Neurocognitive and Personality Mechanisms of Risk Behavior among

Drug Users in Protracted Abstinence

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THESIS

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This thesis is dedicated to my father, Richard Wilson. Ja, ich verstehen.

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LIST OF ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
ASI-L	Addiction Severity Index-Lite
BIS-11	Barratt Impulsiveness Scale-11
BW-AQ	Buss-Warren Aggression Questionnaire
CGT	Cambridge Gambling Task
CSD	Center for the Study of Democracy
DRDT	Delayed Reward Discounting Task
DRB	Drug Risk Behavior
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders-Version IV
DV	Dependent Variable
ECDS	European Center for Disease Prevention and Control
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
GST	Go-Stop Task
HIV	Human Immunodeficiency Virus
HRBS	HIV Risk Behavior Scale
IGT	Iowa Gambling Task
IMP	Trait Impulsivity
IMT	Immediate Memory Task
IQ	Intelligence Quotient
IV	Independent Variable

LIST OF ABBREVIATIONS (continued)

MLR	Multiple Linear Regression
PCL:SV	Psychopathy Check List: Screening Version
PSYC	Psychopathy
SES	Socioeconomic Status
SS	Sensation-Seeking
SSS-V	Sensation-Seeking Scale-V
SCID-SAM	Structured Clinical Interview for DSM-IV: Substance Abuse Module
SRB	Sexual Risk Behavior
UNAIDS	The Joint United Nations Programme on HIV/AIDS
UNODC	United Nations Office on Drugs and Crime
USA	United States of America
WHO	World Health Organization
WIAD	Wissenschaftliches Institut der Ärzte Deutschlands/Scientific Institute of the German Medical Association

SUMMARY

Externalizing personality traits are important risk factors for substance dependence with some evidence indicating that Impulsivity (IMP) and Sensation-Seeking (SS) are associated with elevated risk for stimulant dependence and Psychopathy (PSYC) is associated with elevated risk for heroin dependence. Elevated neurocognitive impulsivity is a well-documented consequence of substance dependence that may also influence propensity for risk-taking behavior, with some evidence that reward-based decision-making deficits are preferentially associated with opiate dependence and response inhibition deficits are more severe in stimulant dependence. Unfortunately, previous research on the respective contributions of these personality and neurocognitive risk factors to public health risk behaviors has been constrained by methodological limitations including high rates of polysubstance use in drug user samples and pooling together of users in different stages of the addiction cycle. The present study sought to address these limitations by examining associations of externalizing personality and neurocognitive impulsivity variables with risk behaviors in a sample of drug users in protracted (< 1 year) abstinence.

The sample was recruited from Bulgaria, where both heroin and amphetamine addictions are highly prevalent but not often overlapping, providing access to unique samples of relatively "pure" monodependent heroin and amphetamine users as well as polysubstance users. This study also evaluated the hypothesis that residual neurocognitive impulsivity would mediate the association between externalizing personality traits and risk behaviors among drug users in protracted abstinence.

Results indicated that PSYC was the most robust and consistent predictor of risk behavior across all drug users. Different dimensions of the externalizing spectrum were found to correlate with specific neurocognitive impulsivity profiles, such that IMP was linked primarily to impulsive motor responding, PSYC was linked to disadvantageous reward-based decision-making under conditions of cognitive complexity, and SS was linked to advantageous reward-based decision-making under explicit risk conditions and disadvantageous reward-based decision-making under ambiguity. Sexual risk behavior in protracted abstinence was linked to poor decision-making under ambiguity in the context of cognitive complexity, while aggression was linked to motor impulsivity and problem gambling was linked to attentional control. Hypotheses that PSYC would be most strongly associated with risk behaviors among former heroin users were largely confirmed. By contrast, hypotheses that IMP and SS would be most strongly associated with risk behaviors among former amphetamine users were largely disconfirmed, indicating that protracted abstinence may change the personality-risk behavior profile associated with amphetamine dependence but not heroin dependence. Contrary to predictions, neurocognitive impulsivity measures did not mediate associations of externalizing personality traits with risk behaviors, likely owing to amelioration of cognitive deficits with maintained abstinence.

I. Introduction

A. Background

The proliferation and abuse of drugs presents a formidable public health challenge for the global community. Approximately 27 million people currently engage in drug use, which is associated with huge burdens to health care and criminal justice systems worldwide, including up to 253,000 deaths in 2010 and 211,000 deaths in 2011 directly attributable to drug abuse worldwide (UNODC 2012, 2013). Although the presence of the international drug market has stabilized in most industrialized nations over the past century, the scope of the illicit drug trade continues to expand in the developing world, with growth in this sector projected to contribute to a 25% increase in global drug use over the next several decades (UNODC, 2012).

Eastern Europe and Central Asia are among the regions of the developing world currently experiencing the most severe increases in rates of problem drug use, defined as "injecting drug use or long-duration / regular use of opiates, cocaine and/or amphetamines" (EMCDDA, 2013). The recent increase in drug availability in the Balkans is attributable to societal changes following the region's transformation from communism to democracy at the end of the twentieth century. Due to relaxation of authoritarian drug use restrictions and border policing, black market drug trafficking and trade made significant encroachments in multiple Eastern European and Central Asian countries, aided by an influx of foreign capital and reduced social control and government deregulation (Davis, 1994; Estievenart, 2005; Gruszczynska, 2004; Hamers et al., 1997). In particular, heroin trafficking along the

Balkan Drug Route from Afghanistan to Western Europe has increased dramatically in recent years. For example, in the small Eastern European country of Bulgaria, heroin seizures by law enforcement agencies in 2009 amounted to 1.18 metric tons, compared to 0.67 tons seized for the entire United States of America (USA) in the same year (EMCDD, 2010). In accordance with this rise in drug trafficking and parallel increase in domestic drug production, problem drug use has reached epidemic levels in Bulgaria. Heroin accounts for 21% of all drug-related offences recorded by Bulgarian officials, and opiates (primarily heroin, and "street-" methadone) are the primary drugs of choice amongst 97.1% of Bulgarians entering addiction treatment (92.8% among first-time treatment clients). The European Monitoring Centre for Drugs and Drug Addiction (2009) estimates that, in 2008, there were 20,000 to 30,000 problem heroin users in Bulgaria and a prevalence rate of 0.38% in ages 15 and over – much higher than in the USA. The rise in international drug trafficking through the Balkans has been complemented by increased activity of domestic criminal syndicates who operate independently and engage not only in international drug trafficking and resale, but also in domestic production and distribution of illicit drugs, primarily synthetic-type stimulants. Accordingly, an increasing number of clandestine sites of amphetamine production have recently been identified within Bulgaria by law enforcement officials (EMCDDA, 2013).

1. Public Health Consequences of the Balkan Drug Epidemic

Converging reports indicate that multiple ongoing public health crises in Eastern Europe and Central Asia are linked to increased rates of substance abuse, particularly of opiate and stimulant type drugs (EMCDDA 2013; Grund et al., 2009; Jolley et al., 2012; Tavitian-Exley, Boily, & Vickerman, 2013; UNDOC, 2013). Increases in the prevalence of multiple infectious diseases associated with drug use and sexual risk behaviors have been noted in the Balkans over recent decades (Hoover, 2009; Hope, Eramova, Capurro, & Donoghoe, 2013; Magdzik,

2000; Naoumov, 1999; Post et al., 2013; Rhodes et al., 1999; Van Rie et al., 2005; van der Werf, Hollo, & Noori, 2013). Other social and public burdens associated with the rise of drug abuse in this region include elevated rates of problem gambling (Kun, Balazs, Arnold, Paksi, & Demetrovics, 2012; Skokauskas & Satkeviciute, 2007) and increasing levels of crime and incarceration (Gruszczynska, 2004; Pridemore, 2007; Stuckler, Basu, McKee, & King, 2008; Shkolnikov, McKee, & Leon, 2001). Three specific domains of public health problems within this region (but also of significant public health consequence to the larger global community) are elaborated below.

a. <u>Human Immunodeficiency Virus</u>

Perhaps of greatest public health concern, a burgeoning Human Immunodeficiency Virus (HIV) epidemic that has been observed in Eastern Europe and Central Asia over the past decade. Approximately 34 million people worldwide currently live with HIV (UNAIDS, 2012). Globally, HIV infection rates and rates of Acquired Immune Deficiency Syndrome (AIDS) mortality are in decline due to widespread public health initiatives and the proliferation of combination antiretroviral therapies. However, there is a substantial regional variation in HIV outcomes, and some parts of the world have experienced significant increases in both rates of HIV infection and AIDS mortality over the past decade (UNAIDS, 2012), with Eastern Europe demonstrating one of the fastest growing HIV rates in the world (UNAIDS, 2012). Parallel increases in rates of infections transmitted by sexual and drug use risk behaviors such as Hepatitis C (Hoover, 2009; Hope et al, 2013; Magdzik, 2000; Naoumov, 1999) and tuberculosis (Post et al., 2013; Rhodes et al., 1999; Van Rie et al., 2005; van der Werf et al., 2013) have also been observed within this population. This trend is of special concern given that financial resources for the treatment of HIV and other

sexually transmitted infections are relatively scarce within the Balkan countries, and clinical utilization of combination antiretroviral therapy remains low in this region (UNAIDS, 2012).

The increased rates of HIV infection in the Balkans has been attributed primarily and directly to high rates of needle sharing and unprotected sex among adult drug users, especially among heroin and polydrug users (Aceijas, Stimson, Hickman & Rhodes, 2004; Dehne, Khodakevich, Hamers & Schwartländer, 1999; Reekie et al., 2012). The country of Bulgaria serves as an illustrative example of this trend: cases of HIV have increased dramatically in Bulgaria over the past decade, leading to the second highest overall HIV prevalence rate (2.7/100,000 individuals) in Eastern Europe (ECDC/WHO, 2012). Analysis of transmission vectors revealed that in 2011, 44.3% of new HIV cases in Bulgaria were spread via unprotected heterosexual sex, while 31.3% of cases were attributable to injection drug use (Bozicevic, Handanagic, Lepej, & Begovac, 2013). The Bulgarian drug user population has proven to be particularly vulnerable to HIV infection, demonstrating significantly higher observed prevalence rates of HIV (7.1%) relative to all other Eastern European drug user populations monitored by the European Centre for Disease Prevention and Control (Bozicevic et al., 2013; Vassilev et al., 2006).

b. <u>Aggression</u>

Increased rates of community aggression linked to the proliferation of drug abuse represent another critical public health issue affecting both the Balkans and the global community at large (Gruszczynska, 2004; Pridemore, 2007; Stuckler et al., 2008; Shkolnikov et al. 2001). Drug abuse is frequently identified as a direct antecedent to interpersonal aggression. For example, between 24 and 40of violent offenders in the USA report being

intoxicated on drugs of abuse while committing an assault and more than half of intimate partner assaults are reportedly precipitated by drug or alcohol use (BJS, 2004). Similar reports from multiple countries identify reliable links between drug abuse and community violence including the United Kingdom (WHO, 2009); Germany and Spain (Hughes et al., 2008); Canada (Pepler et al., 2002; Walsh et al., 2003); Mexico (Watts & Wright, 1990); Australia (Crilly, Chaboyer, & Creedy, 2004); South Africa (Parry et al., 2005); Brazil (Inciardi & Surratt, 1998); the Caribbean (WIAD, 2006); and China (Xu et al., 2005).

Although precise statistics regarding the national incidence and prevalence of drugs and crime are not widely available from Balkan countries, preliminary research in this region indicate significant growth in violent crime and incarceration rates occurring in parallel with increasing rates of drug abuse (Chervyakov, Shkolinkov, Pridemore, & McKee, 2002; CSD, 2005; Fajnzylbera, Lederman, & Loayza, N. 2002; Meslés, 2004; Walberg, McKee, Shkolnikov, Chenet, & Leon, 1998; Shkolnikov et al. 2001). For example, in the Eastern European country of Bulgaria, a drastic increase in violent crime was observed from 1990 to 1992 during the initial establishment of post-Communist drug trafficking. Accordingly, the overall crime rate in Bulgaria was observed to increase dramatically as a direct result of the drug trade and accompanying criminal activity (CSD, 2007, p. 15):

> By the early 1990s [the Bulgarian government] had effectively lost its monopoly on violence […] in the face of the explosion of criminal activity. By official data, in three years alone (1990-1992), overall street crime increased four times with the rate of some types increasing 10 to 20 times.

In particular, drug-trade related violence escalated dramatically in the 1990s (CSD, 2007) and continues to account for 13% of Bulgarian homicides (*e.g*. 156 killings between 2000 and 2005).

c. Problem Gambling

A third major public health concern linked to widespread drug abuse within Eastern Europe is the spread of problem gambling. Problem gambling is a behavioral addiction characterized by recurrent patterns of compulsive, maladaptive gambling behavior. The addiction process in problem gambling is thought to be underpinned by similar mechanisms to substance use disorders, and the two conditions are frequently comorbid, with up to 30% of substance abusers reporting clinically significant gambling problems (Feigelman, Kleinman & Lesieur, 1996; Steinberg, Kosten & Rounsaville, 1992). Tremendous psychosocial burdens are associated with problem gambling, including high financial debts, loss of productivity, legal difficulties, stress to close relationships, and comorbid psychiatric disorders (Erbas & Buchner, 2012; Ladouceur, Boisvert, Pepin, Loranger, & Sylvain, 1994; Petry, Stinson & Grant, 2005; Shek, Chan & Wong, 2012). Problem gambling represents a serious public health problem globally, with point prevalence rates in North America and Western Europe ranging from one to six percent of the populations (Meyer, Hayer & Griffths, 2009).

Although recreational gambling is very popular in Eastern European countries, very few studies have examined the phenomenology of problem gambling in this population (Meyer et al., 2009; Kun et al., 2012). Preliminary epidemiological data indicate notable rates of problem gambling in Hungary (3.3%; Kun et al., 2012), and Lithuania (13-15%; Skokauskas

et al, 2007). Additionally, researchers have identified a growing problem gambling prevalence rate in Romania over the past decade: a 2002 survey of Romanian teenagers indicating a 7% prevalence rate (Lupu, Onaca, & Lupu, 2002), whereas a similar survey ten years later detected a 27% prevalence rate (Lupu & Todirita, 2013). Such trends are expected to continue across Eastern Europe due to the "unprecedented deregulation of gambling" (Fisher & Griffiths, 1995, p. 1) in Balkan countries at the beginning of the twenty-first century.

Further empirical research in native Balkan samples is needed to better understand the impact of problem gambling (Likops & Taube, 2008; Skokauskas, 2009; Tsytsarev & Gilinsky, 2009; Zivny & Okruhlica, 2009). For example, despite its status as one of the most "well-established gaming markets [in Eastern Europe]" (Meyer et al., 2009, p. 14) the country of Bulgaria has received very little research attention from problem gambling investigators. According to Meyer and colleagues (2009) "almost nothing is known empirically about gambling and problem gambling in Bulgaria" (p. 14) despite the presence of multiple societal factors indicating that problem gambling is likely to be prevalent within this country's population, including a high number of legal gambling outlets (e.g. 15,400 known gambling machines as reported by the Bulgarian Trade Association of Manufacturers and Operators in the Gaming Industry, 2008) and a 20% growth in the recreational gambling sector as of 2007 following Bulgaria's acceptance into the European Union (Meyer et al., 2009). Accordingly, a Bulgarian government initiative is currently underway to boost the tourism industry by constructing a large number of hotel casinos in the Bulgarian capital of Sofia (Meyer et al., 2009, and documents drafted by the Bulgarian State Gambling

Commission (2008) focus on directives for prevention and treatment of problem gambling within the local community (Meyer et al., 2009).

2. Implications of Drug-Related Health Problems in the Balkans for Clinical Research

Due to the alarming public health trends accompanying the proliferation of drugs in Eastern Europe, scientific investigations of causal mechanisms between drug use and risk behaviors within these populations are needed, to develop effective interventions and to inform relevant legal and public health policy. Although comprehensive system-level interventions aimed at reducing the marginalization of at-risk populations for drug abuse and risk behaviors will likely be an important factor in reducing the overall prevalence of public health problems in the long-term, it is nonetheless a clinical research priority to identify reliable individual difference factors which function as proximal mechanisms of health risk behaviors in these populations (Krueger, Caspi, & Moffitt, 2001). Given that available resources for treatment and prevention of public health problems are scarce in the Balkans (UNAIDS, 2012), identifying accurate clinical markers of potential for risk behavior within this population is particularly imperative for timely and cost-effective interventions. Unfortunately, there has been little research to date on the functional relationship between drug abuse and risk behaviors in this population despite their current epidemic levels of problem drug use and associated public health problems.

B. A Dual Process Framework for Assessing Propensity for Risk Behavior

Two empirically validated risk factors related to the increased propensity for risk behavior in addicted populations are (a) neurocognitive changes secondary to drug use and (b) elevated presence of externalizing personality traits. Chronic drug use has been shown to cause long-term functional changes in the brains of drug users; therefore, the cognitive neuroscience approach of characterizing drug-related neurocognitive changes offers one promising avenue of research for

identifying and characterizing potential mechanisms underlying the relationship between drug abuse and health risk behaviors. Complicating the theoretical relationship between neurocognitive changes and drug abuse is the fact that not all drugs of abuse are associated with identical neurocognitive deficits, despite the fact that neurocognitive changes to common brain systems are involved in all forms of addictive behavior. Although these differences may be influenced in part by pharmacological differences between different classes of drugs of abuse, there is ample evidence to suggest that premorbid individual differences in externalizing personality traits may differentially influence the motivation to pursue a specific drug of abuse. Neurocognitive differences associated with these premorbid externalizing traits may therefore partly explain differences in neurocognitive performance observed between users of different classes of drugs. Thus, quantification of externalizing personality factors is hypothesized to provide both a means of estimating potential for risk behavior prior to the initiation of drug abuse *and* an individual difference factor which may explain variations in the severity of disinhibited behavior observed among users of different classes of drugs. When employed in conjunction with measures of neurocognitive functioning, a rich multi-faceted data set is formed with significant potential to inform clinical interventions.

The integration of both personality and neurocognitive mechanisms represents an attempt to capture the real-world complexity of psychological factors which influence risk behavior among drug users. Several researchers (Barratt & Slaughter, 1998; Llewelyn, 2008) have proposed that due to the multi-faceted nature of impulsivity, integration across disciplines is essential for empirical progress in understanding problems of impulse control. Specifically, Barratt & Slaughter (1998) argue that the true relationship of impulsivity to behavioral disorders such as drug addiction may be studied best with a "discipline neutral" integrative model that combines measurements from biological, social, behavioral,

and psychological/cognitive areas. Following this recommendation, the current study utilizes a multimodal approach towards elucidating relationships of clinically important risk with the ultimate aim of informing more precisely targeted clinical interventions appropriate for individual patients.

The following sections of this proposal will outline the theoretical basis for examining externalizing personality traits and neurocognitive changes as potential mechanisms underlying health risk behaviors linked to drug abuse. Finally, a study is proposed to examine the relationship between externalizing traits, neurocognitive functioning, and three types of risk behavior, as well as to observe the potential moderating effects of specific class of drug of abuse on these relationships. The proposed study will examine drug users currently in protracted abstinence, a clinical population which is understudied and which is ideally suited for providing quantitative data on residual neurocognitive changes. Further, two of the drug user samples to be examined within the current study were previously monodependent on heroin or on amphetamines and will be compared to formerly polysubstance dependent drug users and healthy controls with no history of drug dependence. This unique between-groups design offers an excellent opportunity to examine residual neurocognitive effects secondary to opiate and stimulant dependence without the risk of data contamination due to acute effects of current intoxication, withdrawal, or polysubstance use, an issue which plagues the addiction literature. Of further note, the proposed study will examine neurocognitive performance not only as an outcome variable, as observed in the bulk of the addiction neuropsychology literature, but will also take a step further and test the hypothesis that neurocognitive performance may serve as a functional mechanism of real-world risk behavior in the context of drug abuse.

1. Neuropsychiatric Consequences of the Addiction Process

Chronic drug use causes long-term functional changes in the brains of drug users, which may be related to the increased propensity for risk behavior in addicted populations. Koob & LeMoal (2008) postulate that in the early stages of addiction, users of all types of drugs of abuse experience increased sensitization to the rewarding psychopharmacologic properties of drugs, mediated by the mesocorticolimbic dopaminergic system. This reward sensitization may lead to increased and impulsive consumption driven by *positive reinforcement mechanisms*. As the brains of drug users are repeatedly exposed to hedonic overactivation through chronic drug use, compensatory neuroadaptive changes in the mesocorticolimbic system are initiated which functionally serve to reduce sensitivity to the rewarding properties of drugs and suppress metabolic activity in prefrontal cortical regions which mediate executive control of behavior. These neurocompensatory changes occur in tandem with increased production of stress hormones and dysregulation of the endogenous opioid system, an opponent process to reward sensitization that is thought to be mediated by a postulated 'anti-reward system' with substrates in the extended amygdala (Koob & LeMoal, 2005). Although theorized to function as a homeostatic regulatory mechanism, the neurocompensatory opponent process of the extended amygdala often serves to functionally maintain drug use behavior via *negative reinforcement mechanisms.* Individuals in this later stage of addiction are often motivated to engage in compulsive seeking and use of drugs in order to achieve relief from the chronic aversive internal state mediated by metabolic up-regulation of neurological "anti-reward" systems and down-regulation of reward system functioning (Koob & Lemoal, 2008).

Addiction-mediated reorganization of mesocorticolimbic reward circuitry is associated with reduced neurometabolic functioning of the prefrontal cortex, a brain region which mediates executive cognitive control and behavioral inhibition. Drug users who successfully maintain abstinence from drugs for an extended period of time demonstrate partial recovery of these functional deficits (Selby & Azrin, 1998; Wang et al., 2004), yet this recovery is incomplete, as evidenced by persisting neurometabolic abnormalities, executive cognitive deficits, and high vulnerability to relapse (Sekine et al., 2006; Verdejo-Garcia, Bechara, Recknor, & Perez-Garcia, 2006; Wang et al., 2004). Thus, addiction can be said to cause persistent neurological 'scarring' effects, which manifest in a chronically negative emotional state and decreased executive control, increasing susceptibility to disinhibition of motivational impulses and risky behaviors--even in extended abstinence from drugs (Durazzo et al., 2011; Scott, Dennis, Laudet, Funk, & Simeone, 2011; Li et al., 2013; Yang, German, Webster, & Latkin, 2011; Wilson, Gonzalez, Bozgunov, Vasilev, & Vassileva, 2013). Therefore, empirically informed efforts to reduce public health risk behaviors associated with drug epidemics must include data from individuals in protracted abstinence—putatively the ultimate end state for any successful addiction therapy.

2. Neurocognitive Dimensions of Impulsivity

Standardized, performance-based measures of neurocognitive functioning offer an effective empirical method for quantitatively operationalizing the long-term neurocognitive effects of the addiction process and are well-suited to examining their association with risk behaviors. Although the neuroadaptive processes of addiction are common to all drugs of abuse, comparative analysis of neurocognitive profiles across different groups of relatively 'pure' (*i.e.* monodependent) drug users offers the ability to quantitatively identify selective residual

neurocognitive deficits specific to distinct pharmacological drug classes (e.g. opiates, stimulants) which may differentially influence downstream behavioral functioning (Badiani, Belin, Epstein, Calu, & Shaham, 2011). Neurocognitive measures of *impulsivity* hold particular promise in this regard. Drug user samples reliably demonstrate impulsive performance on neurocognitive tasks sensitive to impulse control deficits, suggesting that addiction-mediated dysregulation of executive cognitive and motor control systems may contribute to the elevated propensities for risk behavior frequently observed among clinical populations of drug users.

Research findings support a nosology of two broad domains of neurocognitive impulsivity mediated by dissociable neuroanatomical substrates sensitive to neuroadaptive reorganization during the addiction process (Haber 2008; Schoenbaum, Roesch, & Stalnaker, 2006; Sonuga-Barke, 2002; Kim & Lee, 2011; Rubia, 2011): affectively mediated *impulsive choice*, defined as unplanned reward-driven behavior characterized by a strong preference for smaller immediate rewards and discounting of larger but temporally delayed rewards (Bickel & Marsch, 2001; Monterosso & Ainslie, 1999) and failure to fully appreciate reward and punishment contingencies in the context of motivational cues (Bechara, Tranel & Damasio, 2000); and affectively neutral *impulsive action*, defined as a tendency towards rapid, premature responses without assessing context and difficulty inhibiting prepotent motor responses (Evenden, 1999; Perry and Carroll, 2008). Impulsive choice is typically operationalized via neurocognitive measures of decision-making, reward-choice, and risk-taking behavior, mediated by paralimbic structures associated with regulation of emotions and motivated behavior including orbital and ventromedial prefrontal cortex, and limbic structures

including the amygdala (Christakou et al., 2009; Hampton, Adolphs, Tyszka, & O'Doherty, 2007; Rubia, Smith, Taylor, & Brammer, 2007; Northoff et al., 2006; Rubia et al., 2006; Rubia, Hyde, Giampietro, & Smith, 2010; Shoenbaum, Roesch, & Stalnaker, 2006). In contrast, impulsive action is measured by neurocognitive tasks of response inhibition mediated by neural networks associated with attentional and timing functions, including inferior frontal, striatal, parietotemporal, and cerebellar systems (Fellows & Farah, Nikalou, Critchley, & Duka, 2013; Arnsten & Rubia, 2012; Rubia, Smith, Brammer, & Taylor, 2003; Rubia, Halari, Christakou, & Taylor, 2009). Drug users commonly evidence poor impulse control on neurocognitive measures of both impulsive choice and impulsive action (Bolla et al., 2003; Hester and Garavan, 2004; Kaufman, Ross, Stein & Garavan, 2003; Perry & Carroll, 2008). Neurocognitive impulsivity has been demonstrated to effectively predict clinically significant risk behaviors among drug using samples, including age of drug use onset (Tarter et al., 2003); frequency and severity of drug use (Shoal & Giancola, 2001); unsafe sexual practices (Gonzalez et al., 2005; Wardle, Gonzalez, Bechara, & Martin-Thormeyer, 2010); and aggression (Fishbein, 2000).

3. Neurocognitive Differences between Opiate and Stimulant Users

In addition to the common neurocognitive effects of addiction-mediated changes across all drugs of abuse, a limited body of comparative evidence suggests parallel differences in neurocognitive impulsivity between stimulant and opiate users. Ornstein et al. (2000) reported that amphetamine and heroin abusers were discriminated by attentional shifting deficits on a task of cognitive control, such that amphetamine users demonstrated weaknesses in extra-dimensional shifting while heroin users demonstrated impaired intra-dimensional shifting. Other research has demonstrated that relative to heroin users, cocaine users show deficits in response inhibition/impulsive action (Verdejo-Garcia et al., 2007). Rogers et al. (1999) also reported that

amphetamine users demonstrate impaired impulsive choice on the Cambridge Gambling Task, a measure of decision-making on which opiate users displayed intact performance, such that extent of prior drug use was selectively associated with poorer decision-making in stimulant users. However, empirical evidence for equivocal neurocognitive functioning across both stimulant and opiate users has also been demonstrated. Specifically, cocaine and heroin users have both demonstrated greater delayed reward discounting relative to alcohol users (Kirby and Petry, 2004) and have demonstrated greater reflection impulsivity than healthy controls (Clark et al., 2006). However, not *all* drug users demonstrate neurocognitive performance deficits, with some reports indicating that as many as one-third of some drug using samples show intact impulse control relative to healthy controls (Bechara & Damasio, 2002; Bechara & Martin, 2004; Vassileva, Georgiev, Martin, Gonzalez, & Segala, 2011). Impulse control deficits acquired during the addiction process may therefore modulate premorbid individual predispositions towards disinhibited behavior among drug users, such as pre-existing externalizing personality traits. Additionally, it is plausible that acquired neurocognitive impulsivity may have an additive effect with externalizing personality traits in predicting risk behavior.

4. The Relationship between Externalizing Personality Traits and Impulsivity

Neurocognitive impulsivity observed among drug users is multifactorial in origin. Two prominent individual difference etiologic factors to consider in this regard are the influence of addiction-mediated neuroadaptive changes as described above, and the influence of premorbid externalizing personality traits. Neurocognitive measures of impulsivity place more emphasis on current, state-dependent functioning and are sensitive to acquired deficits including addiction-mediated neuroadaptive reorganization of the central nervous system. In contrast, measures of externalizing personality traits capture putatively endogenous and

temporally stable propensities for disinhibited and risky behavior that are typically present prior to initiation of drug use and transition to dependence. Individuals with elevated externalizing personality profiles are at high risk for engaging in clinically significant risk behaviors, including drug abuse and dependence (Krueger et al., 2002; Conrod, Peterson & Pihl, 1997), HIV risk behavior (Muchimba et al., 2013; Tourian et al., 1997), aggression (Frick & White, 2008), and problem gambling (Slutske, Caspi, Moffitt, & Poulton, 2005). Systematic investigations of impulsive behavior among drug users (*e.g.* Gerra et al., 2001; Moeller et al., 2002; Morentin, Callado & Meana, 1998) indicate that underlying externalizing personality traits may account for the high propensity towards risk behavior observed among drug using populations.

Premorbid elevations on specific externalizing personality traits may account for the motivational preference for specific drugs of abuse, supported by evidence that distinct externalizing traits are selectively associated with preferences for the reinforcing effects of specific classes of drugs (Conrod, Pihl, Stewart, & Dongier, 2000). Accordingly, variations in neurocognitive profiles between stimulant and opiate users of may also be partly accounted for by pre-existing personality differences across these populations of drug users. Personality traits which are particularly important to consider in this regard are the widely validated constructs of trait impulsivity, sensation-seeking, and psychopathy, which measure relatively distinct aspects of the externalizing spectrum and show associations with both overlapping and distinct neuroanatomical features (Castellanos-Ryan, Rubia, & Conrod, 2011; Robbins, Gillan, Smith, de Wit, & Ersche, 2012; Raine et al., 1997; Rubia, 2011; Sisk & Foster, 2004; Sisk & Zehr, 2005; Soderstrom et al., 2000; Teicher, Andersen, & Hostetter, 1995; Wittman et al., 2011), neurocognitive performance patterns (Castellanos-Ryan et al. 2011; Collins et al., 2012; Fillmore,

Ostling, Martin, & Kelly, 2009; Hunt et al., 2005; Noel et al., 2011; Vassileva et al., 2007, 2011), and risk behavior profiles (Bornovalova et al. 2005; Fischer & Smith, 2008; Fortune & Goodie, 2010; Hayaki et al., 2006; Lejuez et al., 2005; Smith et al., 2007). These three externalizing constructs appear to represent distinct personality mechanisms for motivational preference for use of distinctive drugs of choice—with trait impulsivity and sensation-seeking associated preferentially with stimulant use (Belin, Mar, Dalley, Robbins, & Everitt, 2007; Dalley et al. 2007; McNamara, Dalley, Robbins, Everitt, & Belin, 2010; Robbins et al., 2012) and psychopathy associated preferentially with heroin use (Alterman, Rutherford, Cacciola, McKay, & Boardman, 1998; Compton, Cottler, Shillington & Price, 1995; Hopley & Brunelle, 2012; Rutherford, Cacciola, Alterman, & McKay, 1996; Vassileva et al., 2007, 2011)—as well as a common shared vulnerability to overall problem drug use (Castellanos-Ryan et al., 2011; Gudonis, Derefinko, & Giancola, 2009); polysubstance dependence (Darke, Kaye, & Finlay-Jones, 1998; Hicks, Vaidyanathan, & Patrick, 2010; Kelly & Parsons, 2008), and health risk behavior (Lejuez, Bornovalova, Daughters, & Curtin, 2005; Muchimba et al., 2013; Tourian et al., 1997).

a. <u>Trait Impulsivity</u>

Impulsivity, the "predisposition toward rapid, unplanned reactions to internal or external stimuli without regards to the negative consequences of these reactions" (Moeller, Barratt, Dougherty, Schmitz, & Swann, 2001) is a psychological factor implicated in a wide variety of risk behaviors. Impulsivity is a multidimensional construct that can be operationalized via both state-dependent measures of neurocognitive functioning as described above, and also as a putatively stable trait-like measures of personality across the lifespan. Personality measures of trait impulsivity (IMP) capture a putatively stable, lifelong tendency towards reduced behavioral control, difficulty inhibiting prepotent responses, low

reflectiveness and planning, and a tendency towards rapid decision-making and action regardless of context (de Wit, 2009; Moeller et al., 2001). Neuroanatomical investigations implicate inferior frontostriatal, parietotemporal, insula, and cerebellar systems as neurobiological substrates of IMP (Robbins et al., 2012; Rubia, 2011; Wittman et al., 2011). Personality measures of IMP have reliably been shown to correlate positively with aggression and negatively with neurophysiological and neurocognitive measures of prefrontal cortex function among a wide range of clinical populations, including drug users (Handley et al., 2011), forensic psychiatric patients (Barratt et al., 1997; Dolan & Anderson, 2002), and healthy individuals (Hoaken, Shaughnessy, & Pihl, 2003; Horn, Dolan, Elliot, Deakin, & Woodruff, 2003).

Correlations between IMP and neurocognitive impulsivity are typically modest but statistically significant (Wingrove & Bond, 1997). Both neurocognitive impulse control deficits and IMP predict common and unique variance in risky behavior (Castellanos-Ryan et al., 2011). Therefore, trait measures of IMP and state-dependent neurocognitive impulsivity may reflect overlapping but distinct aspects of externalizing behavioral tendencies that offer the potential for incremental validity in the prediction of risk behavior. Personality measures of IMP have proven to be robust predictors of externalizing psychopathology and risk behavior including initiation of drug abuse (Conrod, Peterson, & Pihl, 1997; Conrod, Pihl, Stewart, & Dongier, 2000), sexual risk behavior (Hayaki, Anderson, & Stein, 2006; Lejuez et al., 2005), aggression (Critchfield, Levy, & Clarkin, 2004; Dumais et al., 2005), and problem gambling (Clarke, 2006; Lai, Ip, & Lee, 2011).

Comparative research across drug user populations indicates that IMP is typically more highly elevated in stimulant than in opiate users (Lejuez et al., 2005; Vassileva et al., 2014). Preclinical studies also support a relationship between IMP and escalation of stimulant use but not opiate use (Belin et al., 2008; Dalley et al. 2007; McNamara et al., 2002). Additionally, converging evidence indicates that stimulant use and IMP are more closely associated with risk behaviors among primary stimulant users as opposed to primary opiate users (Bornovalova et al. 2005; Hayaki et al., 2006; Lejuez et al., 2005). A recent comparative study of the relationship of IMP with neurocognitive measures of impulsive action and impulsive choice across groups of monodependent heroin and amphetamine users in protracted abstinence demonstrated that high IMP was related to better response inhibition efficiency in heroin users but to worse response inhibition in amphetamine users (Vassileva, et al., 2014). Thus, the specific class of drug of abuse may influence the expression of neurocognitive disinhibition across drug user groups. Consistent with this hypothesis, comparative research indicates that stimulant users demonstrate higher impulsive action than opiate users (Verdejo-Garcia et al., 2007). Also, neurocognitive measures of impulsive action but not impulsive choice have been found to mediate the relationship of personality IMP with both antisocial behavior and the development of problem drug use (Castellanos-Ryan et al., 2011). The specificity of impulsive action as a mechanism of the relationship between stimulant use and clinically relevant impulsive behavior is consistent with the conceptualization of personality IMP as a measure of predilection for disinhibited responding regardless of situational context. In comparison, the reward-based, affect-mediated disinhibition captured by neurocognitive measures of impulsive choice is more closely associated with other externalizing traits, such as sensation-seeking and psychopathy.

b. Sensation-Seeking

Sensation-seeking (SS) is a personality construct encompassing a strong need for sensory stimulation, instrumental risk-taking to achieve new experiences, and intolerance of boredom (Zuckerman, 1979, 1996). In contrast to IMP, SS does not encompass a stable tendency towards rapid decision-making and action across all contexts. Instead, high SS is associated with disinhibited behavior *within the context* of motivational reward cues. SS has been shown to predict an array of risky thrill and adventure-seeking behaviors such as extreme sports (Roberti, 2004), interpersonal aggression (Wilson & Scarpa, 2011), and sexual risk behavior (Gonzalez et al., 2005). By contrast, SS has not been reliably linked to problem gambling, but rather to frequency of gambling behavior (Fischer & Smith, 2008; Fortune & Goodie, 2010; Smith et al., 2007).

Personality neuroscience research indicates that limbic and paralimbic brain circuits involved in social and emotional regulation mediate the expression of SS (Sisk & Foster, 2004; Sisk & Zehr, 2005; Teicher et al., 1995). The neuroanatomical substrates of SS, which include the amygdala, ventral striatum, and the orbito- and medial prefrontal cortices, are sensitive to the reinforcing properties of certain drugs of abuse—particularly stimulants and alcohol. Stimulant intoxication elicits increased approach behavior through activation of dopaminergically-mediated reward-seeking, and individuals high in SS may be particularly prone to these behavioral effects (Hoaken & Stewart, 2003; Pihl & Peterson, 1995). Accordingly, SS has proven to be a robust predictor of stimulant and alcohol use (Brunelle et al., 2006; Conrod et al., 2000; Conrod, Peterson & Pihl, 2006; Kelly et al., 2006; Low & Gandaszek, 2002; Stoops et al., 2007) and

polysubstance use with primary stimulant use (Ball, Carroll, & Rounsaville, 1994; Kelly & Parsons, 2008; Lackner, Unterrainer, & Neubauer, 2013; Zuckerman, 1994). SS has been linked to poor impulse control on neurocognitive measures of both impulsive action (Collins et al., 2012; Fillmore et al., 2009) and impulsive choice (Castellanos-Ryan et al. 2011; Noel et al., 2011), which have been shown to influence associations of SS with HIV risk behavior (Gonzalez et al., 2005) and to longitudinally mediate the relationship between SS and drug abuse (Castellanos-Ryan et al., 2011).

c. <u>Psychopathy</u>

The construct of psychopathy (PSYC) includes tendencies towards poor affective processing, manipulative interpersonal behavior, poor impulse controls, and a propensity towards antisociality (Hare, 2003). Identification of psychopathic traits is of extremely high utility in predicting individual potential for future risk behavior, with evidence indicating that violence risk assessments that integrate clinician-administered psychopathy ratings outperform actuarial instruments in predicting violence and criminal recidivism (Harris., Rice, & Quinsey, 1993; Rice & Harris, 1995; Serin, 1996; Zamble & Palmer, 1996). The expression of PSYC is associated with abnormalities in diffuse neuroanatomical networks, including regions that overlap with neural substrates of SS, (*e.g.* orbitofrontal cortex and amygdala; Kiehl et al., 2001; Muller et al., 2003), as well as in distinct anatomic regions (*e.g.* corpus callosum and angular gyrus; Raine et al., 1997; Soderstrom, Tullberg, Wikkelso, Ekholm, & Forsman, 2000). Psychopathic individuals reliably demonstrate focal neurocognitive deficits in impulsive choice but not impulsive action (Blair et al., 2001; Mitchell, Colledge, Leonard, & Blair, 2002; Vassileva et al., 2007, 2011). Individuals with high levels of PSYC are overrepresented among violent offender populations and engage in

disproportionate levels of public health risk behaviors including unsafe sexual practices (Tourian et al., 1997), aggression (Hare, 2003), and problem gambling (Blaszczynski, Steel & McConaghy, 1997; Steel & Blaszczynski, 1998). PSYC has been widely implicated as a risk factor for problem drug use primarily due to affectively-mediated impulse control deficits and punishment insensitivity (Gudonis et al., 2009; Hart, Hemphill, & Hare, 1994). In particular, psychopathic traits have been linked to injection drug use, especially heroin use (Alterman et al. 1998; Compton et al. 2012; Rutherford et al., 1996; Vassileva et al., 2007, 2011). PSYC is also often elevated among polysubstance using populations with primary opiate use (Darke et al., 1998; Hicks et al. 2010; Piotrowski, Tusel, Sees, Banys, & Hall, 1996).

5. Dual Process Mechanisms of Risk Behavior: Neurocognition and Personality

Clinical prediction of risk behaviors among drug users is likely to be most effective if measures of personality and neurocognitive functioning are integrated (Barratt et al., 1998; Llewellyn, 2008). The research framework summarized above suggests the utility of a dual systems approach to measuring propensity for risk behavior in drug using populations: externalizing personality constructs may be deployed as measures of premorbid tendencies towards disinhibited and risky behavior, whereas performance on neurocognitive impulsivity paradigms provide objective measures of current behavioral functioning that may reflect acquired neurocognitive deficits secondary to the addiction process in addition to the influence of premorbid psychological characteristics. The utilization of a multimodal approach to risk prediction may be particularly important in light of evidence that patterns of neurocognitive impulsivity differ across users of distinct drug classes such as opiates and stimulants (Badiani, et al. 2011). As mentioned above, previous comparative research has indicated that

stimulant users demonstrate greater impulsive action than opiate users (Verdejo-Garcia et al., 2007), while elevations in impulsive choice have been observed across both stimulant and opiate users (Bornovalova, Daughters, Hernandez, Richards, & Lejuez, 2005; Rogers et al., 1999; Verdejo-Garcia et al., 2007). Findings of overlapping yet distinct neurocognitive profiles across stimulant and opiate users are believed to be at least partly related to underlying externalizing personality profiles, such as variations in externalizing personality traits across groups. Psychopathy has been linked specifically to impulsive choice on neurocognitive tasks (Blair et al., 2001; Mitchell et al., 2002; Vassileva et al., 2007, 2011). In contrast, SS has been linked to both impulsive action (Collins et al., 2012; Fillmore et al., 2009) and impulsive choice (Castellanos-Ryan et al., 2011; Noel et al., 2011), while IMP has been most consistently associated with impulsive action (Castellanos-Ryan et al., 2011, Verdejo-Garcia et al., 2007).

Interestingly, computational modeling analysis of one of the most common neurocognitive measures of impulsive choice (*i.e.,* the Iowa Gambling Task) revealed that decision-making performance of groups of monodependent heroin and amphetamine users in protracted abstinence was characterized by distinct neurocognitive processes. Specifically, monodependent amphetamine users demonstrated heightened reward sensitivity on the IGT (analogous to reward-seeking in SS), whereas monodependent heroin users manifested decreased loss aversion (Ahn et al., 2014). These findings are in line with other evidence linking trait SS preferentially to stimulant dependence (Hutchison, Wood, & Swift, 1999; Kelly et al., 2006; Low & Gandaszek, 2002; Stoops et al., 2007; Zuckerman, 1979) and psychopathic traits preferentially to opiate dependence (Darke et al. 1998; Compton et al. 1995; Piotrowski et al.1996; Rutherford et al. 1996; Vassileva et al. 2007, 2011), and may in part reflect

elevated levels of these personality traits within each respective monodependent drug user group (Ahn et al., 2014).

C. Rationale for the Present Study

Despite the body of evidence linking externalizing personality traits and neurocognitive impulsivity as individual risk factors relevant to the prediction of risk behavior, to our knowledge no previous studies have systematically compared associations of these individual risk factors with salient public health risk behaviors across groups of chronic users of different classes of drugs. Consequently, variations in the relationships between personality and neurocognitive risk factors and health risk behaviors as a function of specific drug class remain poorly understood. Given that externalizing personality traits appear to partially explain links between drug abuse and health risk behavior, it is plausible that neurocognitive changes resulting from the addiction process may mediate the relationships of premorbid externalizing personality traits and risk behavior. As mentioned previously, response inhibition deficits on neurocognitive tasks have been found to mediate the relationships of IMP and SS with substance abuse and antisocial behavior outcomes in a longitudinal study of adolescents (Castellanos-Ryan et al., 2011). These findings support the hypothesis that residual neurocognitive impulsivity secondary to neuroadaptive changes from the addiction process may serve as a mechanism for the elevated behavioral manifestation of impulsive, compulsive, and aggressive behavioral states observed in abstinent drug users long after cessation of regular drug use.

In addition to the dearth of studies comparatively examining risk behavior mechanisms across drug user groups, another limitation of the extant literature is that available studies rarely specify the particular stage of the addiction cycle of their participants (*i.e.* initiation of drug use; abuse; dependence; acute intoxication; withdrawal; protracted abstinence). Studies of drug users may

pool together participants at different stages of the addiction cycle, precluding extrapolation of neurocognitive data to clinical subpopulations due to the sensitivity (but not specificity) of neurocognitive tasks to such factors as acute intoxication, withdrawal, and polysubstance use. Studies which have explicitly examined drug users in protracted abstinence may be further complicated methodologically by the presence of current drug use in the form of opioid substitution therapy. Additionally, high rates of polysubstance use are ubiquitous among published studies of drug user samples, even when the goal of the research is to understand the effects of individual classes of drugs (*e.g.* Bond, Verheyden, Wingrove, & Curran, 2004; Sekine et al., 2006). Therefore observed neurocognitive and behavioral patterns cannot necessarily be associated with one particular substance of abuse, limiting the potential for matching appropriate interventions to specific drug user attributes. Finally, virtually no studies have examined mechanisms of risk behavior among drug users in protracted abstinence, despite the preponderance of evidence indicating that this population remains at high risk for drug use relapse and other health risk behaviors.

The proposed study will utilize the theoretical framework articulated above to examine relationships between candidate personality and neurocognitive mechanisms of health risk behaviors among demographically representative samples of problem drug users. The study sample was recruited from the Eastern European country of Bulgaria, where both heroin and amphetamine addictions are highly prevalent but not often overlapping, providing access to unique samples of relatively "pure" monodependent drug users. Additionally, all participants recruited for this study were in protracted abstinence from drug use, allowing a rare opportunity to assess for potential residual neurocognitive effects of pure heroin or stimulant dependence outside of the context of acute drug intoxication or withdrawal. This study proposes to investigate the relationships

between three externalizing personality traits: trait impulsivity (IMP); sensation-seeking (SS); and psychopathy (PSYC); with four dimensions of clinically significant risk behaviors relevant to the ongoing public health difficulties in Eastern Europe and Central Asia: HIV risk behaviors, including unsafe sexual practices and risky injection drug use behaviors; interpersonal aggression; and problem gambling. The study will examine the role of endogenous (*i.e.*, neurocognitive impulsivity) and exogenous (*i.e.*, drug class) mechanisms as potential mediators and moderators of these relationships. Specifically, it is hypothesized that individual differences in performance on neurocognitive tasks of impulsive choice and impulsive action will mediate the relationships between specific externalizing personality traits and specific types of risk behavior. Pharmacologic drug class (heroin, amphetamine, polysubstance) of past dependence is expected to moderate these relationships. We propose to address the following specific aims:

1. **Aim 1: Evaluate the relationships between externalizing personality traits, neurocognitive performance, and risk behaviors**

    a. **Aim 1 Hypotheses**

    IMP and psychopathy are predicted to demonstrate positive associations with all risk behaviors, whereas SS is predicted to demonstrate positive associations with HIV risk behaviors and aggression. Externalizing personality traits are predicted to demonstrate associations with neurocognitive dimensions of impulse control, such that: IMP will be selectively associated with impulsive action; SS will be associated with impulsive choice and impulsive action; and psychopathy will be selectively associated with impulsive choice. Neurocognitive dimensions of impulse control are predicted to demonstrate selective associations with risk behaviors, such that: impulsive choice will be associated with HIV risk

behaviors and problem gambling; and impulsive action will be associated with aggression and problem gambling.

2. **Aim 2: Evaluate whether specific drug class moderates the relationships between personality traits, neurocognitive performance, and risk behaviors**

   a. **Aim 2 Hypotheses**

When examining moderating effects of heroin on associations between externalizing traits and risk behaviors and between externalizing traits and neurocognitive impulsivity, associations of PSYC and dependent variables (DVs) are predicted to be strongest among heroin users. When examining moderating effects of heroin on associations between neurocognitive impulsivity and risk behaviors, associations of impulsive choice with DVs are predicted to be strongest among heroin users. When examining moderating effects of amphetamine on associations between externalizing traits and risk behaviors and between externalizing traits and neurocognitive impulsivity, associations of both SS and IMP with DVs are predicted to be strongest among amphetamine users. When examining moderating effects of amphetamine on associations between neurocognitive impulsivity and risk behaviors, associations of impulsive action with DVs are predicted to be strongest among amphetamine users.

3. Aim 3: Determine whether neurocognitive performance mediates the relationship between externalizing traits and risk behaviors.

a. Aim 3 Hypotheses

Neurocognitive dimensions of impulse control are predicted to mediate specific relationships between externalizing traits and risk behaviors, such that: impulsive choice will mediate associations of SS with HIV risk behaviors; impulsive choice will mediate associations of psychopathy with HIV risk behaviors and problem gambling; impulsive action will mediate relationships of IMP and SS with aggression; and impulsive action will mediate the relationship of IMP with problem gambling. Potential moderating effects of specific drug class on observed mediated relationships will be evaluated in an exploratory fashion.

II. Methods

A. Study Participants and Recruitment

Study participants were recruited in Sofia, Bulgaria as part of a large-scale study on addiction and impulsivity conducted at the Bulgarian Addictions Institute. The study was advertised through flyers placed in community substance abuse clinics and social venues including night clubs, bars and cafes. Participants were screened via telephone or in-person by structured interview assessing basic medical and substance use histories. Study protocol was approved by the Institutional Review Boards of the University of Illinois at Chicago and Medical University in Sofia. All participants provided informed consent. The study protocol consisted of two 3.5- hour sessions. All assessment instruments were translated iteratively into Bulgarian and back-translated into English until a consensus was reached on the final versions of the instruments. Participants were paid 80 Bulgarian Leva (≈US$50) for their participation in the study.

Study inclusion criteria consisted of: (a) age of 18-50 years; (b) minimum completion of eighth grade education; (c) estimated IQ > 75; (d) no history of neurologic/neuropsychiatric illness; (e) no history of penetrating head injury or closed head injury with loss of consciousness > 30 minutes; (f) no current mania or major depression; (g) negative breathalyzer test for alcohol and negative rapid urine toxicology screen for opiates, cannabis, amphetamines, methamphetamines, benzodiazepines, barbiturates, cocaine, MDMA, and methadone. All participants were HIV-seronegative as determined by rapid HIV testing. No participants were currently on opioid substitution therapy.

B. Assessment of Substance Use History

Detailed substance use histories were obtained using the substance abuse module of the Structured Clinical Interview for DSM-IV-Axis I Disorders (SCID-SAM; First, Spitzer, Gibbon Williams, 1996). Inclusion criteria for drug users included a lifetime history of DSM-IV substance dependence on either heroin or amphetamines. Participant substance use history was corroborated via the Addiction Severity Index-Lite (ASI-L; McLellan, Cacciola, & Zanis, 1997) a semi-structured interview assessing history of recent (i.e., past 30 days) and lifetime substance use characteristics. Inclusion criteria for healthy controls (*n* = 102) included no history of dependence on alcohol or any other drugs of abuse. Drug users (total *n* = 205) were designated as either amphetamine monodependent (*n* = 50); heroin monodependent (*n* = 63); or polysubstance dependent (*n* = 78). Length of abstinence in days was recorded via self-report. All drug users met criteria for protracted (*i.e.* > 1 year) abstinence from substance dependence at the time of the study, as determined by the SCID-SAM. The total sample consists of 293 participants.

C. Neurocognitive Assessment of Impulsive Choice

1. Iowa Gambling Task

The Iowa Gambling Task (IGT; Bechara et al. 2000) is a computerized measure of decision-making under uncertainty which involves learning task contingencies by trial-and-error. Participants are given $2000 to start and are presented with four decks of cards. They are instructed to select cards freely from the four decks in order to maximize earnings over the course of 100 trials. Decks A and B are associated with higher rewards, providing an average profit of $100 per trial, but also higher occasional penalties, resulting in an average net loss of $250 every ten trials. In contrast, Decks C and D yield lower rewards,

providing an average profit of $50 per trial, but lower occasional penalties, resulting in an average net gain of $250 every ten trials. Thus, selecting from Decks A and B represent a disadvantageous long-term strategy despite providing higher immediate rewards, while Decks C and B represent a more advantageous long-term strategy despite providing lower immediate rewards. The total number of advantageous - disadvantageous deck selections across all trials will be used as the performance measure.

2. Cambridge Gambling Task

The Cambridge Gambling Task (CGT) is a computerized subtest from the Cambridge Neurocognitive Test Automated Battery (Sahakian et al., 1988) designed to assess decision-making and risk-taking. In contrast to the IGT, the CGT does not involve learning of task contingencies as subjects are explicitly informed of the odds associated with each choice. The examinee is presented with 10 boxes, each colored red or blue, and is instructed to guess if a token is hidden under a red box or a blue box. The ratios of red: blue boxes vary from 1:9 to 9:1 in pseudorandom order. Participants earn points based on correct performance and must also gamble some points based on the confidence of their decisions by selecting from an array of possible bets ranging from 5% to 95% of their points, presented in descending and ascending order. Participants who wish to make a high-risk bet can do so immediately in the descending condition but must wait for the possible bet proportion to increase over time in the ascending condition (Manes et al, 2002); thus, unlike the IGT, the CGT dissociates risk-taking from impulsivity in the ascending condition. The CGT yields several performance indices representing distinct facets of decision-making that will be examined in the present

study, including risk-taking (*i.e.*, mean number of points wagered when the most likely outcome is selected); risk adjustment (*i.e.* mean risk-taking score for both the ascending and the descending conditions), and delay aversion (*i.e.* total difference between risk-taking scores in the ascending and descending conditions).

3. Balloon Analogue Risk Task

The Balloon Analogue Risk Task (BART; Lejuez et al., 2002) is a computerized task of decision-making in which a high-risk approach produces diminishing returns and a higher likelihood for poorer outcomes. Participants simulate pumping air into a balloon with the click of a mouse and earn money based on how full they can pump a balloon without breaking it. The odds of a balloon breaking non-randomly increase with each pump. Specifically, the odds of a balloon breaking on the first trail are 1:128, on the second trial 1:127, and so on until the balloon breaks or the participant reaches the 128^{th} trial, at which point the balloon is guaranteed to explode. With each pump, the balloon inflates slightly and participants win $0.05. The participant can select to take the amount of money earned from the balloon at any time; when this option is selected, their current earnings are added to their total earnings and a new trial begins; participants complete a total of ten trails. If the balloon explodes before the participant collects their earnings, they gain no additional funds. Each pump on a particular balloon trial increases earnings and decreases the chance that an additional pump will be advantageous; on average, balloons explode after 64 pumps. The performance measure from the BART is the adjusted average number of pumps across balloons that did not explode.

4. Delayed Reward Discounting Task

The tendency to discount the value of delayed rewards was assessed via the Monetary Choice Questionnaire (Kirby, Petry & Bickel, 1999), a delayed reward discounting task (DRDT)

which consists of 27 choices between smaller rewards available at the day of testing and larger rewards available in the future, with delay intervals ranging from one week to six months. The DRDT performance measure is the discount-rate parameter, *k*. The discount-rate parameter is computed via Mazur's (1987) hyperbolic discount function V = A/[1 + *k*D]. V is the present value of reward A. Delay D is the delay at which reward A is available..

D. Neurocognitive Assessment of Impulsive Action

1. Go/No-Go Task

The Go/No-Go task (Lane, Moeller, Steinberg, Buzby, & Kosten, 2007) is a computerized task assessing response inhibition. A series of two-element visual stimuli arrays are presented on the screen for 500ms and examinees are instructed to respond only when the elements are identical (Go) and to inhibit responding when the stimuli do not match (No-Go). On No-Go trials, the position (left or right) of the No-Go stimulus element was randomly determined, requiring the examinee to scan both stimulus elements. The performance measure to be used will be the sensitivity index *d'*, measuring the ability to discriminate between target and non-target stimuli.

2. Go-Stop Task

The Go-Stop Task (GST; Dougherty, Mathias, Marsh, & Jagar, 2005) is a computerized stop-signal paradigm. Examinees are presented with a series of five-digit numbers displayed for 500ms each and are instructed to respond when a stimulus is identical to the previous display (Go trial). Additionally, examinees are instructed to withhold responding when the stimulus matches but changes color from black to red (Stop trial). Stop-signals occurred at 50, 150, 250, or 350ms delay intervals from stimulus onset. The performance measure used was the mean

ratio of inhibition failures on Stop trials to correct performance on Go trials collapsed across delay intervals.

3. Immediate Memory Task

The Immediate Memory Task (IMT; Dougherty, Marsh, & Mathias, 2002) is a computerized continuous performance test of high difficulty and sensitivity (Dougherty, Marsh, Moeller, Chokshi, & Rosen, 2000). A series of five-digit numbers are shown for 500ms each, with examinees instructed to respond only if a stimulus is identical to the preceding display. Participants are presented with three target types in approximately equal proportions: correct targets, where the display matches the preceding display; non-target filler trials, where the display numbers clearly do not match the preceding display; and non-target catch trials, where the display numbers vary from the preceding display only by one digit. The performance measure *(d'*) is an index of the ability to discriminate between correct targets and non-target catch trials.

E. Assessment of Externalizing Personality Traits

1. Trait Impulsivity

Trait Impulsivity (IMP) was assessed with the Barratt Impulsiveness Scale (BIS-11; Patton, Stanford and Barratt 1995), a well-validated 30-item self-report questionnaire. Examinees read statements describing themselves and rate their agreement on a 4-point scale. The BIS-11 yields a total trait impulsivity rating underpinned by three dimensions: motor impulsivity (i.e., acting without thinking and difficulty persevering; e.g. “I act on the spur of the moment”); attentional impulsivity (i.e., difficulty concentrating and cognitive instability; e.g. “I am restless at the theater or at lecture”); and non-planning impulsivity (i.e., lack of forethought and

aversion to cognitive complexity; e.g., “I say things without thinking”). Full-scale BIS-11 scores will be used as independent variables in analyses, while relationships of BIS-11 sub-traits to dependent variables will be examined in follow-up analyses on a post-hoc basis.

2. Sensation-Seeking

Participant levels of trait Sensation-Seeking (SS) were assessed via the Sensation-Seeking Scale-V (SSS-V; Zuckerman, 1994), a widely validated self-report measure with good psychometric properties. The SSS-V consists of 40 forced-choice items which measure a unitary SS construct underpinned by four factors: disinhibition (i.e., desire for social and sexual disinhibition; e.g. “I like wild “uninhibited” parties”); boredom susceptibility (i.e., aversion to repetition or routine; e.g. “I can’t stand watching a movie that I’ve seen before”); thrill and adventure seeking (i.e., desire to engage in sports or activities involving speed and danger; e.g. “I often wish I could be a mountain climber”); and experience-seeking (i.e., desire for experience through the mind and sense, travel, and a non-conforming lifestyle; e.g. “People should dress in individual ways even if the effects are sometimes strange”). Full-scale SSS-V scores will be examined as predictor variables in analyses.

3. Psychopathy

Participant psychopathy levels were assessed using the Psychopathy Checklist: Screening Version (PCL:SV; Hart, Cox & Hare, 1995), which has been validated in a Bulgarian community sample (Wilson et al., 2014). The PCL:SV is a 12-item scale based on the 20- item PCL-R (Hare, 1991, 2003) that is rated by trained observers following a semi-structured interview of the participant. Interviews were conducted by a trained team of research assistants and clinicians at the Bulgarian Addictions Institute. Initial training in psychopathy assessment was provided by doctoral-level trainers with substantial clinical and research experience in psychopathy

assessment. The PCL:SV is divided into two six-item factors. Factor 1 assesses a manipulative interpersonal style and deficient affective experience, whereas Factor 2 measures an unstable, impulsive and antisocial lifestyle. Full scale PCL:SV scores will be examined as independent variables in statistical analyses.

F. Assessment of HIV Risk Behaviors

1. HIV Risk Behavior Scale

The HIV Risk Behavior Scale (HRBS; Petry, 2001) is an 11-item questionnaire assessing drug risk behavior (DRB) and sexual risk behavior (SRB), scored on a 6-point scale. We administered both the *past 30 days* and *lifetime* versions of the HRBS. All drug users were in protracted abstinence, which rendered the past 30-days DRB index insensitive to between-group differences ($F(3, 276) = 0.96$, $p > .40$). Thus, only lifetime DRB data from the HRBS will be included in further analyses. Sample items from the HRBS include: "How many people, including clients, have you had sex with?" and "How often did you use condoms when you had sex with casual partner(s) in the past 30 days?"

2. Knowledge of Safe Sexual Practices

Participant knowledge of safe sexual practices was assessed by a self-report scale developed for use with Eastern European populations (Amirkhanian et al., 2001). Seven items assess the respondent's awareness of sexually transmitted infections and effective risk reduction steps (*e.g.* condom use). This measure will be used to determine whether knowledge of safe sexual practices influences any observed between-group differences in HIV risk behavior.

G. Assessment of Aggression

Aggression was assessed with the Buss-Warren Aggression Questionnaire (BW-AQ; Buss & Warren, 2000), a self-report clinical assessment instrument comprised of 34 items answered on a Likert-type scale. The BW-AQ is the latest version of the Buss-Durkee/Buss-Perry Aggression Questionnaire, the most widely used self-report measure of aggression (Buss & Warren, 2000). The instrument measures five theoretically distinct forms of aggression: (a) *physical aggression* (i.e., physical expression of anger; e.g. "I may hit someone if he or she provokes me"); (b) *verbal aggression* (i.e., argumentative style and use of hostile language; e.g. "My friends say that I argue a lot"); (c) *anger* (i.e., agitation and a need for sense of control; e.g. "I let my anger show when I do not get what I want"); (d) *hostility* (i.e., resentment, social isolation, and paranoia; e.g. "I wonder what people want when they are nice to me"); and (e) *indirect aggression* (expression of anger without direct confrontation; e.g. "I sometimes spread gossip about people I don't like"). Total BW-AQ scores will be employed as a dependent variable in analyses.

H. Assessment of Problem Gambling

Symptoms of lifetime problem gambling were indexed using the gambling subscale of the Addiction Severity Index-Lite (ASI-L; Cacciola, Alterman, McLellan, Lin, & Lunch, 2007; Petry, 2003) and DSM-IV criteria (APA, 2000). The ASI-L is completed by a trained research assistant during a semi-structured interview. Examinees reported difficulties over their lifetime and past 30 days on a five-point ordinal rating scale. In addition to problem gambling, life domains assessed by the ASI-L include medical history, employment/financial support (including Hollingshead socioeconomic status), drug and alcohol use, legal problems, family/social support, and psychiatric conditions.

I. Data Analytic Plan

All analyses were conducted in SPSS v21.0. The alpha level for statistical significance was set at p = .05. All continuous variables were centered to reduce multicollinearity. Prior to running analyses, demographic variables that did not systematically vary as a function of participant group (Miller & Chapman, 2001) were examined as potential covariates via a series of bivariate correlations with predictor variables (*i.e.*, drug user type, externalizing personality traits) and dependent variables (*i.e.*, SRB, DRB, aggression, and problem gambling). Non-normally distributed variables were subjected to log10 or square root transformation as needed to approximate normality. Demographic variables which correlated significantly with both independent and dependent variables and did not vary as a function of participant group (Miller & Chapman, 2001) were entered as covariates during analyses. Potential covariates that were examined included years of education, estimated intelligence quotient (IQ) from Raven's Progressive Matrices (Raven, Raven, & Court, 2004), socioeconomic status as estimated by the ASI-L, years of prior drug use, and length of abstinence from drug use.

1. Aim 1 Analyses

The first aim of analyses was be to evaluate the simple relationships between externalizing personality traits, dimension of neurocognitive impulsivity, and risk behaviors. A series of covariate-adjusted partial correlations were calculated to assess the strength of associations between: externalizing personality traits and risk behaviors; externalizing personality traits and measures of neurocognitive impulsivity; measures of neurocognitive impulsivity and risk behaviors. When a series of significant relationships between specific externalizing personality traits, measures of neurocognitive impulsivity, and risk behaviors were identified, these relationships were the basis for constructing mediation models tested in Aim 3 (see below).

2. Aim 2 Analyses

The second aim of analyses was to evaluate the moderating effects of previous dependence on specific classes of drugs (*i.e.* heroin and amphetamine) on the relationships between externalizing traits and risk behaviors; externalizing traits and dimensions of neurocognitive impulsivity; and dimensions of neurocognitive impulsivity and risk behaviors. Multiple linear regression (MLR) models were computed by entering conditional main effects of drug class and either externalizing traits or dimensions of neurocognitive impulsivity as predictor variables. Additionally, two-way interaction terms (i.e. externalizing trait × drug class or neurocognitive impulsivity dimension × drug class) were simultaneously entered as predictor variables.

All continuous variables were standardized and centered (*i.e.* converted to Z-scores based on full sample means) to reduce potential multicollinearity and to ease interpretability when computing interaction effects. Interaction terms were created by multiplying continuous predictor variables (*i.e.* externalizing personality trait or neurocognitive impulsivity dimension) with contrast-coded categorical drug class variables (coding: 1 = drug user group, -1 = healthy control). Significant two-way interactions were followed up by plotting the simple slopes of associations between continuous predictor variables and dependent variables at both levels (*i.e.* drug user or healthy control) of categorical drug class moderator variables.

3. Aim 3 Analyses

Measures of neurocognitive impulsivity were evaluated as a potential mediator of associations between externalizing traits and risk behaviors. According to Baron & Kenny (1986), conducting formal tests of mediation first requires that statistically significant linear

relationships are demonstrated between: the independent variable (IV) and the dependent variable (DV); the IV and the candidate mediator; and the candidate mediator and the DV. Therefore, once significant associations between the IV (*i.e.* externalizing personality trait), candidate mediator (*i.e.* neurocognitive impulsivity parameter), and DV (*i.e.* risk behavior) have been established, formal tests of mediation may be conducted. In order to test for mediation, the effect of the IV on the DV should be computed while controlling for the mediator pathway. If the absolute size of the effect of the IV on the DV is significantly reduced by controlling for the mediation pathway, partial mediation has occurred, while if the effect is reduced to zero, complete mediation has occurred.

Mediation models for Aim 3 were computed using the PROCESS macro for SPSS (Hayes, 2013) which can accommodate up to 10 mediators in parallel. PROCESS mediation analyses utilized 5,000 sample bootstrapping and 95% bias-corrected and accelerated confidence intervals for estimating mediation effects. If significant mediation effects were observed, potential moderating effects of drug classes on these mediated relationships would be examined in an exploratory fashion via follow-up moderated multiple-mediation analyses in PROCESS. A conceptual model detailing the statistical relationships examined in Aim 3 is presented below in Figure 1.

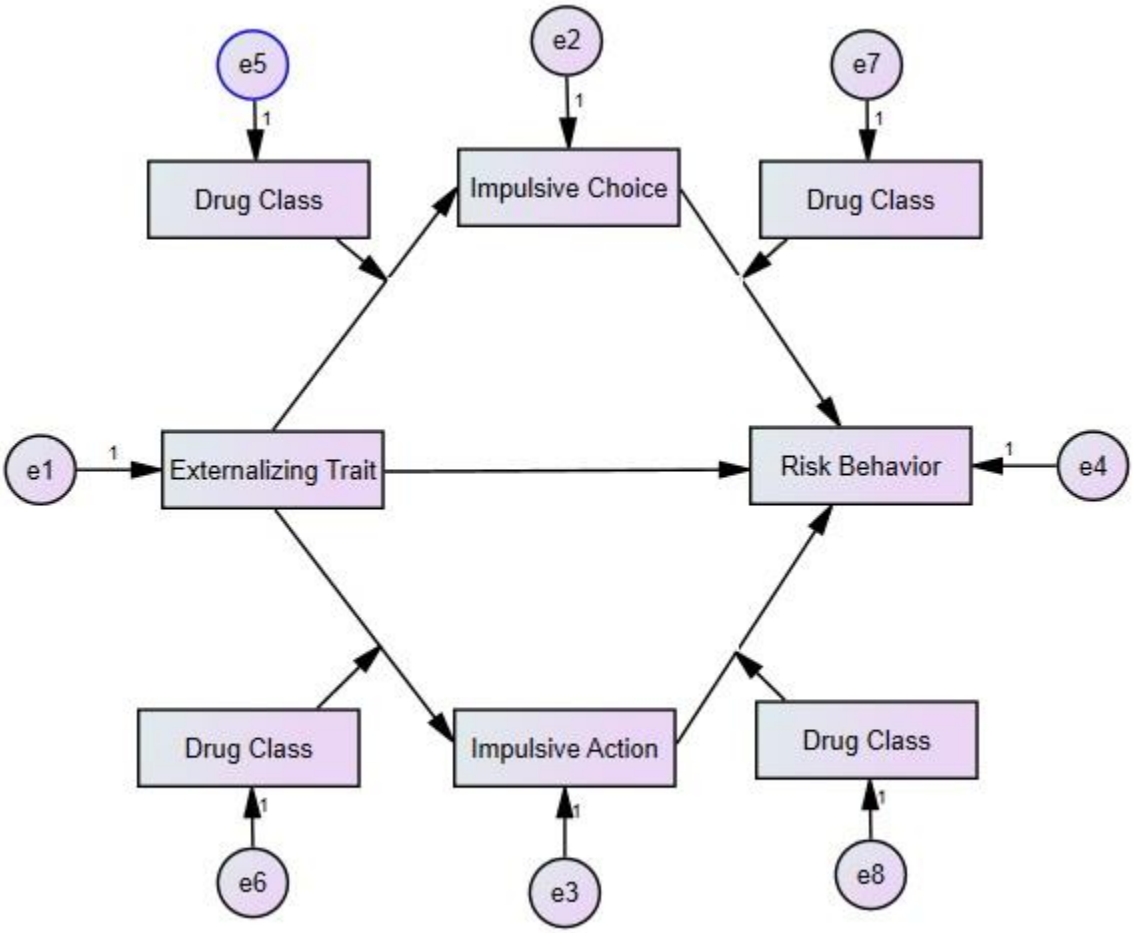

Figure 1. Conceptual model of Aim 3 data analyses.

III. Results

A. Demographics

Participant characteristics are presented in Table I (basic demographics, drug use history, externalizing personality traits) and Table II (risk behaviors, neurocognitive performance). The proportion of female participants did not differ significantly across groups (p = .11). Similarly, participants were well-matched in terms of education level (p = .40), estimated IQ from Raven's Progressive Matrices p =.29), and estimated socioeconomic status (p = .86). Significant between-group age differences were noted; heroin users (M = 29.3, SD = 4.6) were older than all other participant groups (p's $\leq$ .001); and both healthy controls (M = 25.4, SD = 5.9) and polysubstance users (M = 26.3, SD = 5.2) were older than amphetamine users (M = 23.1, SD = 3.9, p's < .02).

B. Drug Use History

In terms of drug use history, heroin users (M = 7.1, SD = 3.4) reported significantly more years of previous heroin use (t = 4.8, p < .001) than polysubstance users (M = 3.6, SD = 4.5). In contrast, duration of prior amphetamine use was equivalent across both amphetamine and polysubstance users (p = .58). Polysubstance users (M = 10.6, SD = 5.6) and heroin users (M = 11.4, SD = 5.5) endorsed equivalent periods of alcohol use (p = .43) significantly longer in duration (p's < .01) than amphetamine users (M = 7.6, SD = 3.8). Additionally, both heroin users (M = 10.4, SD = 3.6) and polysubstance users (M = 10.0, SD = 3.9) reported significantly longer periods of other drug use (p's < .002) than amphetamine users (M = 6.7, SD = 3.2). Among polysubstance users, rates of prior heroin dependence and amphetamine

TABLE I

PARTICIPANT DEMOGRAPHICS

	Controls (*n* = 124)	Heroin (*n* = 57)	Amphetamine (*n* = 43)	Polysubstance (*n* = 71)	
Sex (*# females,*	37 [30]	13 [23]	15 [35]	12 [17]	χ^2 = 6.05
Age (*M, SD*)	25.4[a] (5.9)	29.3[b] (4.6)	23.1[c] (3.9)	26.3[a] (5.2)	*F* = 12.4**
Education (*M,*	13.3 (2.7)	12.9 (2.4)	13.0 (2.3)	13.0 (2.2)	*F* = 0.4
Est. IQ (*M, SD*)	107 (15)	103 (13)	108 (11)	105 (14)	*F* = 1. 3
SES Category	5.0 (2.0)	5.2 (1.7)	4.9 (2.0)	5.1 (1.5)	*F* = 0.3
Years of Drug Use (*M, SD*)					
Heroin Use	0	7.1 (3.4)	0	3.6 (4.5)	*t* = 4.8**
Amphetamine	0.5[a] (1.9)	0.1[a] (0.9)	3.3[b] (2. 1)	3.0[b] (3.2)	*F* = 34.2**
Alcohol Use	9.1[a,c] (5.6)	11.4[b] (5.5)	7.6[a] (3.8)	10.6[b,c] (5.6)	*F* = 5.0**
Other Drug	1.9[a] (3.8)	10.4[b] (3.6)	6.7[c] (3.2)	10.0[b] (3.9)	*F* = 102.5**
DSM-IV Lifetime Substance Dependence (*#, %*)					
Heroin	0	57 [100]	0	34 [48]	χ^2 =218.6**
Amphetamine	0	0	43 [100]	43 [61]	χ^2 = 234.9**
Alcohol	0	0	0	26 [37]	--
Cannabis	0	0	0	56 [79]	--
Cocaine	0	0	0	5 [7]	--
Hallucinogens	0	0	0	4 [6]	--
Sedatives	0	0	0	8 [11]	--
Years since last met dependence criteria (*M, SD*)					
Heroin	--	3.5 (2.5)	--	2.4 (1.7)	*t* = 1.4
Amphetamine	--	--	2.8 (1.6)	2.7 (1.9)	*t* = 1.9
Externalizing Personality Traits					
Impulsivity	59.1[a] (10.4)	65.2[b] (11.1)	67.5[b] (10.1)	67.1[b] (11.4)	*F* = 11.6**
Psychopathy	4.7[a] (3.8)	12.8[b] (4.8)	7.8[c] (4.7)	12.1[b] (4.8)	*F* = 62.6**
Sensation	18.2[a] (7.1)	20.0[a] (6.5)	23.7[b] (5.6)	23.6[b] (5.4)	*F* = 13.9**

Note. Discordant superscripts indicate that group values differ statistically; *p < .05; **p < .01

TABLE II

PARTICIPANT RISK BEHAVIORS AND NEUROCOGNITIVE PERFORMANCE

	Controls (*n* = 124)	Heroin (*n* = 57)	Amphetamine (*n* = 43)	Polysubstance (*n* = 71)	
Risk Behaviors					
Aggression	73.9[a] (17.4)	83.5[b] (17.8)	84.7[b] (17.4)	87.7[b] (19.8)	*F* = 10.3**
Risky Drug Use	.02[a] (.2)	14.7[b] (7.9)	0.3[a] (1.7)	14.6[b] (8.2)	*F* = 93.8**
Risky Sexual	8.7[a] (4.0)	12.3[b] (4.0)	10.8[b] (3.9)	12.2[b] (3.8)	*F* = 16.8**
Problem	0.7[a,b] (1.7)	1.2[b,c] (2.3)	0.3[a] (1.3)	1.5[c] (2.6)	*F* = 3.8*
Impulsive Choice (*M,SD*)					
IGT Block 1	-2.2 (6.4)	-2.0 (6.4)	-1.6 (5.1)	-1.9 (6.0)	*F* = 1.0
IGT Block 5	2.1 (9.0)	1.5 (10.1)	0.9 (7.6)	0.1 (9.5)	*F* = 0.5
CGT Delay	.34 (.23)	.39 (.20)	.34 (.20)	.37 (.22)	*F* = 0.5
CGT Quality	.87 (.13)	.84 (.17)	.85 (.13)	.86 (.13)	*F* = 0.5
CGT Risk	.91 (.95)	.89 (.95)	.88 (.91)	.81 (.79)	*F* = 0.9
CGT Risk-	.62 (.13)	.59 (.14)	.61 (.15)	.61 (.15)	*F* = 0.7
BART Pumps	39.7 (11.2)	38.2 (13.5)	39.8 (14.8)	41.2 (15.0)	*F* = 0.7
DRDT Small	.11 (.09)	.13 (.08)	.15 (.09)	.12 (.08)	*F* = 0.3
DRDT Medium	.10 (.08)	.10 (.09)	.12 (.09)	.08 (.07)	*F* = 0.2
DRDT Large	.08 (.08)	.09 (.09)	.10 (.08)	.07 (.07)	*F* = 0.5
Impulsive Action (*M, SD*)					
Go/No-Go	2.2 (0.8)	2.0 (0.8)	2.0 (0.7)	2.1 (0.8)	*F* = 1.1
IMT *d'*	1.2 (0.5)	1.0 (0.5)	1.1 (0.4)	1.1 (0.5)	*F* = 1.4
Go-Stop Task	92.4[a,c] (10.6)	94.3[a] (9.6)	87.9[b] (17.0)	89.3[b,c] (13.8)	*F* = 3.0*
Go-Stop Task	74.8 (18.0)	75.5 (15.5)	69.7 (22.8)	75.6 (19.5)	*F* = 1.0
Go-Stop Task	52.0 (20.3)	49.5 (18.7)	50.8 (23.8)	50.1 (23.0)	*F* = 0.2
Go-Stop Task	29.4 (19.8)	25.9 (14.0)	30.7 (18.1)	31.1 (21.2)	*F* = 0.9

Note. Discordant superscripts indicate that group values differ statistically; *$p < .05$; **$p < .01$

dependence were 48% (*n* = 34) and 61% (*n* = 43), respectively. Thirty-seven percent (*n* = 26) of polysubstance users met criteria for history of alcohol dependence, 79% (*n* = 56) had a history of cannabis dependence, 7% (*n* = 5) had a history of cocaine dependence; 6% (*n* = 4) had a history of hallucinogen dependence, and 11% (*n* = 8) had a history of dependence on sedatives. Regarding duration of abstinence, polysubstance users (*M* = 2.4, *SD* = 1.7) and heroin users (*M* = 3.5, *SD* = 2.5) reported equivalent years of abstinence from heroin (*p* = .164). Similarly, both amphetamine users (*M* = 2.8, *SD* = 1.6) and polysubstance users (*M* = 2.7, *SD* = 1.9) reported equivalent length of abstinence from amphetamines (*p* = .22).

C. Externalizing Personality Traits

All drug users (heroin *M* = 65.2, *SD* = 11.1; amphetamine *M* = 7.8, *SD* = 4.7; polysubstance *M* = 12.1, *SD* = 4.8) reported significantly elevated levels of IMP (*p*'s $\leq$ .001) relative to healthy controls (*M* = 59.1, *SD* = 10.4). Both heroin users (*M* = 12.8, *SD* = 4.8) and polysubstance users (*M* = 12.1, *SD* = 4.8) were rated as having significantly higher levels of PSYC (*p*'s < .001) than both amphetamine users (*M* = 7.8, *SD* = 4.7) and healthy controls (*M* = 4.7, *SD* = 3.8). Additionally, amphetamine users were rated as more psychopathic than healthy controls (*p* < .001). Finally, amphetamine users (*M* = 23.7, *SD* = 5.6) and polysubstance users (*M* = 23.6, *SD* = 5.4) reported significantly higher levels of SS (*p*'s $\leq$ .005) than both healthy controls (*M* = 18.2, *SD* = 7.1) and heroin users (*M* = 20.0, *SD* = 6.5).

D. Risk Behaviors

All drug users (heroin *M* = 83.5, *SD* = 17.8; amphetamine *M* = 84.7, *SD* = 17.4; polysubstance *M* = 87.7, *SD* = 19.8) reported significantly elevated levels of aggression (*p*'s $\leq$.001) relative to healthy controls (*M* = 73.9, *SD* = 17.4). Additionally, healthy controls (*M* = 8.7, *SD* = 4.0) reported significantly less risky sexual practices (*p*'s < .005) than all drug users (heroin *M* = 12.3, *SD* = 4.0; amphetamine *M* = 10.8, *SD* =

3.9; polysubstance *M* = 12.2, *SD* = 3.8). Both healthy controls (*M* = 0.02, *SD* = 0.2) and amphetamine users (*M* = 0.30, *SD* = 1.7) reported significantly lower levels of risky drug use behaviors (*p*'s <.001) than heroin users (*M* = 14.7, *SD* = 7.9) and polysubstance users (*M* = 14.6, *SD* = 8.2). Additionally, both heroin users (*M* = 1.2, *SD* = 2.3) and polysubstance users (*M* = 1.5, *SD* = 2.6) reported significantly higher levels of problem gambling symptoms than amphetamine users (*M* = 0.3, *SD* = 1.3).

E. Neurocognitive Performance

All participant groups demonstrated equivalent clinical performance on measures of impulsive choice (*p*'s > .05). Similarly, measures of impulsive action did not detect any between-group differences (*p*'s > .05), with the sole exception of motor inhibition performance on the easiest trial (*i.e.* 50ms interval) of the GST. GST 50ms performance was most advantageous among healthy controls (*M* = 92.4, *SD* = 10.6) and heroin users (*M* = 94.3, *SD* = 9.6), while amphetamine users (*M* = 87.9, *SD* = 17.0) performed significantly less advantageously than these two groups (*p*'s < .05).

F. Aim 1 Results: Correlations between externalizing personality traits, neurocognitive performance, and risk behaviors.

Correlation coefficients from all Aim 1 analyses are presented in Table III. As predicted, PSYC was positively associated with all risk behaviors (*r*'s $\geq$ .25, *p*'s < .001). Hypotheses regarding IMP were partially supported; IMP was positively associated with aggression and HIV risk behaviors (*r*'s > .15, *p*'s < .025), but, contrary to expectations, IMP was not significantly associated with problem gambling (*p* = .17). Consistent with hypotheses, SS was positively associated with aggression and risky sexual practices (*r*'s > .20, *p*'s < .001). SS also demonstrated a trend-level association with risky drug use behaviors (*r* = .16, *p* = .06). As predicted, SS was not correlated with problem gambling (*p* = .18). As expected, IMP was negatively associated with several measures of impulsive action (*r*'s $\geq$ .12, *p*'s < .05), but contrary to

TABLE III

PARTIAL CORRELATIONS BETWEEN EXTERNALIZING TRAITS, NEUROCOGNITION, AND RISK BEHAVIORS

	PSYC	IMP	SS	Aggression	Risky Drug Use	Risky Sexual Practices	Problem Gambling
Personality Traits							
PSYC	--	.41**	.26**	.48**	.37**	.31**	.25**
IMP	.41**	--	.41**	.46**	.19*	.20**	.08
SS	.26**	.41**	--	.18*	.16 ǂ	.21**	.08

TABLE III (continued)

PARTIAL CORRELATIONS BETWEEN EXTERNALIZING TRAITS, NEUROCOGNITION, AND RISK BEHAVIORS

	PSYC	IMP	SS	Aggression	DRB	SRB	Gambling
Risk Behaviors							
Aggression	.48**	.46**	.18*	--	.17**	.25**	.18**
DRB	.37**	.19*	.16ł	.17**	--	.35**	.19**
SRB	.31**	.20**	.21**	.25**	.35**	--	.21**
Gambling	.25**	.08	.08	.18**	.19**	.21**	--

TABLE III (continued)

PARTIAL CORRELATIONS BETWEEN EXTERNALIZING TRAITS, NEUROCOGNITION, AND RISK BEHAVIORS

	PSYC	IMP	SS	Aggression	DRB	SRB	Gambling
Impulsive Choice							
BART Pmps AA	-.01	.15*	.16	.04	-.01	-.03	-.02
CGT							
Delay Aversion	.11	.03	-.10	.10	-.06	-.07	-.08
Decision Qual.	-.08	-.09	.03	-.09	-.001	.06	-.05
Risk Adjust.	-.05	-.02	.03	.04	.11	.01	.03
Risk Taking	-.07	.07	.13*	-.05	-.05	.02	.07

TABLE III (continued)

PARTIAL CORRELATIONS BETWEEN EXTERNALIZING TRAITS, NEUROCOGNITION, AND RISK BEHAVIORS

	PSYC	IMP	SS	Aggression	DRB	SRB	Gambling
IGT							
Block 1	.05	-.05	-.14*	-.03	.01	.03	.004
Block 5	-.24**	-.04	-.07	-.01	-.02	-.15*	-.09
Large	.04	-.09	-.03	.03	-.01	-.10	.08
Impulsive Action							
IMT *d'*	-.10	-.06	-.02	-.10	-.08	.08	.11
GNGT *d'*	-.17**	-.14*	.06	-.13*	-.04	-.02	.03

TABLE III (continued)

PARTIAL CORRELATIONS BETWEEN EXTERNALIZING TRAITS, NEUROCOGNITION, AND RISK BEHAVIORS

	PSYC	IMP	SS	Aggression	DRB	SRB	Gambling
GST							
50ms	-.16*	-.07	.11ǂ	-.08	.01	-.01	-.004
150ms	-.04	.01	.17	-.004	.000	.02	-.002
250ms	-.05	-.02	.06	-.05	.02	-.03	-.05
350ms	.05	-.12*	.01	-.03	-.03	-.01	-.02

Note. *$p \leq .05$; ** $p \leq .01$

expectation, IMP was also positively correlated with one measure of impulsive choice: BART pumps adjusted average (r = .15, p = .01). Consistent with hypotheses, SS was associated with multiple measures of impulsive choice. Specifically, SS was negatively associated with IGT Block 1 performance (*r* = -.13, *p* = .04), a measure of decision-making under ambiguity, but was positively associated with CGT Risk-taking (*r* = .14, *p* = .02), a measure of decision-making under explicit contingencies. Contrary to hypotheses, no statistically significant associations of SS and impulsive action measures were noted (*p*'s > .05). PSYC demonstrated the expected inverse relationship with IGT Block 5 performance but was not correlated with other impulsive choice measures (*r* = -.16, *p* =.01). Contrary to predictions, PSYC was also inversely associated with several measures of impulsive action (*r*'s $\leq$ -.13, *p*'s < .04). As hypothesized, impulsive choice measures were correlated with risky sexual practices (IGT Block 5 *r* = -.15, *p* = .02) and problem gambling (DRDT Small *r* = .13, *p* = .04). Contrary to hypotheses, risky drug use practices were not correlated with any measures of neurocognitive impulsivity (*p*'s $\geq$ .25). As expected, aggression was not correlated with any measures of impulsive choice (*p*'s > .06). Additionally, aggression was inversely associated with a measure of impulsive action (GNGT *d*' *r* = -.13, *p* = .04). Contrary to expectations, problem gambling was not significantly correlated with any measures of impulsive action (*p*'s > .05).

G. Aim 2 Results: Moderating Effects of Drug Class on Associations between Externalizing Personality Traits, Neurocognitive Performance, and Risk Behaviors

The second aim of the analyses was to evaluate the moderating effects of previous dependence on specific classes of drugs (*i.e.* heroin and amphetamine) on the relationships between externalizing traits and risk behaviors; externalizing traits and dimensions of neurocognitive impulsivity; and dimensions of neurocognitive impulsivity and risk behaviors. Standardized regression coefficients and test statistics from MLR models examining the influence of

TABLE IV

EFFECTS OF EXTERNALIZING TRAITS AND DRUG TYPE ON RISK BEHAVIORS

	Aggression	DRB	SRB	Gambling
	R^2 = .39***	R^2 = .53***	R^2 = .27***	R^2 = .39***
Heroin	-.13	.62**	.11	-.15
Amphetamine	.05	.01	.03	-.21**
Polysubstance	.02	.31	.20**	-.02
PSYC	.36**	-.001	.43**	.60**
IMP	.43**	.000	.002	.03
SS	-.01	.002	.18*	-.01
PSYC Interactions				
Heroin	.04	.15*	-.07	-.17
Amphetamine	.06	-.01	-.13*	-.12
Polysubstance	-.05	.12	-.20*	-.25**

TABLE IV (continued)

EFFECTS OF EXTERNALIZING TRAITS AND DRUG TYPE ON RISK BEHAVIORS

	Aggression	DRB	SRB	Gambling
	R^2 = .39***	R^2 = .53***	R^2 = .27***	R^2 = .39***
IMP Interactions				
Heroin	-.02	.01	.08	.05
Amphetamine	-.16*	-.01	-.03	.04
Polysubstance	-.01	.05	-.003	-.05
SS Interactions				
Heroin	.05	-.04	-.20**	-.06
Amphetamine	.05	-.003	.04	.01
Polysubstance	-.001	-.06	-.06	-.05

Note. *$p \leq .05$; **$p < .01$; ***$p < .001$

externalizing traits and drug class on risk behaviors are presented in Table IV. MLR models were all statistically significant (*p's* < .001) and accounted for unique variance in all risk behaviors.

Results of MLR analyses examining associations of externalizing traits and drug class on measures of neurocognitive impulsivity are presented in Table V (impulsive choice) and Table VI (impulsive action). Hypotheses regarding the specificity of these associations across specific classes of drugs were largely unsupported, suggesting that the relationships between these constructs change in the protracted abstinence stage. Test statistics and regression coefficients from MLR models examining the influence of neurocognitive impulsivity and drug class on risk behaviors are presented in Table VII. All MLR models accounted for significant variance in risk behavior variables (*p*'s $\leq$ .05).

Hypotheses regarding the specificity of associations between PSYC and risk behaviors among heroin users were largely supported. As predicted, PSYC was positively and selectively associated with risky drug use behaviors among heroin users (PSYC × heroin β = .15, *t* = 1.9, *p* = .05). Further, although PSYC was positively associated with risky sexual practices across all prior drug users (β = .43, *t* = 3.2, *p* < .001), the magnitude of this association was strongest among heroin users relative to relative to other drug users (heroin interaction *p* = .44 indicating the conditional main effect holds across healthy controls and heroin users; amphetamine and polysubstance interaction β's < -.10, *t*'s < -1.8, *p*'s $\leq$ .05 indicating that the strength of the association, although still statistically significant, is weaker in these participant groups). Additionally, in partial support of this hypothesis, PSYC was associated with problem gambling across all drug users (β = .60, *t* = 4.3, *p* < .001) and the magnitude of this association was stronger in

Table V

EFFECTS OF EXTERNALIZING TRAITS AND DRUG TYPE ON IMPULSIVE CHOICE

	DRDT Medium	IGT Block 5	CGT Delay Aversion	CGT Risk Adjustment
	R^2 = .13**	R^2 = .10*	R^2 = .12**	R^2 = .11*
Heroin	-.02	.09	.03	-.06
Amphetamine	.07	.08	-.01	.03
Polysubstance	-.20*	.03	.003	-.01
PSYC	.36**	-.58**	.16	-.10
IMP	-.08	.12	.06	.003
SS	-.20*	.04	-.28**	.18
PSYC Interactions				
Heroin	-.21*	.28**	-.05	.12
Amphetamine	-.12	.12	.04	.05
Polysubstance	-.06	.21*	-.12	-.03

TABLE V (continued)

EFFECTS OF EXTERNALIZING TRAITS AND DRUG TYPE ON IMPULSIVE CHOICE

	DRDT Medium	IGT Block 5	CGT Delay Aversion	CGT Risk Adjustment
	R^2 = .13**	R^2 = .10*	R^2 = .12**	R^2 = .11*
Heroin	-.02	-.07	-.08	.02
Amphetamine	-.16*	-.08	.04	-.20*
Polysubstance	-.03	.01	.07	.11
SS Interactions				
Heroin	.09	-.02	.09	-.17*
Amphetamine	.14	-.03	-.01	.05
Polysubstance	.04	-.02	.13	-.14

Note. *$p \leq .05$; ** $p \leq .01$

TABLE VI

EFFECTS OF EXTERNALIZING TRAITS AND DRUG TYPE ON IMPULSIVE ACTION

	Go/No-Go Task *d'*	Go-Stop Task 50ms	Go-Stop Task 150ms
	R^2 = .18***	R^2 = .11*	R^2 = .12**
Heroin	.05	.09	-.02
Amphetamine	-.15	-.10	-.17*
Polysubstance	-.06	-.07	.09
PSYC	-.03	-.30*	-.02
IMP	-.09	.10	-.02
SS	.26**	.19*	.19
PSYC Interactions			
Heroin	-.21*	.19	.06
Amphetamine	-.06	.03	-.01
Polysubstance	-.05	.02	-.14

TABLE VI (continued)

EFFECTS OF EXTERNALIZING TRAITS AND DRUG TYPE ON IMPULSIVE ACTION

	Go/No-Go Task *d'*	Go-Stop Task 50ms	Go-Stop Task 150ms
	R^2 = .18***	R^2 = .11*	R^2 = .12**
IMP Interactions			
Heroin	.08	-.03	.03
Amphetamine	.05	.03	-.04
Polysubstance	-.09	-.31**	.08
SS Interactions			
Heroin	-.07	-.08	-.08
Amphetamine	-.03	-.03	.15
Polysubstance	-.13	.07	-.02

Note. *$p \leq .05$; ** $p \leq .01$; ***$p < .001$

TABLE VII

EFFECTS OF NEUROCOGNITION AND DRUG TYPE ON RISK BEHAVIORS

	Aggression	DRB	SRB	Gambling
	R^2 =.34*	R^2 = .64***	R^2 = .35*	R^2 = .37*
Heroin	.23**	.74**	.32**	.06
Amphetamine	.17*	.02	.21*	-.05
Polysubstance	.28**	.33**	.29**	-.19*
IGT Block 1	-.19*	.003	.01	-.05
IGT Block 5	-.15	-.002	-.22*	-.11
CGT Delay Aversion	.06	-.004	-.11	-.07
CGT Decision Quality	-.01	.004	-.01	-.05
CGT Risk Adjust	-.02	.004	-.07	.08
CGT Risk-Taking	-.18	-.01	.002	.24
BART Pumps AA	.12	.001	-.17	-.03
DRDT Small	-.27	-.004	-.08	.26
DRDT Medium	.25	-.002	-.07	-.11

TABLE VII (continued)

EFFECTS OF NEUROCOGNITION AND DRUG TYPE ON RISK BEHAVIORS

	Aggression	DRB	SRB	Gambling
	R^2 = .34*	R^2 = .64***	R^2 = .35*	R^2 = .37*
DRDT Large	.12	.004	.03	.15
Go/No-Go Task *d'*	-.12	.002	-.05	.06
IMT *d'*	.01	.003	.07	-.08
Go-Stop Task 50ms	.07	-.002	-.16	-.03
Go-Stop Task 150ms	.12	-.002	-.03	-.02
Go-Stop Task 250ms	.07	.000	.31	.06
Go-Stop Task 350ms	-.23	-.002	-.11	.04
Heroin Interactions (p<.05)				
IGT Block 1	.18*	--	--	--
IGT Block 5	.18*	--	--	--
CGT Delay Aversion	--	-.19*	--	--
IMT *d'*	--	--	--	.18*

TABLE VII (continued)

EFFECTS OF NEUROCOGNITION AND DRUG TYPE ON RISK BEHAVIORS

	Aggression	DRB	SRB	Gambling
	R^2 =.34*	R^2 = .64***	R^2=.35*	R^2=.37*
Polysubstance Interactions (p<.05)				
CGT Risk Adjust	.20*	--	--	--
Go-Stop Task 350ms	.35*	--	--	--
DRDT Medium	--	-.24*	--	--
Go-Stop Task 150ms	--	-.38**	--	-.35*

Note. *$p \leq .05$; ** $p \leq .01$; *** $p < .001$

Note. No statistically significant amphetamine × neurocognitive impulsivity interactions observed.

both heroin and amphetamine users (interaction p's > .07) relative to polysubstance users (β = -.25, t = -2.7, p = .01). In contrast, the hypothesis about the specificity of the associations of externalizing traits and neurocognitive impulsivity among heroin users was not supported. Specifically, although PSYC was associated with performance on tasks of impulsive choice, these associations were either non-significant among heroin users in protracted abstinence (*i.e.* DRDT Medium × heroin β = -.21, *t* = -2.0, *p* = .04; IGT Block 5 × heroin β = .28, *t* = 2.6, *p* = .01) or were not specific to heroin users. The predicted association of impulsive choice performance and risky drug use behaviors specific to heroin users was observed (CGT Delay Aversion × heroin β = -.19, *t* = -2.4, *p* = .02). By contrast, an observed association of impulsive choice with risky sexual practices (IGT Block 5 performance β = -.22, *t* = -2.1, *p* = .04) was not specific to heroin users. Contrary to predictions, no neurocognitive variables were significantly associated with problem gambling in Aim 2 analyses.

Hypotheses were not supported regarding the specificity of associations between externalizing traits and risk behaviors among prior amphetamine users. Specifically, IMP and problem gambling were not significantly associated among drug users in protracted abstinence (*p*'s > .50), while SS was not significantly associated with aggression (*p*'s > .30) when controlling for effects of prior substance dependence in MLR analyses. Similarly, associations of IMP and SS with neurocognitive impulsivity also lacked the predicted specificity to amphetamine users; IMP was associated with impulsive action (*i.e.* GST 50ms) only among polysubstance users (IMP × polysubstance β = -.31, *t* = -3.6, *p* < .001), whereas the associations of SS with impulsive action (*i.e.* GST 150ms) were not moderated by drug class (interaction *p*'s $\geq$ .06). Additionally, the predicted specificity of associations between impulsive action and risk behaviors among amphetamine users was consistently not supported. When controlling for history of drug dependence, no measures of impulsive action were significantly associated with

aggression, with the exception of a unique positive association between impulsive action and aggression among polysubstance users (GST 350ms × polysubstance β = .35, *t* = 2.5, *p* = .01). Finally, no statistically significant main effects of impulsive action were observed for problem gambling, while moderated associations of impulsive action measures and problem gambling were restricted to heroin and polysubstance users.

H. Aim 3 Results: Neurocognitive Impulsivity Parameters as Candidate Mediators of Associations between Externalizing Personality Traits and Risk Behaviors.

Results of Aim 3 analyses indicated that neurocognitive dimensions of impulsivity did not mediate associations of externalizing personality traits and risk behaviors among the current sample of drug users in protracted abstinence. The first computed mediation model examined GNGT *d*′ as a candidate mediator of the association between IMP (IV) and aggression (DV) based on a series of statistically significant partial correlations between these variables observed in Aim 1. Results of the mediation model indicated a marginally significant direct effect of the IV on the candidate mediator (β = -.12, *t* = -1.9, *p* = .06) and a statistically significant direct effect of the IV on the DV (β = .49, *t* = 9.2, *p* < .001). The effect of the candidate mediator in the model on the DV was nonsignificant (*p* = .193) and the confidence interval of the indirect effect of the IV on the DV crossed zero when controlling for the candidate mediator (95% LLCI -.001 ULCI .031), indicating that there was no mediation effect.

The second computed mediation model examined GNGT *d*′ performance as a candidate mediator of the association between PSYC (IV) and aggression (DV) based on a series of statistically significant partial correlations between these variables. Results of the mediation model indicated a

statistically nonsignificant direct effect of the IV on the candidate mediator (p = .622), precluding a possible mediation effect.

The third computed mediation model examined IGT Block 5 performance as a candidate mediator of the association between PSYC (IV) and risky sexual practices (DV) based on a series of statistically significant partial correlations between these variables in Aim 1 analyses. Results of the mediation model indicated a statistically significant direct effect of the IV on the candidate mediator (β = -.20, t = -3.1, p = .002) and a statistically significant direct effect of the IV on the DV (β = .41, t = 6.7, p < .001). However, the effect of the candidate mediator on the DV was nonsignificant (p = .502) and the 95% bias-corrected and accelerated confidence interval of the estimated indirect effect of the IV on the DV when controlling for the mediator crossed zero (β = .008, 95% LLCI -.012 ULCI .037), indicating that there was no mediation effect.

IV. DISCUSSION

A. Aim 1

Correlational analyses largely supported hypotheses regarding the nature and directionality of associations between externalizing personality traits and risk behaviors. Consistent with expectations, PSYC was reliably associated with all dimensions of risk behavior. This finding lends support to previous research indicating PSYC is a valid and useful construct for cross-cultural research on addiction and risk behavior (Berger, Rotermund, Vieth, & Honhorst, 2012; Hare, Clark, Grann, & Thornton, 2000; Wilson et al. 2014), and extends previous findings to the protracted abstinence stage of addiction. Both IMP and SS were associated with aggression and risky sexual and drug use practices, and neither IMP nor SS were associated with problem gambling. The pattern of correlations observed between SS and risk behaviors was in line with previous research (Fischer & Smith, 2008; Fortune & Goodie, 2010; Gonzalez et al., 2005; Roberti, 2004; Smith et al., 2007; Wilson & Scarpa 2011) and also supports the utility of employing SS measures in the prediction of risk behaviors among drug users in protracted abstinence.

Although associations of IMP and risk behaviors also largely conformed to predictions, IMP was not associated with problem gambling as predicted. These results suggest that, although IMP also appears to be a useful construct for predicting clinically significant risk behaviors in general, the nature of relationship between IMP and problem gambling in this sample differs relative to previously observed samples (Clarke, 2006; Lai, Ip, & Lee, 2011). One possibility is that drug users in the protract-

-ed abstinence stage demonstrate better levels of behavioral control than active drug users when motivating cues are not salient, given that IMP refers to a putatively stable impulsive behavioral style, regardless of context (deWit, 2009; Moeller et al., 2001). In contrast, the presence of motivating or reward cues may predispose individuals with elevated levels of traits such as SS and PSYC (which involve context-specific reward-based approach behaviors and failure to learn from punishment, respectively) to be more vulnerable to risk behaviors in the protracted abstinence stage of addiction.

A second round of correlational analyses provided support for hypothesized associations between personality and neurocognitive functioning among drug users in protracted abstinence. IMP was negatively associated with GST inhibition and GNGT *d'*, consistent with the hypothesis that IMP would be selectively associated with disadvantageous performance on measures of impulsive action. Seemingly contrary to this hypothesis, IMP also demonstrated a selective positive association with BART performance; however, given that the BART performance measure was average pump presses per trial, it is plausible that the observed positive association of IMP and number of BART pumps indicates an impulsive motoric responding style. Indeed, IMP was the only externalizing trait associated with BART performance; the selectiveness of that association, coupled with other correlations indicating that IMP is consistently associated with elevated motor impulsivity on measures of impulsive action, may indicate that individuals higher on IMP simply engaged in greater motor responding on the BART regardless of trial context.

As predicted, PSYC was selectively and negatively associated with impulsive choice, although this association was limited to IGT Block 5 performance. The finding of IGT performance as a selective indicator of cognitive deficits associated with PSYC is consistent with previous research indicating that

although psychopathic individuals often perform within the normal range on a variety of neurocognitive tasks, specific measures of reward-based learning such as the IGT may reveal insensitivity to punishment and failure to learn from feedback (Blair et al., 2001; Mitchell et al., 2002; Vassileva et al., 2007, 2011). Notably, among the current sample of drug users in protracted abstinence, PSYC was associated selectively with disadvantageous performance on a measure of reward-based decision-making of high cognitive complexity (IGT Block 5), while PSYC was not associated with performance on a measure of decision-making under explicit risk conditions (*i.e.* CGT) or a pure measure of decision-making under ambiguity (*i.e.* IGT Block 1).

SS was negatively associated with decision-making under ambiguity on IGT Block 1 and positively associated with CGT performance under explicit risk contingencies. This pattern of results confirms hypotheses regarding associations of SS and measures of impulsive choice. Further, results indicate that among drug users in protracted abstinence, SS appears to be differentially associated with risky, *advantageous* reward-based decision-making under unambiguous conditions and risky, *disadvantageous* reward-based decision-making under ambiguity.

The observed variation of associations between neurocognitive impulsivity and IMP, SS, and PSYC highlights the utility of examining neurocognitive associations of multiple externalizing traits simultaneously in drug user populations. Results indicate specific externalizing personality traits appear to be linked to different aspects of neurocognitive impulsivity among drug users in protracted abstinence, with IMP linked primarily to impulsive motor responding, PSYC linked to disadvantageous reward-based decision-making under conditions of cognitive complexity, and SS linked to advantageous

reward-based decision-making under explicit risk conditions and disadvantageous reward-based decision-making under ambiguity.

A third set of correlation analyses evaluated hypotheses regarding specific associations of neurocognitive impulsivity dimensions and risk behaviors. Consistent with hypotheses, measures of impulsive action but not impulsive choice were associated with AGG. Risky sexual practices negatively associated with impulsive choice, specifically IGT Block 5 performance. This finding is consistent with previous studies that have linked reward-based decision-making performance on neurocognitive tasks including the IGT to sexual risk behavior, and extends these findings to drug users in protracted abstinence. The selective correlation of IGT Block 5 performance among the neurocognitive impulsive choice measures suggests that relative cognitive complexity required in learning from mistakes under ambiguous conditions (*i.e.,* a cognitive deficit reliably linked to PSYC) may influence sexual risk behavior among drug users in protracted abstinence. In contrast, less complex and more straightforward forms of reward-based decision-making do not appear to relate to risky sexual behavior in this stage of the addiction cycle.

Contrary to expectations, lifetime risky drug use behaviors were not significantly correlated with any neurocognitive measures of impulsivity. This lack of significant associations may indicate insensitivity of measures of neurocognitive functioning in the protracted abstinence stage to propensities for risky behavior that is not ongoing at the time of neurocognitive assessment and/or is retroactively reported by drug users. Additionally, it is plausible that the association between history of risky drug use behavior and neurocognitive functioning is outweighed by other factors (*e.g.* severity of emotional distress, personal coping resources, availability of clean needles for heroin and

polysubstance users) within this relatively unusual sample of drug users who have been able to maintain protracted abstinence from drugs for one year or more.

Problem gambling was correlated with impulsive choice and impulsive action, consistent with hypotheses. Counterintuitively, advantageous DRDT performance was positively associated with problem gambling. Additionally, better discriminatory ability on a measure of impulsive action (IMT *d'*) was also positively associated with problem gambling. These finding may indicate that among drug users in protracted abstinence--and contrary to previous findings with active drug users (Goudriaan, Oosterlaan, De Beurs, & Van Den Brink, 2006; Lawrence, Luty, Bogdan, Sahakian, & Clark, 2009; Verdejo-Garcia, Lawrence, & Clark, 2008), better selective attention and attention to immediate rewards is evidenced by participants who engage in higher levels of problem gambling, although further exploration of the mechanisms underlying this association is needed before any conclusions may be generated.

B. <u>Aim 2</u>

A set of MLR analyses were computed to evaluate hypotheses regarding moderating effects of drug class on associations of externalizing traits with risk behaviors. Based on prior studies linking PSYC preferentially to heroin dependence over stimulant dependence (Alterman et al. 1998; Compton et al. 1995; Hopley & Brunelle, 2012; Rutherford et al. 1996; Vassileva et al., 2007, 2011), it was hypothesized that associations of PSYC and both HIV risk behaviors and problem gambling would be strongest among heroin users. Results confirmed the importance of PSYC as an important personality mechanism of risk behavior. Among heroin users in protracted abstinence, PSYC was selectively associated with elevated risky drug use behaviors. PSYC was also associated with risky sexual practices across all participants, but statistically significant interaction effects indicated that the strength of this association was *greater* among heroin users than polysubstance or amphetamine users. PSYC was also associated with problem

gambling across heroin users as well as amphetamine users, but not polysubstance users. These findings confirm the reliable associations of PSYC and risk behaviors among heroin users and extend these findings to heroin users in protracted abstinence. Taken together, findings that PSYC was not associated with problem gambling among former polysubstance users and the selective strength of PSYC correlations with risk behavior among heroin users suggest that, rather than a general marker of behavioral and psychological dysfunction in abstinent drug users, PSYC possesses at least some specificity to class of substance dependence. Previous research has indicated that both opiate dependence (Ahn et al., 2014; Upadhyay et al., 2014; Vassileva et al., 2013; Zhang, Zhour, Li, & Shen, 2008) and PSYC (Blair et al., 2004; Cohn et al. 2014; Newman, Patterson, Howland, & Nichols, 1990; Pujara et al. 2014) are linked to decreased loss aversion, which should be evaluated as a candidate mechanism of PSYC's associations with risk behavior among drug users, particularly heroin users.

Based on prior research indicating preferential associations of IMP and SS with amphetamine dependence over heroin dependence (Belin, Mar, Dalley, Robbins, & Everitt, 2007; Dalley et al. 2007; McNamara, Dalley, Robbins, Everitt, & Belin, 2010; Robbins et al., 2012), it was hypothesized that associations of IMP and SS with problem gambling and with AGG, respectively, would be strongest among prior amphetamine users. These hypotheses were not supported. SS was not associated with aggression when controlling for effects of prior substance dependence, while IMP was not associated with problem gambling in any participants. The lack of observed associations in the current sample may speak to a change in personality functioning in the protracted abstinence stage of addiction. Active substance dependence may be a prerequisite for observed associations of SS and aggression in comparatively recent drug users (Murray et al., 2003; Patkar et al., 2002, 2003; Yeater, Lenberg, & Bryan 2012; although see Ramadan, 2005); whereas during the protracted abstinence stage and the absence

of drug-seeking behavior, SS may no longer play a causal role in aggressive behaviors. The lack of association of IMP with problem gambling is consistent with Aim 1 correlational analyses, and may indicate that involvement in problem gambling in the protracted abstinence stage is not a function of trait impulsivity as it may be in active substance dependence.

A second set of MLR analyses was computed to examine whether drug class moderated associations of externalizing traits and performance on tasks of neurocognitive impulsivity. Based on prior research (Castellanos-Ryan et al., 2011; Verdejo-Garcia et al., 2007; Vassileva et al., 2014) indicating that heroin and amphetamine dependence are preferentially associated with impulsive choice and impulsive action, respectively, it was hypothesized that associations of PSYC and impulsive choice would be strongest among former heroin users while associations of IMP and impulsive action would be strongest among former amphetamine users. These hypotheses were not supported. IMP was only associated with impulsive action performance among polysubstance users. PSYC was associated with disadvantageous performance on multiple measures of impulsive choice, but these associations were nonsignificant among heroin users, indicating that although elevated levels of psychopathic traits were generally associated with poorer impulsive choice, heroin users in protracted abstinence appear to be exempt from these effects. One plausible explanation for this pattern of results may be that although PSYC is likely to be a primary mechanism driving poor reward-based decision-making among heroin users engaged in active substance dependence, successful recovery and sustained abstinence from heroin use may and reduce the cognitive deficits more typically associated with PSYC in active heroin users.

Previous research has linked SS to impairments on both tasks of impulsive action (Collins et al., 2012; Fillmore et al., 2009) and impulsive choice (Castellanos-Ryan et al., 2011; Noel et al., 2011), with some evidence of preferential associations of SS to stimulant dependence (Hutchison, Wood, & Swift, 1999; Kelly et al., 2006; Low & Gandaszek, 2002; Stoops et al., 2007; Zuckerman, 1979). Thus, SS was hypothesized to show preferential associations with measures of impulsive action among amphetamine users. This hypothesis was not supported, in that SS was positively associated with performance on tasks of impulsive action, but this association was generalized to all participants.

A third set of MLR models was computed to examine the moderating effects of prior substance dependence on associations between neurocognitive measures of impulsivity and risk behaviors. Associations of impulsive choice and HIV risk behaviors were hypothesized to be strongest among heroin users, a hypothesis that was partially supported for risky drug use behaviors but not risky sexual practices. Counterintuitively, delay aversion under explicit risk conditions was associated with less risky drug use behaviors among heroin users, while low delayed reward discounting was associated with higher risky drug use behaviors among heroin users. Conversely, on measures of impulsive action, better motor response inhibition (*i.e.* GST) was associated with lower risky drug use behaviors and risky sexual practices across both heroin and polysubstance users. Taken together, these findings highlight the importance of reward appraisal and deliberative reward-based decision-making as opposed to rapid and careless responding as a pathologic cognitive process in heroin users that may be observed in the protracted abstinence stage of addiction. Additionally, performance on IGT Block 5 was negatively associated with risky sexual practices across all participants, strengthening the inference that reward-based decision-making is a relevant process for elevated levels of HIV risk behavior in drug users, but

indicating that at least in protracted abstinence, this association is not necessarily specific to opiate users.

Neurocognitive performance on measures of impulsive action was predicted to be associated with risk behaviors most strongly among prior amphetamine users. These hypotheses were not supported. No selective associations of these risk behaviors with neurocognitive performance were observed among former amphetamine users, suggesting that neurocognitive deficits in motor impulse control associated with amphetamine dependence are either ameliorated or are subject to greater cognitive control in protracted abstinence.

C. Aim 3

Results of Aim 3 analyses indicated that neurocognitive dimensions of impulsivity did not mediate associations of externalizing personality traits and risk behaviors among the current sample of drug users in protracted abstinence. This finding may potentially be due to the absence of acute drug-related cognitive deficits seen in more recent addiction/acute withdrawal, an inference supported by the lack of significant between-group differences on almost all neurocognitive measures (see Table II). Contrary to hypotheses, residual neurocognitive 'scarring' from drug dependence does not appear to be a mechanism that explains the association between externalizing personality traits and risk behaviors in protracted abstinence, although further studies and replication of these findings is necessary before generalizable conclusions can be made. One possibility is that neurocognitive impulsivity parameters may potentially *moderate* but not *mediate* the effects of externalizing personality traits on risk behaviors in protracted abstinence, a possibility that will be investigated in a future study of this population.

D. Limitations

There are several methodological limitations to this study that are important to note in the consideration of these findings. First, this study was cross-sectional in nature, and it may be that neurocognitive impulsivity measures may *longitudinally* mediate associations between premorbid externalizing traits and subsequent risk behaviors, as has been previously observed in longitudinal studies of more active drug users (Castellanos-Ryan et al. 2011), although this possibility does not affect the finding that neurocognitive functioning in protracted abstinence does not appear to significantly contribute to risk behavior in this stage of the addiction cycle. Secondly, although every effort was made to ensure accurate translation and cross-cultural validity of psychometric instruments, potential cross-cultural effects may influence the generalizability of the present findings to samples from other cultures. Third, alternate operationalizations of some constructs such as risk behaviors (*e.g.* using behavioral measure of aggression) may provide better ecological validity for risk behavior in protracted abstinence than was available from the current study design. Additionally, most participants did not engage in any *recent* (*i.e.* past 30-day) drug use risk behavior, which may limit inferences that can be drawn from statistical modeling of this particular domain of risk behavior.

E. Future Directions

There are several directions for future research that would effectively build on the present study. Replication of these patterns of associations in a second sample of abstinent drug users would provide convergent validity for the observed effects. Similarly, conducting the same analyses in active drug users drawn from the same culture for a direct comparison would serve to clarify whether many of the conclusions/inferences from this study are accurate. Optimally, a longitudinal study that measures these relationships during addiction, during withdrawal, during acute abstinence, and during protracted abstinence will be possible in the future.

Previous computational modeling of IGT performance (Ahn et al., 2014) has identified unique and dissociable cognitive processes that influence performance in abstinent heroin and amphetamine users (*i.e.* decreased *loss aversion* and *increased reward sensitivity*, respectively). Modeling the underlying processes for other neurocognitive tasks in this study and examining these parameters may prove more illuminating for detecting neurocognitive mechanisms of risk behavior in protracted abstinence.

The current study relied on unitary constructs from psychometric instruments as predictors of risk behavior. Formal cross-cultural construct validation (*e.g.* exploratory/confirmatory factor analyses and establishment of convergent/discriminant criterion validity) of psychometric instruments may produce alternative factor solutions of the personality trait constructs which may prove more sensitive to risk behaviors and cognitive deficits. Additionally, utilizing known factor solutions in this population (*e.g.* the 2-factor solution for the PCL:SV identified in Wilson et al., 2014) may further elucidate specific traits which preferentially influence risk behaviors in this population.

F. Conclusions

In summary, the present study extends findings regarding the utility of externalizing personality traits in the prediction of risk behavior to drug users in protracted abstinence. PSYC emerged as the most robust and consistent predictor of risk behavior, while SS showed the expected pattern of correlations with risk behaviors. Correlations of IMP and risk behaviors also largely conformed with expectations, although IMP was not associated with PG, which may indicate that sustained PG in protracted abstinence is not a function of impulsivity per se. Results from this study indicated that

different dimensions of the externalizing spectrum correlate with specific neurocognitive impulsivity profiles, such that IMP was linked primarily to impulsive motor responding, PSYC was linked to disadvantageous reward-based decision-making under conditions of cognitive complexity, and SS was linked to advantageous reward-based decision-making under explicit risk conditions and disadvantageous reward-based decision-making under ambiguity. Analyses of relationships between neurocognitive impulsivity and risk behavior indicated that sexual risk behavior in protracted abstinence was linked to poor decision-making under ambiguity in the context of cognitive complexity, aggression was linked to impulsive action, and problem gambling was linked to intact attentional control.

Hypotheses regarding associations between externalizing personality traits among specific classes of drug dependence were particularly illuminating. Hypotheses that PSYC would be most strongly associated with risk behaviors among former heroin users were largely confirmed. By contrast, predicted associations of IMP and SS with risk behaviors among former amphetamine users were largely disconfirmed, indicating that protracted abstinence may change the risk behavior profile associated with amphetamine dependence but not heroin dependence, apparently owing in part to persistence of PSYC's functioning as a highly sensitive risk indicator in protracted abstinence from heroin. Contrary to predictions, neurocognitive impulsivity measures did not mediate associations of externalizing personality traits with risk behaviors in protracted abstinence, likely owing to the amelioration of cognitive deficits with successful abstinence from drugs of abuse.

The body of results obtained in the present study indicates that a multivariate approach to categorizing personality has clinical utility in predicting risk behavior among drug users in protracted abstinence. The personality measures utilized in this study are relatively cheap and easy to administer

in real-world clinical settings and may prove advantageous to informing intervention approaches aimed at reducing the incidence and severity of risk behavior associated with drug dependence, potentially including relapse from abstinence. These personality patterns map on to variations in neurocognitive impulse control functioning in the protracted abstinence stage of addiction. Although these neurocognitive variables do not appear to explain associations of externalizing traits and risk behaviors, future replication analyses and direct comparisons of the relationships between the same constructs in more active drug users will inform conclusions about how the putative personality-neurocognitive dual process mechanism of risk behavior varies across different stages of the addiction cycle.

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Vassilev, Z. P., Hagan, H., Lyubenova, A., Tomov, N., Vasilev, G., Krasteva, D. et al. (2006). Needle exchange use, sexual risk behaviour, and the prevalence of HIV, hepatitis B virus, and hepatitis C virus infections among Bulgarian injection drug users. *International Journal of STD & AIDS, 17,* 621-626.

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Wardle, M. C., Gonzalez, R., Bechara, A., & Martin-Thormeyer, E. M. (2010). Iowa Gambling Task performance and emotional distress interact to predict risky sexual behavior in individuals with dual substance and HIV diagnoses. *Journal of Clinical and Experimental Neuropsychology, 32,* 1110-1121.

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Wilson, M. J., Abramowitz, C., Vasilev, G., Bozgunov, K., & Vassileva, J. (2014). Psychopathy in Bulgaria: The cross-cultural generalizability of the Hare Psychopathy Checklist. *Journal of Psychopathology and Behavioral Assessment, 36*(3), 389-400.

Wilson, M.J., Vasilev, G., Bozgunov, K., & Vassileva, J. (2013, June). *Relationships of "hot" cognitive and "cool" motor impulsivity with HIV risk behaviors in abstinent drug users.* Poster session presented at the 11th meeting of the American Academy of Clinical Neuropsychology, Chicago, IL.

Wingrove, J. & Bond, A. J. (1997). Impulsivity: A state as well as trait variable. Does mood awareness explain low correlations between trait and behavioural measures of impulsivity? *Personality and Individual Differences, 22,* 333-339.

Wingrove, J. & Bond, A. J. (1997). Impulsivity: A state as well as trait variable. Does mood awareness explain low correlations between trait and behavioural measures of impulsivity? *Personality and Individual Differences, 22,* 333-339.

Wittmann, M., Simmons, A. N., Flagan, T., Lane, S. D., Wackermann, J., & Paulus, M. P. (2011). Neural substrates of time perception and impulsivity. *Brain Research, 1406,* 43-58.

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Zuckerman, M. (1994). *Behavioral expressions and biosocial bases of sensation seeking*. Cambridge university press.

Zuckerman, M. (1996). Item revisions in the Sensation Seeking Scale form V (SSS-V). *Personality and Individual Differences, 20,* 515.

VITA

Michael J. Wilson

EDUCATION

University of Illinois at Chicago (UIC)
Ph.D. Clinical Psychology, defended June 2015, conferral expected August 2016
M.A. Clinical Psychology, May 2012

University of Maryland, College Park
B.S. Biology & B.S. Psychology, August 2006

CLINICAL EXPERIENCE

Minneapolis VA Health Care System
Clinical Neuropsychology Intern, August 2015-August 2016

- Major Rotations: Polytrauma/Rehabilitation Neuropsychology, General Adult Neuropsychology, Inpatient TBI Rehabilitation Psychology
- Adjunctive Rotations: Clinical Ethics Consultation, MMPI-2-RF Assessment Clinic, Motivational Interviewing, Prolonged Exposure Therapy, Vocational Rehabilitation
- Elective Experiences: Administrative Assistant for VA Impaired Driver Policy workgroup; Cognitive Rehabilitation Group Facilitator (COGSMART); Neuropsychological Examiner for vEEG-monitored seizure patients and interdisciplinary chronic pain rehabilitation program

Supervisors: Greg Lamberty, Ph.D., ABPP-CN; Samantha Glass, Ph.D., ABPP-CN; Anita Sim, Ph.D., ABPP-CN; Paul Arbisi, Ph.D, ABPP; Wayne Siegel, Ph.D., ABPP

Jesse Brown VA Medical Center
Inpatient Psychiatry & Neuropsychology Practicum Student, June 2014-June 2015

- Provided individual & group psychotherapy for veteran psychiatric inpatients
- Conducted neuropsychological & diagnostic inpatient & outpatient evaluations
- Consulted with interdisciplinary medical treatment teams

Supervisors: Leon Kaufmann, Psy.D.; Robert Walters, Ph.D.

UIC Medical Center, Clinical Neuropsychology Service
Clinical Neuropsychology Practicum Student, June 2013-June 2014

- Conducted outpatient & inpatient neuropsychological & medicolegal evaluations

Supervisors: Neil Pliskin, Ph.D., ABPP-CN; Darren Feurst, Ph.D.; Julie Janecek, Ph.D.

UIC Office of Applied Psychological Services
Psychotherapy & Assessment Practicum Student, January 2011-July 2014

- Conducted evidence-based psychotherapies with community outpatients
- Completed integrated psychological assessments & provided feedback

Supervisors: Gloria Balague, Ph.D.; Nancy Dassoff, Ph.D.

RESEARCH EXPERIENCE

Minneapolis Veterans Affairs Health Care System
Clinical Neuropsychology Intern, August 2015-Present

- Developed clinical research project examining neurocognitive functioning of veterans in a comprehensive pain rehabilitation program

Supervisors: Greg Lamberty, Ph.D., ABPP-CN; Carly Anderson, Ph.D.

UIC Department of Psychiatry, Cognitive Neuroscience of Addiction Lab
Graduate Research Assistant, January 2012-August 2016

- Conducted original research projects examining neurocognitive & psychological dimensions of impulsivity among different classes of drug users
- Examined neurocognitive & personality mechanisms of risk behavior & neurocognitive sex differences among abstinent drug users

Supervisor: Jasmin Vassileva, Ph.D.

UIC Medical Center, Neuropsychiatric Institute
Graduate Clinical Research Assistant, August 2013-June 2014

- Assisted with consumer-oriented clinical neuropsychology outcome studies

Supervisor: Neil Pliskin, Ph.D., ABPP-CN

Marjorie Kovler Center for the Treatment of Survivors of Torture
Research Clinician, October-December 2012

- Consulted on a National Capacity-Building Project for Torture Treatment services
- Conducted pilot neuropsychological evaluations of refugee survivors of torture

Supervisors: Neil Pliskin, Ph.D., ABPP-CN; Nancy Dassoff, Ph.D.

University of Chicago Department of Psychiatry
Research Clinician, June 2011-March 2012

- Performed psychiatric screenings of volunteers for psychoactive drug administration research & administered brief substance use interventions

Supervisors: Harriet DeWit, Ph.D.; Royce Lee, M.D.

UIC Department of Psychiatry, HIV/Addiction Neuroscience Lab
Graduate Clinical Research Assistant, August 2010-December 2011

- Conducted original clinical research project investigating neurocognitive effects of HIV, substance use disorders, & neuropenetrant antiretrovirals in community drug users

Supervisor: Eileen Martin, Ph.D., ABPP-CN

Johns Hopkins University Department of Neurology
Clinical Research Coordinator, April 2008-July 2010

- Assisted with clinical research studies on neurocognitive effects of stimulant use

Supervisors: Una McCann, M.D.; George Ricaurte, M.D., Ph.D.

PEER-REVIEWED MANUSCRIPTS

1. Wilson, M. J., & Vassileva, J. (accepted). Neurocognitive and psychiatric dimensions of "hot" impulsivity, but not "cool" impulsivity, predict HIV sexual risk behaviors among drug users in protracted abstinence. *The American Journal of Drug and Alcohol Abuse, 42(2),* 231-241. doi: 10.3109/00952990.2015.1121269

2. Wilson, M. J., Abramowitz, C., Vasilev, G., Bozgunov, K., & Vassileva, J. (2014). Psychopathy in Bulgaria: The cross-cultural generalizability of the Hare Psychopathy Checklist. *Psychopathology & Behavioral Assessment, 36*(3), 389-400. doi: 0.1007/s10862-014-9405-6

3. Vassileva, J., Paxton, J., Moeller, F.G., Wilson, M. J., Bozgunov, K., Martin, E., Gonzalez, R., & Vasilev, G. (2014). Heroin & amphetamine users display opposite relationships between trait & neurobehavioral dimensions of impulsivity. *Addictive Behaviors, 39*(3), 652-659. doi: 10.1016/j.addbeh.2013.11.020

4. Wilson, M. J., Martin-Engel, L., Vassileva, J., Gonzalez, R., & Martin, E.M. (2013). An investigation of the effects of antiretroviral CNS penetration effectiveness on procedural learning in HIV+ drug users. *Journal of Clinical & Experimental Neuropsychology,35*(9)*,* 915-925*.* doi: 10.1080/13803395.2013. 838939

5. McCann, U.D., Edwards, R.R., Smith, M.T., Kelley, K., Wilson, M. J., Sgambati, F., & Ricaurte, G. (2010). Altered pain responses in abstinent (+)3,4-methylenedioxymethamphetamine (MDMA, "Ecstasy") users. *Psychopharmacology, 217*(4), 475-484. doi: 10.1007/s00213-011-2303-7

6. McCann, U.D., Wilson, M. J., Sgambati, F.P. & Ricaurte, G.A. (2009). Sleep deprivation differentially impairs cognitive performance in abstinent methylenedioxymethamphetamine ("Ecstasy") users. *The Journal of Neuroscience*, *29*(44), 14050-14056. doi: 10.1523/jneurosci.4654-09.2009

ORAL PRESENTATIONS

1. Wilson, M. J. (2015, October). *Neurocognitive functioning of chronic pain patients participating in a four-week comprehensive rehabilitation program.* Oral research communication presented at the 2015 meeting of the Minneapolis VAHCS Psychology Research Group.

2. Wilson, M. J., Vasilev, G., Moeller, F. G., & Vassileva, J. (2014, June). *Sex differences in cognitive & motor impulsivity among users of different classes of drugs in protracted abstinence.* Oral research communication presented at the 76th meeting of the College on Problems of Drug Dependence, San Juan, PR.

3. Wilson, M. J., & Vassileva, J. (2014, May). *Biological sex influences neurocognitive functioning in abstinent drug users: Preliminary findings.* Oral research communication presented at the UIC Gender & Sexuality Center.

4. Wilson, M. J. (2014, April). *Longitudinal neuropsychological evaluation of a postoperative stroke patient with visual field deficits.* (2014, May). Clinical case conference presented at the UIC Neuropsychiatric Institute.

5. Wilson, M. J. *Antiretroviral neuropenetrance and neurocognitive functioning in HIV+ inner city drug users.* (2012, April) Oral research communication presented at the UIC clinical psychology graduate seminar series.

POSTER PRESENTATIONS

1. Wilson, M., Anderson, C., Keenan, P., Krause, L., Finn, J., Lamberty, G. J. (accepted). Neurocognitive functioning of veterans participating in a comprehensive pain rehabilitation program. Poster session to be presented at the 14th meeting of the American Academy of Clinical Neuropsychology, Chicago, IL. *The Clinical Neuropsychologist, 30*(3), 442.

2. Vassileva, J., Wilson, M.J., Martin, E.M., & Vasilev, G. (accepted). Sex differences in 'impulsive choice' and 'impulsive action' among opiate and stimulant users in protracted abstinence. Poster session to be presented at the 29th meeting of the European College of Neuropsychopharmacology, Vienna, Austria.

3. Wilson, M.J., & Vassileva, J. (2016, February). Effects of Sex and Drug Class on Neurocognitive Impulsivity among Drug Users in Protracted Abstinence. Poster session presented at the 44th meeting of the International Neuropsychological Society, Boston, MA. *Journal of the International Neuropsychological Society, 22*(S1).

4. Buehler, S., Botbol, E., Zalizniak, K., Carrión, C., Bjorquist, O. Leon, A. Gierut, K., Wilson, M. J., … Pliskin, N. (2014, August). *Measurement of outcome following neuropsychological evaluation: The impact of the evaluation on the consumer.* Poster

session presented at the 122nd meeting of the American Psychological Association, Washington, D.C.

5. Vassileva, J., Moeller, F. G., Bozgunov, K. , Wilson, M. J., & Vasilev, G. (2014, June). *Unique & common neurocognitive effects of opiate & stimulant dependence persist with protracted abstinence.* Poster session presented at the 76th meeting of College on Problems of Drug Dependence, San Juan, PR.

6. Rosado, D., Buehler, S., Botbol, E., Zalizniak, K., Carrión, C., Bjorquist, O., Leon, A., Gierut, K., Wilson, M. J., ... Pliskin, N. (2014, June). *Impact of thorough review of neuropsychological testing results on caregiver coping & perceptions of care-recipient functioning*. Poster session presented at the 12th meeting of the American Academy of Clinical Neuropsychology, New York, NY. *The Clinical Neuropsychologist, 28*(3), 485.

7. Wilson, M. J., Vasilev, G., Bozgunov, K., & Vassileva, J. (2014, February). *Reward-based decision-making & pathological gambling in different types of drug users.* Poster session presented at the 42nd meeting of the International Neuropsychological Society, Seattle, WA. *Journal of the International Neuropsychological Society, 20*(S1), i-294. doi:http://dx.doi.org/10.1017/S1355617714000381

8. Wilson, M.J., Vasilev, G., Bozgunov, K., & Vassileva, J. (2014, February). Effects of psychopathy on reward-based decision-making in opiate, stimulant, & polysubstance users. Poster session presented at the 42nd meeting of the International Neuropsychological Society, Seattle, WA. *Journal of the International Neuropsychological Society, 20*(S1), i-294. doi:http://dx.doi.org/10.1017/S1355617714000381

9. Wilson, M.J., Vasilev, G., Bozgunov, K., & Vassileva, J. (2014, February). *Neurocognitive decision-making performance shows differential associations to pathological gambling across abstinent users of different classes of drugs.* Poster session presented at the 10th NIH Fogarty International Center symposium for Brain Disorders in the Developing World, Washington, D.C.

10. Vasilev, G., Wilson, M. J., Abramowitz, C., Bozgunov, K., & Vassileva, J. (2014, February). *The cross-cultural generalizability of the Hare Psychopathy Checklist.* Poster session presented at the 10th NIH Fogarty International Center symposium for Brain Disorders in the Developing World, Washington, D.C.

11. Vasilev, G., Wilson, M. J., Bozgunov, K., Gonzalez, R., & Vassileva, J. (2014, February). *Relationships of trait & state indices of cognitive & motor impulsivity with HIV risk behaviors in abstinent opiate & stimulant users.* Poster session presented at the 10th

NIH Fogarty International Center symposium for Brain Disorders in the Developing World, Washington, D.C.

12. Vassileva, J., Moeller, F. G., Wilson, M. J., Buzgunov, K., Martin, E. M., Gonzalez, R., & Vasilev, G. (2014, February). *Heroin & amphetamine users display opposite relationships between trait & neurobehavioral dimensions of impulsivity.* Poster session presented at the 10th NIH Fogarty International Center symposium for Brain Disorders in the Developing World, Washington, D.C.

13. Wilson, M. J., Vasilev, G., Bozgunov, K., & Vassileva, J. (2013, June). *Relationships of "hot" cognitive & "cool" motor impulsivity with HIV risk behaviors in abstinent drug users.* Poster session presented at the 11th meeting of the American Academy of Clinical Neuropsychology, Chicago, IL. *The Clinical Neuropsychologist, 27*(4), 646.

14. Wilson, M. J., Bozgunov, K., & Vassileva, J. (2013, June) Differential relationships between psychopathy & HIV risk behavior in abstinent drug users & controls. Poster session presented at the 5th meeting of the Society for the Scientific Study of Psychopathy, Washington, D. C.

15. Wilson, M. J., Vasilev, G., Bozgunov, K., Raynov, I., Naslednikova, R., & Vassileva, J. (2013, May). Differential effects of psychopathy on neurocognitive performance in heroin & stimulant users. Poster session presented at the 85th meeting of the Midwestern Psychological Association, Chicago, IL.

16. Bozgunov, K., Wilson, M. J., Vassileva, J. (2012, November). *Psychopathy in Bulgaria: Preliminary findings*. Paper presented at the National Student Congress of Psychology, Veliko Tarnovo, Bulgaria.

17. Wilson, M. J., Vasilev, G., Bozgunov, K., Raynov, I., Naslednikova, R., & Vassileva, J. (2012, September). *Personality mediators of psychopathy & risk behavior in non-incarcerated substance users & healthy controls.* Poster session presented at the 3rd UIC Psychiatry Research Forum, Chicago, IL.

18. Wilson, M. J., Vassileva, J., Gonzalez, R., Ladd, L. & Martin, E. M. (2012, February). *Effects of antiretroviral CNS penetration effectiveness on procedural learning task performance in HIV+ drug users.* Poster session presented at the 40th meeting of the International Neuropsychological Society, Montreal, Quebec. *Journal of the International Neuropsychological Society, 18*(S1), i-293. doi: http://dx.doi.org/ 10.1017/S1355617712000537

19. Martin, E.M., Vassileva, J., Martin, L., Wilson, M. J., Liu, R., Paxton, J. & Gonzalez, R. (2010, September). *Effects of HIV, antisociality, & drug use on motor impulsivity.* Poster session presented at the 1st UIC Psychiatry Research Forum, Chicago, IL.

20. Wicks, S., Wilson, M. J., Gonzalez, R., Vassileva, J., & Martin, E. M. (2010, September). *Effects of HIV & ADHD symptoms on procedural learning.* Poster session presented at the 1st UIC Dept. of Psychiatry Research Forum, Chicago, IL.

21. Wilson, M. J., Ricaurte, G. A., Smith, M. T., Sgambati, F. P., & McCann, U. D. (2009, December). *The relationship between altered sleep patterns & pain perception in abstinent* (±)*3,4- methylenedioxymethamphetamine users*. Poster session presented at the 4th Johns Hopkins Bayview Research Symposium, Baltimore, MD.

22. Wilson, M. J., Sgambati, F. P., Ricaurte, G. A. & McCann, U. D. (2008, December). *Effects of sleep deprivation on cognitive performance in abstinent* (±)*3,4-methylenedioxymethamphetamine users*. Poster session presented at the 3rd Johns Hopkins Bayview Research Symposium, Baltimore, MD.

PEER REVIEWER

- Journal of Gambling Studies
- World Journal of Psychiatry

AWARDS & HONORS

American Academy of Clinical Neuropsychology

- Student Travel Scholarship ($500), 2016

National Institute on Drug Abuse

- Junior Investigator Travel Award ($750), 2014

University of Illinois at Chicago

- Psychology Dept. Award for Outstanding Research & Scholarship, 2013, 2014, 2015
- Psychology Dept. Travel Award ($400), 2012, 2013, 2014
- Liberal Arts & Sciences Graduate College Travel Award ($500), 2012, 2013, 2014

University of Maryland, College Park

- Dean's List Scholar 2002, 2005, 2006
- College of Chemical & Life Sciences Outstanding Student Award 2005, 2006

PROFESSIONAL AFFILIATIONS

American Academy of Clinical Neuropsychology
American Psychological Association Division 40 (Neuropsychology) & Division 50 (Addictions)

TEACHING EXPERIENCE

UIC Department of Psychology

Graduate Teaching Assistant, August 2010-July 2015

- Abnormal Psychology
- Behavioral Neuroscience
- Developmental Psychology
- Field Work in Applied Psychology
- Introduction to Psychology
- Laboratory in Clinical Psychology
- Personality Theories
- Professional Writing in Psychology
- Psychological Testing

LECTURES

UIC Department of Psychology

- *Perception & Sensorineural Processing*
  Lecture addressed to undergraduate class in Behavioral Neuroscience (June, 2015)

- *Neuropsychological Assessment/Forensic Psychological Assessment*
  Lectures addressed to undergraduate class in Psychological Testing (October/November 2014)

- *Clinical Neuropsychology 101*
  Lecture addressed to undergraduate Clinical Psychology Lab class (November, 2013)

- *Writing an Empirical Paper*
  Lecture addressed to undergraduate class in Applied Psychology (March, 2013; November 2012)