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Men and Women from the STRIDE Clinical Trial: An Assessment of Stimulant Abstinence Symptom Severity at Residential Treatment Entry

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Abstract

Background and Objectives—Gender-specific factors associated with stimulant abstinence severity were examined in a stimulant abusing or dependent residential treatment sample (*N*=302).

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Declaration of Interest

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Method—Bivariate statistics tested gender differences in stimulant abstinence symptoms, measured by participant-reported experiences of early withdrawal. Multivariate linear regression examined gender and other predictors of stimulant abstinence symptom severity.

Results—Women compared to men reported greater stimulant abstinence symptom severity. Anxiety disorders and individual anxiety-related abstinence symptoms accounted for this difference. African American race/ethnicity was predictive of lower stimulant abstinence severity.

Discussion and Conclusions—Women were more sensitive to anxiety-related stimulant withdrawal symptoms.

Scientific Significance—Clinics that address anxiety-related abstinence symptoms, which more commonly occur in women, may improve treatment outcome.

Keywords

gender; stimulant abstinence severity; early withdrawal symptoms; anxiety

BACKGROUND AND OBJECTIVES

Current U.S. population surveys indicate more general drug use and higher rates of illicit drug dependence for men than women.[1] However, male and female patterns of use and disorders differ by the specific drug used. Combined annual data from the most recent National Survey on Drug Use and Health showed no significant gender difference in the abuse of cocaine.[2] Studies suggest that female users exceed males on the severity of dependence regardless of the stimulant used,[3,4] and addiction severity at treatment entry for drug abuse has been linked to poorer outcomes in clinical samples.[5]

Specifically for stimulant abuse, more severe abstinence symptoms have been associated with early treatment termination and greater problems on the Addiction Severity Index drug use subscale.[6,7] Stimulant abstinence symptoms are signs of early withdrawal and include sleep and eating disturbances, anxiety, and depression.[7] The relationship of gender to stimulant abstinence symptoms and the specific factors associated with stimulant abstinence symptom severity are not well described. This secondary analysis examined gender characteristics among baseline participants in a multisite randomized clinical trial testing the addition of vigorous exercise compared to health education as a treatment strategy for stimulant abuse or dependence. Our central aim was to test gender differences in stimulant abstinence symptom severity, as well as the demographic, drug use, and psychiatric factors associated with more severe stimulant abstinence symptoms.

METHODS

Participants

Participants (women n = 121 and men n = 181) were from the Stimulant Reduction Intervention using Dose Exercise (STRIDE) trial, a National Institute on Drug Abuse Clinical Trials Network study (CTN-0037). Full details about the protocol are described elsewhere.[8] Briefly, recruitment occurred during residential treatment in nine geographically diverse community treatment programs that had a 21- to 30-day residential length of stay

and post-residential outpatient services. Eligible participants reported illicit stimulant drug use (e.g., cocaine, methamphetamine, or amphetamine) in the 30 days prior to residential treatment program (RTP) entry and received medical clearance for exercise. Individuals with an opioid dependence diagnosis, general medical conditions that contraindicated exercise, and those with psychosis or other psychiatric conditions that posed a potential safety risk were excluded. Participants provided informed consent.

Measures

All measures utilized for the STRIDE trial were described in Trivedi et al., 2011.[8] Demographic variables included *age*, *race/ethnicity*, *level of education*, *employment status*, and *marital status*.

The Addiction Severity Index-Lite (ASI-Lite) provided lifetime measures of *years of primary stimulant use* (cocaine, amphetamine, or methamphetamine) and assessed problems associated with drug use in seven domains: medical, employment, alcohol, drug use, legal, family/social, and psychiatric. The Timeline Followback (TLFB) measured *days of stimulant use* in the 30 days prior to RTP entry.

The Composite International Diagnostic Interview (CIDI) was used to determine *stimulant use disorders* (categorized here as: cocaine only, cocaine and other stimulants, or other stimulants--not cocaine--only), as well as *other substance use disorders* using Diagnostic and Statistical Manual-IV (DSM-IV) criteria. The Fagerstrom Test for Nicotine Dependence (FTND) measured current *nicotine dependence intensity*.

The Mini International Neuropsychiatric Interview (MINI) measured DSM-IV psychiatric disorders, including major depression, dysthymia, mania, post-traumatic stress disorder (PTSD), panic disorder, social phobia, and obsessive compulsive disorder (OCD).

The Stimulant Selective Severity Assessment (SSSA; based on the Cocaine Selective Severity Assessment (CSSA)) measured self-reported *stimulant abstinence symptom severity* for the past 24 hours.[7] The SSSA covered cocaine, methamphetamine, and other stimulants. Domains included carbohydrate craving, mood, appetite, sleep, energy, and pulse rate. Participants indicated the frequency or intensity of their withdrawal experiences for 16 individual symptoms on a scale of 0 to 7, including, for example, anxiety (i.e., 0 usually doesn't feel anxious; 3-4 anxious half the time; and 7 anxious all the time) and irritability (i.e., 0 most things are not irritating; 3-4 many things are irritating; and 7 mostly everything is irritating or upsetting). The CSSA stimulant craving items were not included in this SSSA measure.

Analysis

Bivariate tests for gender comparisons on sample characteristics were conducted using chi-square and *t* tests, for categorical and continuous variables, respectively. A multivariate linear regression model tested the relationship of gender to stimulant abstinence symptom severity while controlling for other variables. Gender and variables found to be significant ($p < .05$) on bivariate tests were entered into the regression model simultaneously. ASI subscales were not included because of the overlap with other more informative variables

(e.g., the psychiatric problems subscale versus specific psychiatric diagnoses). For the modelled days of cocaine and methamphetamine use variables, we set days of use for non-users to zero. Non-users were participants who responded 'no' to screening questions for any past-30 day cocaine or methamphetamine use. Diagnostics showed that normality and other standard assumptions for linear regression were met.

To further characterize the relationship between gender and stimulant abstinence symptom severity, two post hoc analyses were conducted. First, one variable at a time was removed from the linear regression model to examine the change in the relationship between gender and abstinence symptom severity. We removed comorbid psychiatric diagnosis variables with the smallest *p*-values. Additionally, *t* tests were conducted for gender and each individual abstinence symptom item.

RESULTS

Gender characteristics

On demographic variables, women were younger than men, *M*=35.67 (*SD*=9.9) versus *M*=41.17 (*SD*=10.8) years, and more likely to be Hispanic, 17.36% versus 5.52%, *p*-values < .001. Men were more likely to have a high school degree or more education (86.19% versus 74.38%, *p*=.023) and to be employed (39.23% versus 19.83%) and African American (51.93% versus 29.75%), *p*-values < .001.

Table 1 shows gender comparisons on measures of stimulant drug use, drug use problems, and comorbid drug use and psychiatric disorders. Men reported more years using stimulants as their primary drug. Women reported higher median cocaine and methamphetamine use days prior to RTP entry, and were more likely to report dual stimulant use disorders (cocaine use disorder plus another non-cocaine stimulant use disorder). Most men met the diagnosis for a cocaine use disorder only. Women had higher ASI subscale scores on employment, family/social, and psychiatric problems, while men had higher scores for alcohol problems. Men were also more likely to be diagnosed with alcohol dependence as well as marijuana dependence, and had greater nicotine dependence intensity. Women had a higher prevalence of current manic episode, panic disorder, and OCD diagnoses.

Stimulant abstinence symptom severity

On the SSSA, women reported greater stimulant abstinence symptom severity compared to men (Table 1). In the multivariate model, gender was no longer associated with abstinence symptom severity, *p*-value > .05. Model results are presented in Table 2. African American race/ethnicity was associated with lower abstinence symptom severity than non-African Americans after controlling for other variables in the model. Other modelled variables were non-significant; however, after two variables were removed from the model, i.e., 1) panic disorder and 2) OCD diagnoses, gender was associated with a higher stimulant abstinence severity score compared to men. Post hoc tests also identified higher scores for women on four individual abstinence symptoms, including anxiety (men: *M*=1.02, *SD*=1.7; women: *M*=1.74, *SD*=2.1, *p*=.001), tension (men: *M*=0.72, *SD*=1.5; women: *M*=1.09, *SD*=1.8, *p*=.

047), attention (men: *M*=0.62, *SD*=1.4; women: *M*=1.12, *SD*=1.9, *p*=.008), and irritability (men: *M*=0.80, *SD*=1.4; women: *M*=1.55, *SD*=2.1, *p*<.001).

DISCUSSION AND CONCLUSIONS

We identified differences between men and women on measures of stimulant use and associated disorders. Women were more likely to report dual stimulant use disorders (i.e., cocaine and other stimulant use disorders), while most men met diagnosis for a cocaine use disorder only. These dual stimulant diagnoses corresponded with both more methamphetamine use days and more cocaine use days for women than men. Preclinical and clinical studies provide some evidence to indicate that women, via increased estrogen levels, are more vulnerable to the reinforcing effects of stimulant drugs.[9]

Women reported greater drug use problems in employment, family/social, and psychiatric domains compared to men. Men reported greater problems related to alcohol and were more likely to have an alcohol dependence diagnosis. This is consistent with other studies involving stimulant abusers, with women reporting more employment and economic issues and men more alcohol problems.[10,11] Women in treatment also report significantly greater depressive symptomatology and a history of abuse and violence in their lives,[10,5] although in the current study, major depression, dysthymia, and PTSD were not significantly different in men and women.

We found greater stimulant abstinence symptom severity in women compared to men. More severe early withdrawal symptoms appeared to be positively associated with anxiety-related symptoms (e.g., anxiety, tension, difficulty concentrating, and irritability), and panic disorder and OCD diagnoses appeared to account for the association between gender and stimulant abstinence symptom severity. Being African American was negatively associated with stimulant abstinence symptom severity. African Americans in the STRIDE sample, relative to other racial/ethnic groups, were majority male, reported better mental health status, and had low psychiatric comorbidity,[12] which may help describe our findings here. Women may be more sensitive to the anxiety-related stimulant withdrawal symptoms. STRIDE women compared to men reported higher rates of anxiety-related disorders (i.e., panic disorder and obsessive compulsive disorder). Greater psychological severity in women is associated with poorer treatment retention and outcomes.[5] Individuals who remain anxious during treatment may be at greater risk for using substances to reduce anxiety symptoms.[13]

There were some limitations to this study, including the retrospective assessment of drug use, drug use problems, and drug and psychiatric disorders. Self-report measures may be subject to recall bias (e.g., years of primary stimulant use), although most time periods assessed were relatively short (e.g., 24 hours and past 30 days for the SSSA and TLFB, respectively). The generalizability of our findings may be limited by the trial's sampling criteria. In particular, eligible participants agreed to participate in a clinical trial and were medically cleared and willing to exercise.

SCIENTIFIC SIGNIFICANCE

Addiction severity at treatment entry is associated with treatment retention and abstinence outcomes. The CSSA is one measure of stimulant abstinence severity that has been shown to predict attrition from treatment,[6] and could be used by clinic staff during the admissions process to identify and target stimulant abusing patients with greater risk for poor treatment outcomes. It is a brief self-administered measure, which potentially makes it well adaptable to a clinical setting. It could also be an effective tool for identifying specific symptoms (e.g., anxiety, tension, and irritability) to discuss with patients in treatment sessions. This study emphasized anxiety-related withdrawal experiences as salient topics for clinicians to address in treatment to reduce stimulant abstinence symptoms and potentially the risk for relapse to substance use. Mood and anxiety disorders are more prevalent in women and non-Hispanic whites.[14] There are mixed findings related to gender and treatment retention,[5] but women who complete stimulant treatment are reported to have similar or better outcomes than men.[15] Future prospective studies could help clarify the relationships we identified between gender, race/ethnicity, stimulant abstinence symptom severity, and associated anxiety-related factors.

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Table 1

Sample Characteristics and Stimulant Abstinence Symptom Severity by Gender

Baseline variables	Total *M* (*SD*) or % *N* = 302	Male *M* (*SD*) or % *n* = 181	Female *M* (*SD*) or % *n* = 121	*p*
Drug Use Characteristics				
Years of Primary Stimulant Use	11.14 (9.3)	13.42 (10.9)	9.14 (7.1)	0.012
Days of Cocaine Use (TLFB)[a]	9.00	8.00	11.00	0.002
Days of Methamphetamine Use (TLFB)[b]	12.00	9.50	20.00	0.006
Drug Use Diagnoses (CIDI)				
Stimulant Use Disorders (%)				0.001
Cocaine only	58.80	65.75	48.33	
Cocaine and other stimulant	30.56	28.18	34.17	
Other stimulant (not cocaine)	10.63	6.08	17.50	
Alcohol Dependence (%)	50.33	57.46	39.67	0.002
Marijuana Dependence (%)	31.89	36.46	25.00	0.037
Drug Use Problems (ASI-Lite)				
Alcohol	0.21 (0.2)	0.26 (0.3)	0.13 (0.2)	< 0.001
Drugs	0.17 (0.1)	0.16 (0.1)	0.17 (0.1)	0.454
Employment	0.71 (0.3)	0.67 (0.3)	0.76 (0.3)	0.006
Family/Social	0.22 (0.2)	0.20 (0.2)	0.25 (0.2)	0.046
Legal	0.14 (0.2)	0.13 (0.2)	0.15 (0.2)	0.441
Medical	0.16 (0.3)	0.15 (0.3)	0.18 (0.3)	0.373
Psychiatric	0.27 (0.2)	0.22 (0.2)	0.34 (0.2)	< 0.001
Nicotine Dependence Intensity (FTND)				
	3.45 (2.1)	3.76 (2.2)	3.02 (1.8)	0.011
Comorbid Psychiatric Diagnoses (MINI)				
Major Depressive Episode (%)	22.85	19.34	28.10	0.076
Dysthymia (%)	9.44	11.64	5.75	0.137
Manic Episode (%)	4.97	2.76	8.26	0.031
Post-traumatic Stress Disorder (%)	9.60	8.29	11.57	0.343
Panic Disorder (%)	6.02	3.31	10.17	0.015
Social Phobia (%)	10.93	10.50	11.57	0.770
Obsessive Compulsive Disorder (%)	5.96	3.31	9.92	0.018
Stimulant Abstinence Severity				
SSSA Score	11.77 (11.5)	10.44 (11.1)	13.78 (11.9)	0.013

Notes: TLFB = Timeline Followback; CIDI = Composite International Diagnostic Interview; ASI = Addiction Severity Index; FTND = Fagerstrom Test for Nicotine Dependence; MINI = Mini International Neuropsychiatric Interview; SSSA = Stimulant Selective Severity Assessment;

[a]Median days of use computed for those who used cocaine in the 30 days prior to residential treatment program (RTP) entry (Men *n* = 157 and Women *n* = 82); and

[b]Median days of use computed for those who used methamphetamine in the 30 days prior to RTP entry (Men *n* = 38 and Women *n* = 43).

Table 2

Regression Analysis for Gender and other Variables Predicting Stimulant Abstinence Symptom Severity

	B	SE	p
Gender	2.710	1.5	0.071
Age	0.014	0.1	0.847
High School or more Education	0.101	0.3	0.766
Employed	0.682	1.5	0.642
African American	−4.651	1.6	0.005
Hispanic	−2.994	2.3	0.202
Years of Primary Stimulant Use	−0.020	0.1	0.820
Days of Cocaine Use	−0.047	0.1	0.553
Days of Methamphetamine Use	−0.046	0.1	0.647
Alcohol Dependence	2.155	1.4	0.119
Marijuana Dependence	1.015	1.5	0.485
Nicotine Dependence Intensity	0.519	1.5	0.722
Manic Episode	3.450	3.2	0.288
Panic Disorder	5.636	3.2	0.076
Obsessive Compulsive Disorder (OCD)	4.545	2.9	0.119

Notes. A follow-up analysis, showed that gender (*B*=3.23, *SE*=1.5, *p*=.031) was associated with abstinence symptom severity after two variables were removed from the model, i.e., 1) panic disorder and 2) OCD.