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Heroin and amphetamine users display opposite relationships between trait and neurobehavioral dimensions of impulsivity

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HIGHLIGHTS

- Assess relationships between trait and neurobehavioral impulsivity
- Compare heroin and amphetamine addicts
- Discovered opposite relationships in heroin vs. amphetamine addicts
- Trait impulsivity is associated with worse response inhibition in amphetamine addicts.
- Trait impulsivity is associated with better response inhibition in heroin addicts.

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ABSTRACT

The multidimensional construct of impulsivity is implicated in all phases of the addiction cycle. Substance dependent individuals (SDIs) demonstrate elevated impulsivity on both trait and laboratory tests of neurobehavioral impulsivity; however our understanding of the relationship between these different aspects of impulsivity in users of different classes of drugs remains rudimentary. The goal of this study was to assess for commonalities and differences in the relationships between trait and neurobehavioral impulsivity in heroin and amphetamine addicts. Participants included 58 amphetamine dependent (ADIs) and 74 heroin dependent individuals (HDIs) in protracted abstinence. We conducted Principal Component Analyses (PCA) on two self-report trait and six neurobehavioral measures of impulsivity, which resulted in two trait impulsivity (action, planning) and four neurobehavioral impulsivity composites (discriminability, response inhibition efficiency, decision-making efficiency, quality of decision-making). Multiple regression analyses were used to determine whether neurobehavioral impulsivity is predicted by trait impulsivity and drug type. The analyses revealed a significant interaction between drug type and trait action impulsivity on response inhibition efficiency, which showed opposite relationships for ADIs and HDIs. Specifically, increased trait action impulsivity was associated with worse response inhibition efficiency in ADIs, but with better efficiency in HDIs. These results challenge the unitary account of drug addiction and contribute to a growing body of literature that reveals important behavioral, cognitive, and neurobiological differences between users of different classes of drugs.

1. Introduction

Impulsivity, defined as a predisposition toward rapid unplanned reactions to internal and external stimuli without regard to the negative consequences of these reactions to self or others (Moeller, Barratt, Dougherty, Schmitz, & Swann, 2001) is one of the strongest predictors of the initiation and maintenance of drug addiction (de Wit, 2009; Moeller & Dougherty, 2002; Verdejo-Garcia, Perales, & Perez-Garcia, 2007) and is also reliably associated with increased risk for relapse and treatment failure (Moeller et al., 2001; Perry & Carroll, 2008). Impulsivity is a complex and multidimensional construct characterized by a variety of personality and neurocognitive manifestations (Cyders & Coskunpinar, 2011; Dick et al., 2010; Evenden, 1999). In general,

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measures of trait impulsivity assess self-reported and relatively stable personality characteristics, whereas measures of neurobehavioral impulsivity index performance on laboratory tests of behavior reflecting state-dependent neurocognitive processes.

Self-report trait impulsivity is itself multidimensional, with the number of proposed dimensions ranging from 2 to 15 depending on the specific measures used and samples tested (in Kirby & Finch, 2010). Although there is a considerable disagreement in the literature over the number and nature of trait impulsivity dimensions, they typically include lack of planning (Kirby & Finch, 2010; Patton, Stanford, & Barratt, 1995; Whiteside & Lynam, 2001), lack of perseverance (Patton et al., 1995; Whiteside & Lynam, 2001) and sensation seeking (Whiteside & Lynam, 2001; Zuckerman, 1994), among others. Although informative, self-report measures are limited by their reliance on subjective judgment (de Wit, 2009) and cannot be directly related to preclinical biological models of impulsivity (Evenden, 1999). Neurobehavioral measures of impulsivity overcome most of the problems associated with assessment of trait impulsivity (Rogers & Robbins, 2001). They are often based on preclinical models of impulsivity (Winstanley, Olausson, Taylor, & Jentsch, 2010) and their neural substrates are well delineated by neuroimaging studies with humans (Ersche et al., 2012; Moeller et al., 2005). Neurobehavioral impulsivity is typically measured with tests falling into one of two broad categories (Winstanley et al., 2010): (a) *Impulsive choice* (*cognitive impulsivity*), assessed with decision-making tasks involving various risk, reward, and delay contingencies; and (b) *Impulsive action* (*motor impulsivity*), indexed by response inhibition tasks reflecting inability to inhibit motor responses. Recently, Weafer, Baggott, and de Wit (in press) demonstrated moderate to high test-retest reliability of "cognitive" (r range: .76–.89) and "motor" impulsivity dimensions (r range: .65–.73), indicating that they are reliable measures of impulsive behavior. Other "state-like" neurobehavioral measures of impulsivity assessing impulsive choice and impulsive action (e.g. Kirby, 2009; White, Lejuez, & de Wit, 2008) show comparable reliability to trait-like measures (Odum, 2011). These neurobehavioral dimensions of impulsivity are shown to be mediated by dissociable brain substrates and neurotransmitter systems (Kim & Lee, 2011; Sonuga-Barke, 2002) and to load separately in factor analyses (Broos et al., 2012; Lane, Cherek, Rhodes, Pietras, & Tcheremissine, 2003; Rogers et al., 1999; Sonuga-Barke, 2002).

A notable finding in the literature is that although many substance dependent individuals (SDIs) show impaired impulse control on neurobehavioral measures of impulsivity, certainly not *all* SDIs manifest such impairments, with some studies reporting that more than 1/3rd of SDIs demonstrate relatively spared impulse control even after many years of chronic drug use (Bechara & Damasio, 2002; Bechara & Martin, 2004). This raises the question of whether individual differences in some additional risk factors such as trait impulsivity may increase one's vulnerability to neurobehavioral impairments in impulsivity. Most studies of this nature have focused on healthy individuals and reveal equivocal findings (in Cyders & Coskunpinar, 2011). Of the few studies that have included drug users, Kjome et al. (2010) found that in a mixed group of controls and cocaine users, higher trait impulsivity was associated with impulsive action (response inhibition), but not with impulsive choice (decision-making). Another study using factor analysis found that results varied based on participant group, such that impulsive choice (delay discounting) loaded with self-reported trait impulsivity for controls, but with sensation seeking for drug users and individuals at risk for addiction (Meda et al., 2009). Clearly, more research is needed to understand the associations between trait and neurobehavioral impulsivity and how they relate to substance abuse factors (Dick et al., 2010; Meda et al., 2009; Winstanley et al., 2010).

Much of the research investigating impulsivity in SDIs has focused on the common effects of addiction to different types of drugs, based on findings that addictive drugs increase dopamine concentrations in the mesolimbic system, considered to be the neurobiological substrate of the rewarding effects of most drugs of abuse (Di Chiara & Imperato, 1988; Wise, 1978). More recently, researchers have emphasized the importance of investigating potential differences among commonly abused drugs such as heroin and amphetamines, given that they lead to increased dopamine transmission through different neural mechanisms (Badiani, Belin, Epstein, Calu, & Shaham, 2011; Wise, 1978) and have distinct effects on other neuromodulatory and neuropeptide systems (George & Koob, 2010). This line of research has begun to reveal different behavioral manifestations of impulsivity in heroin and amphetamine users (Fernandez-Serrano, Perez-Garcia, & Verdejo-Garcia, 2011; Verdejo-Garcia, Bechara, Recknor, & Perez-Garcia, 2007). For instance, stimulant users show greater deficits on tests of impulsive action compared with opiate users (Verdejo-Garcia, Perales et al., 2007), whereas tests of impulsive choice reveal more variable results (Bornovalova, Daughters, Hernandez, Richards, & Lejuez, 2005; Rogers et al., 1999; Verdejo-Garcia, Bechara et al., 2007; Verdejo-Garcia, Perales et al., 2007). Research in this field is significantly complicated by the high rates of polysubstance abuse and dependence among SDIs in North America and Western Europe, which makes it virtually impossible to investigate the unique effects of different types of drugs on neurocognitive functioning. Further, despite unequivocal evidence that impulsivity is not a unitary construct, very few studies to date have performed within-subjects comparisons of various trait and neurobehavioral dimensions of impulsivity (Broos et al., 2012) and to our knowledge, no study has investigated the relationships between trait and neurobehavioral impulsivity among stimulant and opiate users.

The current study used a within-subject multi-method design to assess for commonalities and differences in the relationships between different aspects of trait and neurobehavioral impulsivity among SDIs with a history of dependence on either amphetamines or heroin. The main goal of the study was to determine whether aspects of trait impulsivity would differentially predict neurobehavioral impulsivity in heroin and amphetamine addicts. In order to limit the confounding effects of polysubstance abuse and dependence, the study included SDIs who were largely mono-substance dependent on either amphetamines or heroin. Given evidence that amphetamine is associated with increased difficulties in impulsive action, we hypothesized that increased trait impulsivity would be associated with increased impulsive action in amphetamine, but not in heroin users. Further, in light of evidence that higher trait impulsivity is associated with impulsive action but not with impulsive choice, we expected no differential associations between trait impulsivity and impulsive choice among heroin and amphetamine users.

2. Materials and methods

2.1. Participants

Participants included 58 individuals meeting DSM-IV diagnostic criteria for past dependence on amphetamines (ADIs) and 74 individuals meeting diagnostic criteria for past dependence on heroin (HDIs), evaluated at the Bulgarian Addictions Institute in Sofia, Bulgaria. Inclusion criteria included: 1) age between 18 and 50 years; 2) minimum of 8th grade education; 3) estimated IQ > 75; 4) no history of neurologic illness (including dementia secondary to substance abuse); 5) no history of penetrating head injury or closed head injury with a loss of consciousness >30 min; 6) no history of psychotic or mood disorders, or current use of psychotropic medication; 7) HIV seronegative status; 8) no history of dependence on both amphetamines and heroin or current dependence on any substance; and 9) negative breathalyzer test for alcohol and negative urine toxicology screen for opiates, cannabis, amphetamines, methamphetamines, benzodiazepines, barbiturates, cocaine, MDMA, and methadone.