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Sex modulates approach systems and impulsivity in substance dependence

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ABSTRACT

Background: Personality traits such as pathological engagement in approach behaviors, high levels of impulsivity and heightened negative affect are consistently observed in substance dependent individuals (SDI). The clinical course of addiction has been shown to differ between sexes. For example, women increase their rates of consumption of some drugs of abuse more quickly than men. Despite the potential influence of personality and sex on features of addiction, few studies have investigated the interaction of these factors in substance dependence.
Methods: Fifty-one SDI (26 males, 25 females) and 66 controls (41 males, 25 females) completed the Behavioral Inhibition/Behavioral Activation System (BIS/BAS) Scales, the Barratt Impulsiveness Scale, and the Positive and Negative Affect Schedule (PANAS-X). Data were analyzed with 2 × 2 ANCOVAs testing for main effects of group, sex and group by sex interactions, adjusting for education level.
Results: Significant group by sex interactions were observed for BAS scores [$F(1,116) = 7.03$, $p < .01$] and Barratt Motor Impulsiveness [$F(1,116) = 6.11$, $p < .02$] with female SDI showing the highest approach tendencies and impulsivity followed by male SDI, male controls, and finally female controls. SDI scored higher on negative affect [$F(1,116) = 25.23$, $p < .001$] than controls. Behavioral Inhibition System scores were higher in women than men [$F(1,116) = 14.03$, $p < .001$].
Conclusion: Higher BAS and motor impulsivity in SDI women relative to SDI men and control women suggest that personality traits that have been previously associated with drug use may be modulated by sex. These factors may contribute to differences in the disease course observed in male compared to female drug users.

1. Introduction

While substance use disorders more frequently afflict men than women on the order of two or three times, evidence suggests that women with these disorders exhibit an accelerated clinical course (Greenfield et al., 2007). Women appear to advance more quickly from initial substance experimentation to regular use and dependence (Hernandez-Avila et al., 2004; Johnson et al., 2005; Randall et al., 1999). Though sex has not consistently been shown to predict treatment outcomes (Greenfield et al., 2007), studies find that women exhibit longer periods of use following relapse (Gallop et al., 2007), increase their rates of consumption of some drugs of abuse more quickly (Brady and Randall, 1999; Hernandez-Avila et al., 2004), and relapse at similar rates following abstinence in spite of better utilization of treatment options, e.g., more frequent participation in group counseling (Fiorentine et al., 1997; Gallop et al., 2007). Thus far, neuroendocrine investigations related to these clinically observed sex differences in SDI have provided insight into these phenomena. However, relatively few studies of sex differences in drug dependence have directly investigated multiple dimensions of personality related to addiction. Our objective was to investigate behavioral approach/inhibition systems, impulsivity, and affect in male and female substance dependent individuals (SDI) and control groups to examine whether group differences in personality constructs were modulated by sex.

Personality traits, such as heightened impulsivity, may play an integral role in the development and disease course of substance dependence. Increased impulsivity can be defined as having

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decreased inhibitory control over responses to rewarding or distracting stimuli (Ersche et al., 2010). Preclinical models of addiction support the idea that this type of dysregulation can lead to uncontrolled substance use and drug seeking behaviors (Everitt et al., 2008). Studies indicate that SDI samples are more impulsive than controls (Moeller and Dougherty, 2002; Nielsen et al., 2012) and such increases in impulsivity appear to contribute to substance use severity and vulnerability to dependence (Lejuez et al., 2010; Moeller et al., 2001; Verdejo-Garcia et al., 2008), but these studies do not indicate whether sex differences influence these relationships highlighting a need to understand possible sex differences in SDI on this trait.

Most studies utilizing self-report measures of trait impulsivity in SDI samples do not report on findings related to sex (Bjork et al., 2004; Ersche et al., 2011; Lane et al., 2007), have not sought group by sex interactions, or were limited by small or single sex samples. At least one prior study found SDI women were both more impulsive (Barratt Impulsiveness Scale) and more often dependent on psychostimulants than men (Lejuez et al., 2007). However, this study did not include a control group and therefore could not evaluate group by sex interactions. Another study comparing SDI and controls on measures of impulsivity reported no main effect of sex and no group by sex interactions (Allen et al., 1998), but results are limited as drug categories used by this SDI sample were not reported and abstinence was not monitored. The current investigation includes a large sample of controls, detailed characterization of substance use, and verifiable abstinence among SDI.

Similar to impulsivity, heightened sensitivity of the behavioral approach or activation system (BAS) as measured by the BIS/BAS scales (Carver and White, 1994) may also play an important role in the development and disease course of substance dependence. The BAS is said to motivate behaviors that would approach or move in a direction toward an appetitive outcome, goal, or reward and to generate positive affective states in this context (Gray, 1981). Gray (1994) views individuals higher in BAS sensitivity as predisposed to substance use disorders via their propensity for pathological engagement in approach behaviors. Previous studies have supported Gray's theory that the BAS has clinical significance to substance dependence. For example, BAS sensitivity appears to be elevated in SDI samples (Ersche et al., 2011; Franken et al., 2006; Johnson et al., 2003) and the BAS has been directly correlated with substance use severity (Franken and Muris, 2006; Knyazev, 2004) and craving (Franken, 2002). Previous studies that have reported higher BAS scores in SDI did not find that BAS was modulated by sex but few studies comparing SDI to controls have employed direct measures of the BAS (Franken et al., 2006).

As another potential driving force in substance dependence, affect might underlie differences in clinical course modulated by sex. Negative affect, especially in concert with increased impulsivity, may motivate substance use (Verdejo-Garcia et al., 2007) and SDI groups generally demonstrate higher levels of negative affect compared with controls (Jackson and Sher, 2003; Watson and Clark, 1994). Given that depressive symptoms have long been recognized as more prevalent in women (Weissman and Klerman, 1977), investigation of group by sex interactions on affect seems warranted. Such interactions found on this dimension of personality could help account for the accelerated clinical course characteristic of female substance dependence.

The goal of this study was to compare SDI and controls on personality traits thought to be instrumental to substance dependence and to further examine modulation of these traits according to sex. Taken together, findings of increased behavioral approach, impulsivity, and negative affect specifically related to drug addicted women could further account for the clinical differences seen between male and female SDI groups.

2. Materials and methods

2.1. Participants

One-hundred seventeen participants were included in this study ($n = 41$ male control, $n = 26$ male SDI, $n = 25$ female control, $n = 25$ female SDI). SDI participants were in a sex specific long term residential treatment program at University of Colorado School of Medicine's Addiction Research and Treatment Services (ARTS) and were abstinent from all drugs of abuse excluding tobacco for a minimum of 60 days and closely monitored for drug use while in treatment. All SDI met DSM-IV criteria for dependence upon psychostimulants (methamphetamine and/or cocaine). Control participants were recruited from the community and excluded for dependence upon alcohol or other drugs aside from tobacco. All participants received structured diagnostic interviews to screen DSM-IV criteria related to substance use and relevant mental disorders. Participants were excluded if they met diagnostic criteria for current depression (within last 2 months), schizophrenia, and bipolar disorder. All participants provided written informed consent approved by the Colorado Multiple Institution Review Board.

2.2. Screening assessment

2.2.1. Composite International Diagnostic Interview-Substance Abuse Module (CIDI-SAM). This computerized structured interview (Cottler et al., 1989) assesses substance diagnoses and symptom counts for alcohol, tobacco, and other drugs of abuse (stimulants, cocaine, marijuana, hallucinogens, opioids, inhalants, sedatives, club drugs, and PCP) using DSM IV criteria. All participants were administered this detailed interview to verify a diagnosis of cocaine and/or methamphetamine dependence in our substance dependent group as well as to rule out dependence on alcohol or other drugs excluding tobacco in control participants.

2.2.2. Diagnostic Interview Schedule-version IV (CDIS-IV). This computerized structured interview assesses psychiatric diagnoses using DSM IV criteria (Robins et al., 1995) and was administered to all participants and utilized to exclude those with a positive history of schizophrenia, bipolar disorder, or current major depression (within last 2 months).

2.2.3. IQ: Wechsler Abbreviated scale of Intelligence (WASI). The WASI 2-subtest (Vocabulary and Matrix Reasoning) was administered to all participants to assess general intelligence. Participants were excluded for IQ $\leq$ 80.

2.3. Personality and affect questionnaires

2.3.1. The Behavioral Inhibition System/Behavioral Activation System (BIS/BAS) scales. The BIS/BAS scales (Carver and White, 1994) consist of a 20 item self-report questionnaire used to measure the responsiveness of two basic motivational systems. The behavioral inhibition system (BIS) scale (7 items) assesses the tendency to respond with negative affect and behaviors that withdraw from aversive conditioned stimuli. The behavioral activation system scales (BAS, 13 items) assess the tendency to respond with positive affect and behaviors that approach appetitive stimuli. BAS is divided into 3 subscales: Drive (4 items) which relates to persistent pursuit of goals, Fun-Seeking (4 items) which involves the tendency to seek out novel rewards, and Reward Responsiveness (5 items) which assesses the tendency to experience positive affect in response to rewarding stimuli. Prior studies have demonstrated that the BIS/BAS scales possess adequate reliability (Carver and White, 1994; Leone et al., 2001).

2.3.2. Barratt Impulsiveness scale-version 11 (Barratt). This is a 30-item self-report questionnaire used to measure impulsivity (Patton et al., 1995). Participants rate whether phrases describing aspects of impulsivity pertain to themselves along a 4 point scale. The Barratt can be broken into 3 subscales assessing different facets of impulsivity. The Motor impulsivity subscale involves acting on the spur of the moment and includes statement such as, "I do things without thinking". The Attentional impulsivity subscale assesses ability to maintain focused attention on a task and includes statements such as "I concentrate easily". The nonplanning impulsivity subscale pertains to a lack of concern for the future and includes statements such as, "I plan tasks carefully". Studies indicate that the Barratt and its subscales are reliable measures of impulsiveness (Patton et al., 1995; Stanford et al., 2009).

2.3.3. The Positive (+) and Negative (−) Affect Schedule-Expanded Form (PANAS-X). PANAS-X assesses positive and negative affect through 60 words or phrases that refer to specific emotions (Watson and Clark, 1994). Participants are asked to self-rate the extent to which they have felt that emotion over the past few weeks on a 5 point scale (1 = very slightly or not at all to 5 = extremely). The PANAS-X has been shown to be a reliable measure of positive and negative affect (Watson and Clark, 1994).

2.4. Data analysis

Distributions of all dependent variables were evaluated and found to be approximately normal; therefore, parametric statistical procedures were utilized. Pearson