparing the STIM+ and STIM− groups on demographic characteristics (ie, gender, age, race, marital status, and education), psychiatric diagnoses (ie, lifetime history of bipolar I and II disorder, dysthymia, anxiety disorder, psychotic disorder, and lifetime or current non-stimulant use disorders and major depressive disorder), and current depressive symptoms (ie, anhedonia, amotivation, and depressed mood). ANOVA and chi-square tests were used for tests of continuous and categorical variables, respectively. Separate univariate logistic regression analyses were used to examine the relation

between stimulant use disorder history and the three depressive symptoms. These analyses were followed up with multivariate logistic regression analyses to determine whether the influence of stimulant use disorder history on each symptom remained present when controlling for other relevant factors. The control variables included demographic and diagnostic characteristics that significantly differed across groups as well as CGI-S ratings. Results from logistic regression analyses are reported in odds ratios (ORs) with 95% confidence intervals (CIs). Analyses were performed using SAS.[20] For all comparisons, statistical significance was set at $p < .05$, and all tests were two-tailed.

RESULTS

An examination of demographic and diagnostic characteristics by group indicated that those in the STIM+ group, compared to the STIM− group, were significantly younger, more likely to be male, and more likely to have a lifetime anxiety disorder, current major depressive disorder, history of non-stimulant substance use disorder, or current non-stimulant substance use disorder (see Table 1).

Logistic regression analyses examining the association between stimulant disorder history and current depressive symptoms showed the most robust effects for anhedonia, followed by amotivation and depressed mood, respectively (see unadjusted results in Table 2). Multivariate logistic regression analyses predicting depressive symptoms from stimulant use disorder history, when controlling for demographic and psychiatric characteristics with significant effects in the group comparisons described in Table 1 (ie, gender, age, history of anxiety disorder, history of non-stimulant substance use disorder, current non-stimulant substance use disorder, current major depressive episode), and current CGI-S ratings were also conducted (see adjusted results in Table 2). These analyses showed that stimulant use disorder history had a significant effect on current anhedonia and trend effect on amotivation when adjusting for the covariates. The effect on depressed mood was not significant when covariates were included the model.

Post hoc analyses using only the STIM+ subjects compared individuals with past stimulant abuse ($n = 66$, 32.4%) to individuals with past stimulant dependence ($n = 138$, 67.6%) to examine whether there were differences based on the severity of the stimulant use disorder. These analyses showed no significant differences in anhedonia ($p = .44$), amotivation ($p = .34$), or depressed mood ($p = .38$). Thus, patients with stimulant use disorder history had similar prevalence of depressive symptoms regardless of whether they met criteria for stimulant abuse or dependence.

DISCUSSION

The present study found that current anhedonia and amotivation were more prevalent in psychiatric outpatients with a fully remitted stimulant use disorder, as compared to those with no history of stimulant use disorder. The association with stimulant use disorder history was stronger for these two symptoms than it was for depressed mood. Analyses that controlled for relevant clinical and demographic characteristics showed that the association between stimulant use disorder and anhedonia remained robust. The association with amotivation remained present (OR = 1.39), but its significance was at a trend level ($p = .06$). These findings indicate that the relation between past stimulant use disorders and current anhedonia was not fully accounted for by demographics, psychiatric disorders, other comorbid substance use disorders, or overall clinical severity. In contrast, the association with amotivation was partially explained by these characteristics.

These findings are consistent with results from Kalechstein et al.,[6] who demonstrated that anhedonia and amotivation were elevated in cocaine-dependent individuals after five days of abstinence in comparison to a non-abusing control group.[6] The present study extends those findings to longer periods of remission (ie, two months or longer) and to a treatment-seeking outpatient sample with comorbid psychopathology. Kalechstein et al.[6] examined anhedonia and amotivation using the apathy subscale of the Neuropsychiatric Inventory; thus, these two symptoms were not distinguished. The current results suggest that anhedonia is more prominent during protracted abstinence than amotivation. However, both of these symptoms are more common than depressed mood.

Although anhedonia may represent a protracted effect of heavy stimulant use, it is also possible that it is a risk factor for stimulant use disorders that precedes the initiation of use. Investigations demonstrating that greater levels of baseline anhedonia predict enhanced subjective reports of the reinforcing effects of stimulants among drug-naïve individuals[7,8] indicate that anhedonic individuals may be more prone to stimulant use disorders after initial exposure to the drug. However, given its cross-sectional nature, this study cannot elucidate whether anhedonia is a preexisting risk factor or a protracted effect of heavy stimulant use. Accordingly, further investigation of this issue using prospective research designs is necessary to effectively disentangle the temporal nature of this relationship.

Previous studies of anhedonia and amotivation in stimulant use disorders have screened out individuals with psychiatric comorbidity, which limited their generalizablity but enhanced specificity of the findings.[6] In contrast, the STIM+ group in the present report included individuals with other psychiatric disorders, which in turn increases generalizablity. As a result, STIM+ individuals had higher rates of psychiatric comorbidity, including increased prevalence of non-stimulant substance use disorders. This is notable because non-stimulant drug use may also be associated with anhedonia and amotivation.[21,22] In order to account for this potential confound, we statistically controlled for the effects of other psychiatric and substance use disorders. These adjusted models suggested that the association between stimulant use disorder and anhedonia was specific and not accounted for by other factors, including comorbid substance use disorders. Nevertheless, given that anhedonia is potentially elevated in both stimulant and non-stimulant drug use disorders,[6,21,22] future investigation of the complex relationship between anhedonia and specific classes of drugs (stimulants, opiates, alcohol, cannabis) may be warranted.

There are some limitations to the current study. There was no biochemical verification of substance use status. Therefore, it is possible that some patients who reported that their stimulant use disorder was in full remission were actually still using and perhaps continued to experience stimulant use disorder symptoms, which could influence the present findings. Accordingly, the use of drug toxicology screening would be preferred to verify abstinence. Another limitation was the use of single item measures of depressive symptoms. Although these measures demonstrated excellent interrater reliability, the use of multi-item scales would more adequately assess specific constructs linked to individual depressive symptoms, including anhedonia.[23] Even though the sample may generalize well to stimulant abusers with psychiatric comorbidity, the current study used individuals seeking psychiatric treatment who may be different from stimulant abusers who are not treatment-seeking. Also, we did not have information about treatment prior to or during the evaluation. Thus, we cannot assess whether the STIM+ and STIM− groups had different rates of antipsychotic or antidepressant medication use, which could potentially impact current depressive symptoms. Finally, the MIDAS dataset does not contain information on age of substance use offset. Therefore, it is not possible to elucidate whether depressive symptoms are more severe, less severe, or unchanged following longer versus shorter periods of remission.

Limitations notwithstanding, this study provides evidence of a specific link between anhedonia and stimulant use disorders during full remission. The biological plausibility of this relationship is supported by evidence that both anhedonia and stimulant abuse are underpinned by dysregulation of dopamine pathways.[24] Taken together, results from the current study and findings from previous investigations suggest that treatments that target dopamine neurotransmitter systems (eg, bupropion) may be effective for stimulant-prone individuals with anhedonia. Psychological treatments that raise hedonic tone (eg, behavioral activation therapy) might also be beneficial for anhedonic individuals vulnerable to stimulant use disorders. Given the potential treatment implications, continued investigations into the relationship between affective symptoms and the time course of stimulant misuse would be clinically useful.

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TABLE 1

Demographic and diagnostic characteristics by history of stimulant use disorder in psychiatric outpatients without current active stimulant use disorder

	STIM– (*n* = 2070)	STIM+ (*n*= 204)	F/χ^2	*p*
Demographic characteristics				
Female, %	62.2	48.5	14.5	.0001
Age, *M* (*SD*)	38.4 (13.2)	36.4 (7.9)	4.9	.03
Race: white, %	87.8	86.8	0.2	.66
Marital status, %	—	—	1.2	.75
Single	30.9	30.4		
Married/living together	46.8	44.6		
Divorced/separated	20.5	23.5		
Widowed	1.9	1.5		
Level of education, %	—	—	7.0	.07
Less than high school diploma	9.7	14.2		
High school graduate	22.6	25.0		
At least some college	31.2	31.4		
College degree or higher	36.6	29.4		
Diagnostic characteristics, %				
Lifetime history				
Major depressive disorder	64.4	70.6	3.1	.08
Bipolar disorder (I and II)	7.2	9.8	1.8	.18
Dysthymia	8.6	11.3	1.7	.19
Anxiety disorder	62.8	73.1	7.5	.006
Psychotic disorder	3.2	2.5	0.3	.56
Non-stimulant substance use disorder	39.8	90.7	193.1	<.0001
Alcohol abuse	17.5	22.6	3.2	.07
Alcohol dependence	17.9	56.4	164.0	<.0001
Cannabis abuse	6.8	35.8	184.2	<.0001
Cannabis dependence	5.6	18.1	46.5	<.0001
Other drug abuse	2.9	23.0	168.0	<.0001
Other drug dependence	4.8	20.1	74.4	<.0001
Current major depressive episode, %	44.0	53.0	6.0	.01
Current non-stimulant substance use disorder, %	10.0	21.6	25.6	<.0001
Alcohol abuse	3.6	5.9	2.7	.10
Alcohol dependence	4.1	9.8	14.0	.0002
Cannabis abuse	1.1	3.4	7.7	.006
Cannabis dependence	1.3	2.9	3.8	.05
Other drug abuse	.5	1.0	0.9	.35
Other drug dependence	.8	2.5	5.1	.02
CGI-S rating, *M* (*SD*)	2.2 (1.2)	2.4 (1.6)	2.1	.15

Abbreviations: STIM− = participants with no lifetime history of stimulant use disorder; STIM+ = participants with a past stimulant use disorder in full remission; CGI-S = Clinician Global Impression—Severity.

TABLE 2

Depressive symptoms by history of stimulant use disorder in psychiatric outpatients without current active stimulant use disorder

			Unadjusted		Adjusted*	
	STIM− (*n* = 2070)	STIM+ (*n* = 204)	OR (95% CI)	*p*	OR (95% CI)	*p*
Anhedonia, %	43.0	56.9	1.75 (1.31–2.34)	.0002	1.58 (1.10–2.29)	.01
Amotivation, %	45.4	57.8	1.65 (1.24–2.21)	.0007	1.39 (0.98–1.97)	.06
Depressed mood, %	52.7	60.8	1.39 (1.04–1.87)	.03	1.27 (0.77–2.09)	.35

*Adjusted for gender, age, history of anxiety disorder, history of non-stimulant substance use disorder, current non-stimulant substance use disorder, current major depressive episode, and current Clinical Global Impression–Severity ratings.

Abbreviations: STIM− = participants with no lifetime history of stimulant use disorder; STIM+= participants with a past stimulant use disorder in full remission; OR = odds ratio; CI = confidence interval.