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Sex differences in disinhibition and its relationship to physical abuse in a sample of stimulant-dependent patients

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Abstract

BACKGROUND—Research suggests that impulsivity is a vulnerability factor for developing stimulant dependence, that women develop dependence more quickly than men, and that physical abuse can increase impulsivity and may have greater adverse health consequences in women. This study sought to tie these findings together by evaluating: 1. sex differences in disinhibition prior to lifetime initiation of stimulant abuse and 2. the relationship between physical abuse and disinhibition in stimulant-dependent patients.

METHOD—The Frontal Systems Behavior Scale (FrSBe) is a reliable and valid self-report assessment of three neurobehavioral domains associated with frontal systems functioning (Apathy, Disinhibition, and Executive Dysfunction, summed for a Total), that assesses pre-morbid functioning and has a specific cutoff for defining clinically significant abnormalities. Six sites evaluating 12-step facilitation for stimulant abusers obtained the FrSBe from 118 methamphetamine- and/or cocaine-dependent participants. Lifetime physical abuse was measured by the Addiction Severity Index (ASI).

RESULTS—The proportion reporting clinically significant disinhibition was significantly higher in women (64.9%) than in men (45.0%, $p=0.04$), with no significant difference on the other FrSBe scales. Physical abuse in women, but not men, was associated with worse functioning, with physically abused, relative to non-abused, women having a significantly greater proportion with clinically significant disinhibition ($p<0.01$) and total neurobehavioral abnormalities ($p<0.01$).

CONCLUSION—These findings suggest that women may have significantly greater disinhibition than men prior to lifetime initiation of stimulant abuse and that physical abuse in women is associated with greater disinhibition.

Keywords

impulsivity; stimulant dependence; sex; physical abuse

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Contributors

Dr. Winhusen was the principal investigator for the ancillary study. Mr. Lewis, with input from Dr. Winhusen, undertook the statistical analysis, and Dr. Winhusen wrote the first draft of the manuscript. Both authors contributed to and have approved the final manuscript.

Conflict of Interest

The authors have no potential conflicts of interest to report.

1. INTRODUCTION

Pre-clinical (Belin et al., 2008; Dalley et al., 2011) and clinical research (Adinoff et al., 2007; de Wit, 2009; Ersche et al., 2012, 2010) suggests that impulsivity increases vulnerability to developing stimulant dependence. Epidemiological data suggest that women develop cocaine dependence more quickly than men (O'Brien and Anthony, 2005) and that they have greater problems with lower cocaine doses relative to men (Chen and Kandel, 2002). If impulsivity does, in fact, increase vulnerability, one might expect impulsivity to be greater in women, relative to men. Consistent with this, a study by Lejuez (2007) found that impulsivity, measured by the Barratt Impulsiveness Scale-11, was significantly greater in cocaine-dependent women than in cocaine-dependent men and that impulsivity was a risk factor for cocaine-dependence in women, an effect not observed in men. However, the study was limited by measuring current impulsivity, as opposed to impulsivity pre-dating stimulant abuse. Thus, the observed sex differences might have reflected the impact of stimulant use itself, which is a limitation for much of the research examining the interrelationship between stimulant abuse and impulsivity (de Wit, 2009).

The finding of greater impulsivity in women is also counter to the general finding of no significant sex differences on impulsivity (Feingold, 1994; Patton et al., 1995). Of interest, research suggests that childhood abuse increases impulsivity (Braquehais et al., 2010) and that such abuse may result in more adverse health outcomes (Thompson et al., 2004), including the development of substance abuse problems (Hyman et al., 2006), in women than in men.

Impulsivity is a multi-dimensional construct (Robbins et al., 2012) and measures of its various aspects typically do not correlate, possibly indicating that they reflect different brain processes (de Wit, 2009; Ersche et al., 2011). Behavioral disinhibition, an aspect of impulsivity, has been found to predict substance use disorders in prospective studies (Kirisci et al., 2007; Sher et al., 2000). Thus, understanding the relationship between childhood abuse, pre-existing disinhibition (i.e., prior to stimulant abuse), and vulnerability to becoming addicted might shed light on a potential etiological pathway to stimulant addiction.

In an ancillary study (Winhusen et al., 2012) to a National Drug Abuse Treatment Clinical Trials Network (NIDA CTN) trial on 12-step facilitation for stimulant abusers (STAGE-12), the Frontal Systems Behavior Scale (FrSBe), which assesses both pre-morbid and post-damage functioning for three neurobehavioral domains: apathy, disinhibition, and executive dysfunction (Grace and Malloy, 2001; Malloy and Grace, 2005), was completed by cocaine- and/or methamphetamine-dependent patients. A body of research supports the reliability (Grace and Malloy, 2001; Velligan et al., 2002) and validity (Cahn-Weiner et al., 2002; Chiaravalloti and DeLuca, 2003; Lane-Brown and Tate, 2009; Malloy and Grace, 2005; Malloy et al., 2007; Paulsen et al., 1996) of the FrSBe. In the ancillary study, stimulant-dependent patients completed the FrSBe with the pre-morbid time-frame defined as the period before they started abusing stimulants. Because all participants were stimulant dependent, the relationship between disinhibition and the risk of becoming stimulant dependent, as opposed to continuing recreational use, could not be evaluated. However, the data enabled an exploration of sex differences in disinhibition prior to lifetime onset of stimulant abuse; a finding of greater pre-existing disinhibition in women would support the potential import of impulsivity as a vulnerability factor for developing stimulant dependence. The ancillary study did not specifically evaluate childhood abuse but did assess lifetime abuse, and, thus, the relationship between lifetime abuse and pre-existing disinhibition was explored. It was predicted that women would evidence significantly greater pre-existing disinhibition than men, and that lifetime abuse would be associated with greater pre-existing disinhibition in women while this association might not be seen in men.

2. METHOD

2.1 Participants and Procedures

Six of the ten STAGE-12 sites (Donovan et al., 2012) participated in the present study. Eligible participants were randomized into STAGE-12, met criteria for current stimulant dependence, endorsed methamphetamine or cocaine as the primary drug of choice, did not have a seizure disorder or a history of stroke, and completed the FrSBe (N=180). The present study evaluated the "Before" FrSBe rating, which rated the time before participants initiated stimulant abuse. Since the FrSBe is designed for use in adults only, the Before ratings could only be used for individuals who were at least 18 years of age when they initiated stimulant use (N=118). Thus, 118 participants were included in the present analyses. Additional information about the participants and procedures for STAGE-12 (Donovan et al., 2012) and this ancillary study (Winhusen et al., 2012) can be found elsewhere.

2.2 Measures

The FrSBe is written at a 6th-grade reading level and consists of 46 self-report items, with responses in a five-point Likert-type scale. The FrSBe assesses three domains: Apathy (14 items), Disinhibition (15 items), and Executive Dysfunction (17 items); these three domains are summed to yield a total score. The FrSBe instructs the respondent to rate the frequency with which each of the 46 behaviors was engaged in during two time-frames: "Before the illness or injury," referred to as the "Before" rating, and "At the present time." The ASI-Lite is derived from the Fifth Edition of the ASI (McLellan et al., 1992), a structured clinical interview that yields scores for seven areas of functioning typically impacted by addiction. The ASI includes single items to assess whether the participant has a lifetime history of physical and/or sexual abuse and these were used to designate the presence or absence of lifetime physical and sexual abuse for each participant.

2.3 Data analysis

All raw FrSBe scores from the Before ratings were converted into T-scores using the tables provided in the FrSBe manual, which are categorized according to age, sex, and educational level (Grace and Malloy, 2001). For all FrSBe scales, T-scores ≥65 indicate clinically significant neurobehavioral abnormalities (Grace and Malloy, 2001). The planned analyses for sexual abuse could not be completed due to an insufficient number of sexually abused men (n=4). An evaluation of sex baseline differences revealed a significant difference only for race (see Table 1). As such, race was evaluated via corrected Akaike Information Criteria (AICC), for inclusion in the maximum likelihood logistic regressions testing for sex differences on the FrSBe and for the regressions evaluating the association between physical abuse and FrSBe scores within each sex. Race was not selected for inclusion by AICC for any regression. To briefly explore additional relationships, we employed ordinary least squares regressions using disinhibition, physical abuse status and their interaction, to predict ASI Drug and ASI Alcohol composite scores. These regressions, which were completed for the whole sample and for each sex separately, yielded no disinhibition or disinhibition x physical abuse interaction effects.

3. RESULTS

3.1 Sample Characteristics

Table 1 provides participant characteristics as a function of sex. The 118 participants were approximately 40 years of age and had 12 years of education on average. There was a significant sex difference for race, which reflects a greater proportion of African Americans in the male sample and a greater proportion of other/mixed race in the female sample.

3.2 Sex differences for pre-existing neurobehavioral abnormalities

Table 1 provides the proportion of participants with clinically significant neurobehavioral abnormalities as a function of sex. There was one significant sex difference, which reflected a significantly greater proportion of women (64.9%), relative to men (45.0%), with clinically-significant disinhibition.

3.3 Pre-existing neurobehavioral abnormalities and lifetime physical abuse

The relationships between lifetime physical abuse and retrospectively reported pre-existing neurobehavioral abnormalities, including disinhibition, are provided in Table 2. The proportion of women reporting lifetime abuse was high, with 82% reporting physical abuse. As a result, the sample size for the non-abused subsample was limited (n=14). Regardless, a significantly greater proportion of women with lifetime physical abuse had clinically-significant disinhibition (73.0%) and total neurobehavioral abnormalities (74.2%) relative to women without such abuse (28.6% and 35.7%, respectively). The proportion of men reporting lifetime physical abuse was 30%. There were no significant effects for lifetime physical abuse, which may have been related to the smaller sample size for the male analyses.

4.0 DISCUSSION

This study revealed that a significantly greater proportion of stimulant-dependent women, relative to men, retrospectively reported clinically significant disinhibition prior to lifetime initiation of stimulant abuse, as measured by the FrSBe. This sex difference was not observed for the other FrSBe scales. This finding contributes to research suggesting that impulsivity is a vulnerability trait for developing stimulant dependence (Ersche et al., 2010) in that women develop stimulant dependence more quickly than men (O'Brien and Anthony, 2005) and pre-clinical evidence suggests that females may be more vulnerable to compulsive cocaine use than males (Hyman et al., 2008). This study also found that women with a lifetime history of physical abuse had a significantly higher rate of clinically significant Disinhibition and Total scores relative to women without such history. This relationship was not observed for the other FrSBe scales. For men, no significant association was found between lifetime physical abuse and FrSBe scales, which might be due to the limited sample size for those analyses. In addition, there is evidence to suggest that the ASI underestimates the incidence of physical abuse in men (Langeland et al., 2003) which could also account for the lack of association between physical abuse and disinhibition. However, a finding of poorer functioning in physically abused, relative to non-abused, women and no poorer functioning observed in abused, relative to non-abused, men is consistent with research finding that childhood abuse may have more adverse health consequences in women than men (Thompson et al., 2004).

The present results must be considered in light of several limitations. First, a single item from the ASI was used to assess lifetime physical abuse, which did not provide information about the abuse nor when it occurred (e.g., pre-stimulant-abuse initiation vs. later). Thus, some of the participants endorsing physical abuse may have experienced the abuse following the onset of stimulant use, which would serve to weaken the association observed between physical abuse and pre-existing disinhibition. In addition, research suggests that the severity of the neurobiological consequences of childhood adverse events, such as abuse, depend on the age at which they are experienced (Andersen and Teicher, 2009). Thus, future research should collect more thorough information about childhood abuse, including the age at which it was experienced, in order to further elucidate the relationships between childhood abuse and disinhibition.

Second, the ratings of pre-stimulant abuse functioning entailed retrospective rating of behavior that occurred many years prior and the reliability of the FrSBe for such retrospective reporting has not been published. Third, the sample sizes for the physical abuse analyses were small, particularly in the men, and, thus, our analyses were likely underpowered and the results may have limited generalizability. Another limitation was the sole focus on physical abuse. While lifetime sexual abuse was assessed, the sample of sexually abuse men (n=4) was too small for analysis. Also, it must be noted that this study is correlational in nature and so cause and effect determinations cannot be made and, of course, disinhibition can result from a number of factors other than physical abuse (Enoch et al., 2010). In addition, all participants were stimulant-dependent and, thus, the association between disinhibition and vulnerability to addiction could not be assessed. Finally, since the FrSBe is designed for use with adults, the 62 participants (34% of the sample) who started using stimulants prior to age 18 were excluded. Thus, this study did not address participants who may have turned to substances at an early age to cope with abuse or may have been particularly impulsive.

The present findings, which indicate a significant sex difference in pre-existing disinhibition and that physical abuse in women is associated with greater disinhibition, is relevant to investigation of risk factors for addiction. For example, it has been suggested that studies of possible gene x environment interactions could significantly advance our understanding of the causes of, and possible treatments for, substance use disorders (Caspi and Moffitt, 2006). Should the present results be replicated and extended to find a relationship between pre-existing disinhibition and vulnerability to addiction, the FrSBe, in combination with physical abuse measures might be useful in defining more homogenous subsamples for genetic studies. Thus, conducting a study which includes a larger and more diverse sample (i.e., including recreational users), more in-depth assessment of physical/sexual abuse, and an evaluation of the test-retest reliability of FrSBe ratings for pre-stimulant-abuse-initiation may be warranted.

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Table 1

Demographics, clinical characteristics, and pre-stimulant-use neurobehavioral abnormalities of stimulant-dependent patients as a function of sex

	Female (N=78)	Male (N=40)	Sex Analysis Test Statistic
Age (years)	39.7 (8.8)	42.5 (6.7)	W = 1.8
Education (years)	12.2 (1.6)	12.3 (1.2)	W= 0.2
Race (%):			F=0.0 *
African American	49.4%	70.0%	
Caucasian	39.0%	30.0%	
Other/Mixed	11.7%	0.0%	
Ethnicity-Hispanic (%)	3.9%	5.0%	F=0.3
Cigarette smoker	80.8%	77.5%	P (1)=0.2
Stimulant positive UDS[a] (%)	19.2%	17.5%	P(1)=0.1
Non-Stimulant SUD[a] Diagnosis (%)	69.2%	80.0%	P (1)=1.6
Stimulant-Dependence Diagnosis:			F=0.0
Methamphetamine	25.6%	12.8%	
Cocaine	70.5%	87.2%	
Both	3.8%	0.0%	
FrSBe [c] Scales (T-scores ≥65)			
Significant Apathy	71.4%	80.0%	X^2 (1)=1.0
Significant Disinhibition	64.9%	45.0%	X^2 (1)=4.2 *
Significant Executive Dysfunction	46.2%	53.8%	X^2 (1)=0.6
Significant Total	67.1%	69.2%	X^2 (1)=0.1

Note: Where not specifically indicated, numbers represent means (standard deviations). W=Wilcoxon Rank Sum, P(df)= Pearson's Chi Square, F=Fisher's Exact, X^2(df) = Type III Wald Chi Square from logistic regression.

* $p < 0.05$.

[a] Urine drug screen;

[b] Substance use disorder;

[c] FrSBe=Frontal Systems Behavior Scale

Table 2

Proportion of participants with pre-existing neurobehavioral abnormalities as a function of sex, FrSBe[a] scale, and lifetime physical abuse

	Clinically Significant Apathy	Clinically Significant Disinhibition	Clinically Significant Executive Dysfunction	Clinically Significant Total
Female (N=78)				
Physical abuse (n=64)	76.2%	73.0%	50.0%	74.2%
No physical abuse (n=14)	50.0%	28.6%	28.6%	35.7%
X^2 (1) for physical abuse	3.63	8.49 **	2.04	6.83 **
Male (N=40)				
Physical abuse (n=12)	83.3%	58.3%	54.5%	81.8%
No physical abuse (n=28)	78.6%	39.3%	53.6%	64.3%
X^2 (1) for physical abuse	0.12	1.21	0.00	1.10

Note:

[a]Frontal Systems Behavior Scale.

** p<.01