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The Influence of Neurocognitive Impairment on HIV Risk Reduction Intervention Outcomes among Drug Dependent Methadone-Maintained Patients

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By

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ABSTRACT

Injection drug users (IDUs) represent a significant vector for contracting and transmission of HIV infection, which occurs through preventable drug- and sex-related risk behaviors. Accordingly, IDUs remain a target population of HIV risk reduction behavioral interventions. Previous findings show that it is feasible to provide a brief behavioral risk reduction group intervention to high risk HIV-infected IDUs in a community-based setting to reduce HIV risk-related outcomes. In order for behavioral interventions to be effective, a relatively high level of cognitive abilities is required. Evidence shows that chronic drug use can affect the central nervous system and this may result in neurocognitive impairment that could potentially interfere with optimal participation in such behavioral interventions. Few efforts have been made to determine how neurocognitive impairment may negatively impact intervention participation and, in turn, outcomes in this population. In this study high-risk HIV-negative opioid-dependent drug users seeking drug treatment in a community based methadone program received 4-session of Community-Friendly Health Recovery Program (CHRP) vs. a Control condition to evaluate whether there is a significant association between cognitive impairment and HIV risk reduction intervention outcomes.

Table of Contents

INTRODUCTION

There are currently over 1 million people living with HIV/AIDS in United States U.S. and, 20% of those people are unaware of their infection (Center for Disease Control and Prevention [CDC], 2008). HIV infection is caused by Human Immunodeficiency Virus. This virus can gradually destroy the immune system and lead to Acquired Immune Deficiency Syndrome (AIDS). HIV is transmitted via body fluids including blood, semen, vaginal fluid, and breast milk. The most common routs of HIV transmission are: unprotected sex and sharing needles, syringes, rinse water, or other unsterilized injection equipment. HIV transmission via birth, breastfeeding, and blood transfusion is not a main concern in U.S. anymore although it is still a key route of transmission in many developing countries. In the U.S., men who have sex with men (MSM), heterosexual intercourse, and injection drug use (IDU) are the major modes of HIV transmission (see Figure below).

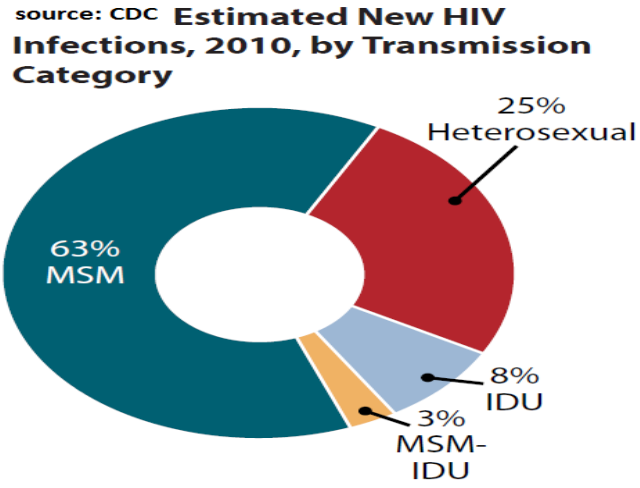

Figure1. Estimated New HIV Infection by Transmission Category (CDC, 2010)

Despite a range of HIV prevention efforts, CDC estimated, HIV incidence was approximately 48,100 new HIV infections in the United States in 2009 (CDC, 2009). About 8% of these new HIV infections in 2010 occurred among injecting drug users (IDUs; CDC, 2010). People who have unprotected sex with an injection drug user also are at risk of infection through the sexual transmission of HIV. Trading sex for money or for drugs are also activities that put drug dependent individuals at risk for contracting or transmitting HIV (CDC, 2009).

In 2000, 11635 AIDS cases in U.S. were evaluated regarding their route of HIV contraction and the results showed that 73% of AIDS cases were directly associated with IDU while, the 27% of AIDS cases were indirectly associated with IDU and were seen among sex partners of IDUs, male-IDUs who had sex with men and children of IDUs or their sex partners (see Figure below).

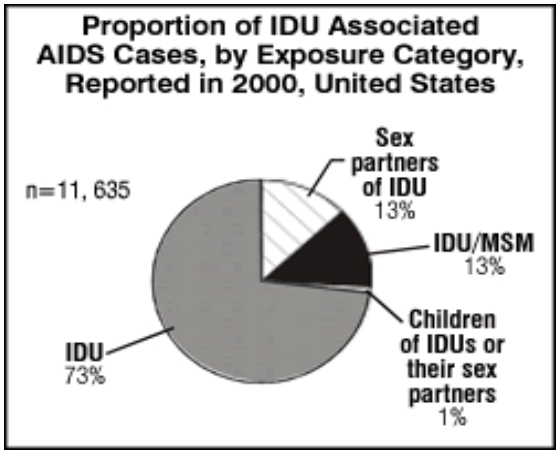

Figure2. Proportion of IDU associated AIDS cases, by exposure category in 2000, United States.

Studies have shown that substance abusers tend to practice HIV-related risk behaviors such as sharing needles or having unprotected sex especially while under the influence of drugs (National Institute on Drug Abuse [NIDA], 2012).

There is currently no effective vaccine to prevent new HIV infections while previous studies show that through behavioral interventions, risky sexual and needle sharing behaviors can be effectively reduced. Maintaining consistently safe sex- and drug-behaviors over time and increasing knowledge of HIV status and personal risk factors through behavioral interventions could eliminate the high risk of HIV transmission among populations at risk. Accordingly, behavioral interventions remain a primary tool for reducing the risk of HIV transmission (Semaan et al., 2002). There are some evidence-based behavioral intervention approaches targeting HIV-infected and HIV-negative IDUs (Holistic Health Recovery Program-HHRP+). The goal of these approaches is to improve antiretroviral medication adherence and reduce HIV transmission risk for HIV-infected patients and reduce HIV risk behaviors for high risk HIV-negative patients (Avants, Margolin, Usubiaga, & Doebrick, 2004; Margolin, Avants, Warburton, Hawkins, & Shi, 2003). These interventions consist of a series of group 'treatment' sessions, where HIV-infected participants are provided information on antiretroviral medication adherence, risk behaviors, and how to maximize their outcomes. Participants are also taught harm reduction skills, such as how to properly use condoms and how to sterilize needles (Avants et al., 2004; Margolin et al., 2003).

Evidence shows that these behavioral interventions are also applicable in community based organizations that offer OAT (opioid agonist therapy) for drug dependent patients (M. M. Copenhaver, Lee, & Margolin, 2007). OAT -a type of drug

abuse treatment- is also an effective intervention used as HIV prevention. The goal of OAT is to reduce illicit drug use and consequently to limit exposure to needle sharing and to increase the practice of safer sex among IDUs. Methadone maintenance therapy (MMT) is the most widely applied and researched OAT. Methadone blocks the euphoric effects of other opioids and evidence shows that MMT has been effective in reducing illicit opioid use (Metzger & Zhang, 2010).

On the other hand, both chronic drug abuse and OAT exacerbate neurocognitive impairment (NCI) which can lead to HIV risk-taking behaviors and also could reduce the effectiveness of risk reduction behavioral interventions (Anand, Springer, Copenhaver, & Altice, 2010). Most drugs of abuse cross the blood-brain-barrier and directly affect the central nervous system (CNS), resulting in NCI symptoms (Tamrazi & Almast, 2012). Deficits in attention, working memory, episodic memory, and executive function have been observed in individuals with drug abuse (Rapeli et al., 2006). NCI symptoms can range from very mild to very severe, and studies suggest that symptoms tend to worsen with prolonged drug use (Heaton et al., 1995).

In order to be effective, risk-reduction interventions must therefore take into account the impact of on learning and behavior. Some interventions use cognitive remediation strategies that are designed to take into account the possibility of NCI in the target populations and accordingly consider the specific intervention needs of drug users with NCI (M. Copenhaver, Avants, Warburton, & Margolin, 2003). Based on these findings, access to proven risk reduction behavioral interventions, and also continued research activities to develop optimal interventions suitable for high-risk population in the U.S. is highly recommended. The purpose of the current study was to examine the

relationship between NCI and HIV risk reduction intervention outcomes in a sample of high-risk HIV-negative drug-dependent patients seeking drug treatment in a community based methadone program. The participants participated in a Community-Friendly Health Recovery Program (CHRP) for HIV-negative drug users in New Haven, Connecticut.

LITERATURE REVIEW

Drug dependence and HIV/AIDS are still major public health problems in the U.S. and many other parts of the world. According to the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) substance abuse is defined as having problems at work, home, and school; problems with family or friends; physical danger; and trouble with the law due to substance use while the dependence status is defined as health and emotional problems, attempts to cut down on use, tolerance, withdrawal, and other symptoms associated with substances use (American Psychological Association, 1994). The National Institute on Drug Abuse (NIDA) lists 10 different categories for drugs of abuse including: legal recreational substances (e.g. alcohol), prescription medications (e.g. opioids), and illegal substances (e.g. heroin, cocaine and marijuana; NIDA, 2011). According to Substance Abuse and Mental Health services Administration's (SAMHSA) 2011 estimate of substance dependence or abuse in the past year, 20.6 million persons (8% of the population aged 12 or older) were classified with substance dependence or abuse based on criteria specified in DSM-IV. Of these, 2.6 million were classified with dependence or abuse of both alcohol and illicit drugs and 3.9 million had dependence or abuse of illicit drugs but not alcohol. According to SAMHSA's 2011 survey, the rate of current illicit drug use (one month prior to survey) generally declined with age and was higher for males. Among persons aged 12 or older, the rate of current illicit drug use was lowest among Asians followed by Hispanics, whites, blacks, Native Hawaiians or Other Pacific Islanders, American Indians or Alaska Natives. Among adults aged 18 or older, the rate of current illicit drug use was positively associated with unemployment and negatively associated with the level of education.

Among persons aged 12 or older, the rate of current illicit drug use in 2011 was highest in the West followed by the Northeast, Midwest and South of the US (SAMHSA, 2011). The fact is that drug abuse or drug dependence is associated with significant morbidity and mortality. For example, IDU can increase the risk of infection through needle contamination with HIV, hepatitis, and other organisms.

It is estimated that 34.2 million people were living with HIV in 2011 worldwide. East and Southern Africa remains the area most heavily affected by the HIV epidemic (UNAIDS, 2011). HIV is transmitted through six common categories including male-to-male sexual contact, IDU, male-to-male sexual contact and IDU, heterosexual contact, mother-to-child (perinatal) transmission, and other (like blood transfusions and unknown cause). IDU is a major risk factor of HIV transmission or contraction. In 2010, IDU was the third most frequently reported risk factor for HIV infection in the U.S. (CDC, 2010). In Northeastern United States, as many as 44% of all new HIV infections are directly or indirectly attributable to drug use (CDC, 2009). In 2010, IDUs and male who have sex with male (MSM) and are IDUs accounted for approximately 8% and 3% of all the new cases of HIV infection. According to the CDC in the same year, MSM accounted for 61% and heterosexual intercourse accounted for 28% of new HIV infections. The highest rates of people living with a diagnosis of HIV infection at the end of 2008, was reported in the South and the Northeast of the U.S. In 2009, African Americans accounted for 44% of all new HIV infections in the U.S. while they represent only 14% of the U.S. population (CDC, 2009).

The impact that drug use and abuse can have on the spread of HIV/AIDS is not only through IDU and needle sharing but also through the risky behaviors that occur

in the context of drug use. Drug intoxication affects mental status and judgment and can lead to risky sexual behavior (e.g. unprotected sex or having multiple sex partners) that puts participants at risk of contracting or transmitting HIV and other sexually transmitted diseases. Moreover, substance use can weaken the immune system and consequently facilitate the progress of HIV infection. Substance abuse is one of the focus areas of Healthy People 2020 and one of the proposed objectives of Healthy People 2020 is: 'increase the number of admission to substance abuse treatment for injection drug use'. Co-occurring of HIV and substance abuse is also mentioned in one of the proposed objectives: 'increase the proportion of substance abuse treatment facilities that offer HIV/AIDS education, counseling, and support'.

With such a significant number of HIV cases directly or indirectly related to drug use, effective substance abuse treatment and HIV-prevention interventions should be delivered to this high risk population. NIDA's research has showed that comprehensive HIV prevention including substance abuse treatment and community-based outreach, in combination with testing and counseling for HIV and other infections is an effective approach (NIDA, 2005). Drug abuse and HIV/AIDS are related issues and based on this fact, drug treatment becomes a crucial HIV prevention method while it limits exposure to needle sharing and increases the practice of safer sex. Most of the drug involved people, are poly-drug users (users of more than one drug) and will require treatment for all of the substances that they abuse. Detoxification of drugs is also accompanied by withdrawal syndrome, which is managed with medications prescribed by a physician in an inpatient or outpatient setting. Medications are used to prevent relapse and decrease cravings and also help reestablish normal brain function. Different types of

medications are applied to control the withdrawal symptoms such as opioids, benzodiazepines, alcohol, nicotine, barbiturates, and other sedatives (NIDA, 2012).

Opioid agonist therapy (OAT) is one of the substance abuse treatments applied to reduce illicit drug use. OAT is defined as the consumption of regular, controlled doses of opioid agonists for extended periods (e.g. > 6 months). Methadone, buprenorphine and, for some individuals, naltrexone are effective medications for the treatment of opiate addiction. Methadone maintenance therapy (MMT) is the most widely applied and researched OAT. Methadone is used orally and blocks the euphoric effects of other opioids. Its metabolism is slow, lasts longer than many illicit opioids, and is acceptable to many patients (Metzger & Zhang, 2010). Evidence shows that MMT has been effective in reducing illicit opioid use and has helped patients disengage from drug seeking and related criminal behavior and become more receptive to behavioral treatments (NIDA, 2009).

Neurocognitive impairment among drug involved population:

Most drugs of abuse cross the blood-brain-barrier and directly affect the central nervous system (CNS), resulting in Neurocognitive impairment (NCI) symptoms. There are different types of substances with serious brain complications including cocaine, heroin, alcohol, amphetamines, toluene, and cannabis. The CNS complications of these drugs include neurovascular complications, encephalopathy, atrophy, infection and other changes in brain structure (Tamrazi & Almast, 2012). Deficits in attention, working memory, episodic memory, and executive function have been observed in individuals with drug abuse (Rapeli et al., 2006). Previous studies indicate that there is an

extensive overlap between the brain regions and neural processes that underlie addiction and those that support cognitive functions like learning, memory, and reasoning. On the other hand, cognitive deficits followed by continued drug use exacerbate the difficulty of establishing sustained abstinence. The developing brain is particularly susceptible to the effects of drugs of abuse; accordingly, prenatal, childhood, and adolescent exposures produce long-lasting changes in cognition (Gould, 2010). Some studies suggest that the association between chronic drug use and different types of cognitive deficit may be because of the direct impact of specific drugs on brain or because of impact of drugs on deficits that have already happened and could possibly make that person susceptible to the effects of drug abuse (Ersche, Clark, London, Robbins, & Sahakian, 2006). Neuroimaging studies suggest that methamphetamines can make changes in serotonin and dopamine function and also can make difference in cerebral blood flow. These studies suggest that methamphetamine use is associated with mood and anxiety disorders, psychosis, and cognitive deficits. Changes in inhibitory control -one of the domains of cognitive function- caused by methamphetamine use are associated with continued use of this substance and high tendency to relapse (Price et al., 2011). Methamphetamine users experience generalized difficulties with prospective memory even after abstinence (Rendell, Mazur, & Henry, 2009). Other studies indicate that long-term heavy cannabis use can result in memory impairment in adults. The results also show that even brief exposure to cannabis adversely affects the developing brain of adolescents, as this population demonstrates memory deficits similar to those reported in adult long-term heavy users (Solowij et al., 2011). Le Berre et al. showed that in their sample of chronic alcoholics both episodic memory and metamemory for novel information has been

affected. Executive dysfunction was also seen in this clinical population (Le Berre et al., 2010). In one study 19 recently abstinent cocaine-dependent males were compared to 16 control subjects on a battery of neuropsychological tests. The results showed that the performance of cocaine-dependent subjects was inferior to the control group on tasks assessing higher level verbal skills, and on a task requiring logical sequencing of complex visual stimuli. Cocaine users also performed poorly on a delayed visual memory task and on a verbal generation task, but performed better than the control group on a task assessing simple visual-motor speed (Gillen et al., 1998). One study estimated the prevalence of NCI in different components of executive functions in poly-substance users who were enrolled in therapeutic communities. Study results showed a significant prevalence of executive function impairment in poly-substance users compared to non-substance users. Working memory was the component with the highest impairment proportion, followed by fluency, shifting, planning, multi-tasking and interference (Fernandez-Serrano, Perez-Garcia, Perales, & Verdejo-Garcia, 2010). In St. Petersburg, Russia a group of Heroin addicts were compared with three comparison groups including alcoholics, addicts who used both alcohol and heroin, and non-abusers. The results showed that heroin addicts exhibited significantly more disadvantageous decision making and longer deliberation times while making risky decisions compared to other groups (Fishbein et al., 2007). Some studies indicated that heroin addicts with history of poly-drug abuse perform worse than controls but better than amphetamine users on functions like: impulsivity, attention and learning, working memory and pattern recognition (Ersche et al., 2006; Ornstein et al., 2000).

There are other common issues among drug involved patients which are associated with NCI, such as; drug-related infections (e.g. HIV and Hepatitis C viral infection), traumatic brain injury, and mental illness, and opioid substitution therapy. Studies have shown that following HIV infection, cognitive performance (such as learning of new information, information processing speed and attention) and daily functioning are highly affected (Anand et al., 2010). Among HIV-associated CNS disorders, HIV-associated neurocognitive disorders (HAND), is the most significant one (Boisse, Gill, & Power, 2008). Evidence shows that brain injury acquired during advanced immune suppression might be only partially reversible with antiretroviral therapy (Letendre, Ellis, Ances, & McCutchan, 2010). Moreover, opioid dependence can reduce immune system integrity and stimulate viral replication in HIV-seropositive drug users and consequently exacerbate HAND (Anand et al., 2010). Studies show that patients with mental illness are also at high risk for substance abuse, and the adverse impact of drug abuse on cognition may be particularly deleterious in combination with cognitive problems related to their mental disorders (Gould, 2010). Findings show that OAT is also associated with NCI (Anand et al., 2010). Some psychomotor and cognitive dysfunctions have been seen in methadone-maintained patients compared to matched control groups (Darke, Sims, McDonald, & Wickes, 2000). Some studies indicate that abstinence from certain drug groups may cause some cognitive improvements (Ersche et al., 2006; Papageorgiou et al., 2004; Verdejo, Toribio, Orozco, Puente, & Perez-Garcia, 2005). However, one study comparing methadone-maintained patients with current cocaine dependence to methadone-maintained abstainers shows no differences on measures of cognitive functions between these two groups (Henry et al., 2012). Previous

studies indicate that NCI symptoms tend to worsen with prolonged drug use (Heaton et al., 1995). Drug dependence and drug induced NCI could both affect the quality of life, and possibly the craving and relapse. NIDA has estimated that in 2002 illicit drug use alone has accounted for $181 billion in health care, productivity loss, crime, incarceration and drug enforcement office (Office of National Drug Control Policy, 2004).

Substance abuse and HIV related risk behaviors:

Evidence shows that the NCI due to substance abuse is associated with increased HIV related risk behaviors, which are caused by drug-induced poor judgment. NCI due to substance abuse is also associated with significant barriers to HIV risk reduction behavioral interventions which also cause the increased HIV related risk behaviors (Avants, Warburton, Hawkins, & Margolin, 2000). Studies have shown that drug dependent people are involved in sex- and drug-related HIV risk behaviors more than other people. Epidemiological studies have identified multi-person use of contaminated drug injection equipment, such as needles and syringes as a major route for transmitting HIV among IDUs (Needle et al., 1998). The results of one study evaluating 2091 IDUs in the capitals of 29 provinces in Iran showed that 35.8% of sample reported lifetime experience of needle and syringe sharing (Rafiey et al., 2009). In Pakistan in a sample of 161 IDUs, sharing syringes was reported by 79.5% of participants (Altaf et al., 2007). In another study 54 drug injection networks were observed by researchers in seven cities of seven different states of the U.S. Sharing injection paraphernalia or drug solution occurred in 94% of injection events and serial use of syringes or needles occurred in 14% of events. While, reuse of cookers, cotton and water respectively occurred in 84%, 77%

and 77% of events (Needle et al., 1998). Besides, generalization of the HIV epidemic from high-risk groups to the general population may be driven by risky sexual behavior among drug users. One study has examined the role of risky sexual behaviors on HIV infection among 426 IDUs and non-injection drug users in China. The results showed that considerable proportions of sample reported engagement in risky sexual behaviors including: multiple sexual partners (37% of IDUs), concurrent sexual partnerships (46% of IDUs) and commercial sex partners (24% of IDUs). Only 42% of IDUs reported condom use with non-regular partners and 27% reported condom use with regular partner (Li et al., 2011). Unprotected sex was reported by 64% of research participants in a sample of 161 Pakistani IDUs (Altaf et al., 2007). The results of a survey done in Mauritius, an Indian Ocean Island revealed that among 511 IDUs, 61% reported injecting 2-3 times/day and 29.3% reported past month injection with a previously used needle. Amongst the 60% of IDUs who reported having sexual intercourse in the past three months, 39.5% did so with ≥2 partners. Almost all IDUs (98.1%) reported inconsistent condom use in the past 12 months (Johnston, Saumtally, Corceal, Mahadoo, & Oodally, 2011). CDC's National HIV Behavioral Surveillance System (NHBS) interviewed and tested 10,073 IDUs in 20 metropolitan statistical areas in 2009. Among the 9,565 IDUs with HIV-negative or unknown HIV status before the survey, 69% reported having unprotected vaginal sex, 34% reported sharing syringes, and 23% reported having unprotected heterosexual anal sex during the 12 previous months (CDC, 2009).

The sex- and drug- related risk behaviors remain a driver of HIV, hepatitis C virus (HCV) and hepatitis B virus (HBV) transmission and other sexually transmitted diseases (STDs) throughout the world. In one study among the 407 IDUs recruited from a

region with higher incidence of STDs, HCV and HIV prevalence were 60.6% and 10.1%, respectively; and 98% of HIV positive individuals were co-infected with HCV (Pilon et al., 2011). While, HIV prevalence among 511 IDUs in Mauritius was 47.4%, HCV 97.3%, HBV 9.0%, and syphilis 2.7%; and 99.7% of those infected with HIV were also infected with HCV (Johnston et al., 2011). In Puerto Rico, 255 young IDUs (16-24 years old) were evaluated regarding the factors associated with HIV-seropositivity. More than 23% of subjects were HIV-seropositive (Marrero Rodriguez et al., 1993).

HIV related risk behaviors and neurocognitive impairment:

Once drug- and sex-related risk behaviors determined to be major transmission routes for HIV infection, identifying and understanding the reasons behind choosing drug- and sex-related risk behaviors among substance dependent individuals is crucial. Drug-related NCI reduces the individual's perception of personal risk and consequently is a significant barrier in managing risk behaviors. Lots of studies have shown that there is a mutual relationship between NCI and HIV related risk behaviors. Increased risk behaviors exacerbate NCI and NCI reduces the effectiveness of interventions aimed at reducing HIV related risk behaviors (Anand et al., 2010). Findings indicate that more intensive efforts may be required to reduce the risky behaviors among those IDUs with lower cognitive scores in higher risk social groups. On the other hand**,** risk-reduction interventions must consider the impact of NCI on learning and behavior (Anand et al., 2010).

The results of 52 reviewed studies showed that HIV related risk behaviors were correlated with cognitive-behavioral factors, substance use, psychiatric illness,

childhood abuse, and social relationships. In these studies the majority of sexually active adults with severe mental illness were engaged in HIV related risk behaviors (such as unprotected sex, multiple sex partners, and injection drug use) (Meade & Sikkema, 2005). One study evaluated the effects of implicit cognition, behavioral and personality variables (like poly-drug use and sensation seeking), on risky sexual behaviors (like lack of condom use, sex after drug use, and multiple sexual partners) among high risk and low risk adults from a community population. Results showed that the implicit cognition (unconscious influences such as knowledge, perception, or memory, that influence a person's behavior) was a significant, independent predictor of lack of condom use in the high-risk sample. Poly-drug use and sensation seeking (a personality trait common among drug users) also had important predictive effects (Stacy, Newcomb, & Ames, 2000). Another study examined the effect of executive neurocognitive functions, sensation seeking, and HIV serostatus in predicting risky sexual practices among poly-substance users (with a history of dependence primarily for cocaine or cocaine/heroin). The impact of executive functions was less clear but findings indicated that continued risk behavior among HIV infected drug users may be driven by sensation seeking (Gonzalez et al., 2005). One study in Baltimore examined the association among knowledge of someone who had died from AIDS, cognitive functioning, and drug and sex-related HIV risk behaviors among 229 IDUs of heroin. Among IDUs with lower cognitive scores, knowing someone who had died from AIDS was associated with increased risk and among IDUs with greater cognitive reserves, knowing someone who had died from AIDS was associated with decreased risk. This suggests that cognitive performance can provide protection to individuals in riskier social environments. These

findings can help in targeting HIV prevention efforts toward higher risk individuals within the IDU population (Mitchell, Severtson, & Latimer, 2007).

Behavioral interventions applied to reduce risk behavior in drug users

There is currently no effective vaccine to prevent new HIV infections while previous studies show through behavioral interventions, risky sexual and needle sharing behaviors among IDUs can be reduced. Accordingly, behavioral interventions remain a primary tool for reducing the risk of HIV transmission (Semaan et al., 2002). Evidence shows that these behavioral interventions are applicable in a wide range of settings such as community based organizations that offer OAT for drug dependent patients. Margolin et al. (2003) randomly assigned 90 HIV-seropositive, methadone-maintained IDUs either to an experimental group receiving 12-session HHRP+ intervention or to a control group receiving harm reduction components recommended by the National AIDS Demonstration Research Project. Participants in experimental group received information on antiretroviral medication adherence and also received training on harm reduction skills, such as how to properly use condoms and how to sterilize needles. Subjects were followed at 6 and 9 months after the intervention. Reduction in risk behaviors was seen in both groups. However, patients receiving HHRP+ were less likely to use illicit opiates during intervention. Moreover, participants in experimental group showed lower addiction severity scores and less high-risk behaviors at follow up points (M. M. Copenhaver et al., 2007; Margolin et al., 2003). Avants et al. (2004) focused on 220 HIV-negative methadone-maintained IDUs. Participants in the control group received standard care which involved 2 hours of counseling per month and a single-session risk reduction

intervention and experimental group's participants received standard care plus 12-session HHRP intervention. The goal of the HHRP intervention was to promote health and increase quality of life through HIV prevention information, motivation to engage in HIV prevention and opportunities to practice behavioral skills for HIV prevention. Results indicated that experimental group's participants were more likely to be abstinent from cocaine and to report fewer unsafe sexual practices (Avants et al., 2004).

Because further evidence showed that 12-session HHRP intervention was very lengthy, complex, and costly in terms of training, implementation, and monitoring, Copenhaver et al. (2007) reduced the content and duration of HHRP intervention. The resulting intervention was a shortened, adapted version called the Community-friendly Health Recovery Program (CHRP) since it was designed to be more acceptable within the clinical context of community-based organizations. In this study, 226 HIV-negative methadone-maintained IDUs received 4-session CHRP intervention in an uncontrolled condition. Post-test results showed significant reductions in drug-and sex-related HIV risk behaviors. Moreover, the CHRP intervention demonstrated the potential to be fully integrated within drug treatment community based organizations (M. M. Copenhaver et al., 2007). Another study done in California compared a 4-month enhanced intervention (consist of nine sessions of HIV counseling, and testing) to a 2-session standard counseling and testing intervention developed by NIDA. The purpose of the study was to determine the efficacy of two different types of intervention in terms of reducing drug-and sex-related risk behaviors among IDUs. For both interventions, most risk behaviors were significantly reduced but enhanced intervention significantly increased IDUs' use of their own injection equipment. According to these results, the theory-based cognitive-

behavioral intervention showed limited advantage over the standard intervention in terms of both magnitude and frequency of HIV risk reduction achieved by high-risk drug users (Hershberger, Wood, & Fisher, 2003).

Based on the previous information, risk-reduction behavioral interventions available for neurocognitively-impaired drug-involved people must consider the impact of NCI on learning and behavior. Some interventions provide cognitive remediation delivery strategies which are designed to take into account the possibility of NIC in the target populations and accordingly accommodate the specific intervention needs of drug users with NCI during intervention delivery (M. Copenhaver et al., 2003). Some of the cognitive remediation strategies thought to accommodate intervention participants with NCI include: training front-line clinical staff, especially addiction counselors to identify NCI, to communicate effectively with other health care providers and with neurocognitively-impaired clients, and to establish a trusting relationship with the client. The cognitive remediation strategies include developing a treatment plan, multimodal presentation of material (visual and verbal), experimental learning (practice, role-play, and behavioral games), use of simple language, frequent review of material, assessment with immediate feedback (observation of behavior and quizzes), having structured sessions and consistent times/locations, use of memory aids and stress management (M. Copenhaver et al., 2003).

Both the HHRP and CHRP interventions are based on the Information–Motivation–Behavioral Skills model of health behavior (Fisher & Fisher, 1992) which specifies that HIV prevention Information, Motivation, and Behavioral Skills are the fundamental determinants of HIV risk and HIV risk reduction behavior. From this

perspective, HIV prevention Information that is directly relevant to an individual's practice of risk reduction behavior is a prerequisite for engaging in risk reduction action. Similarly, HIV prevention Motivation to act on what one knows about HIV prevention - including personal motivation (attitudes about personally taking preventive actions) and social motivation (perceived social support/social pressure to take preventive actions) - is an additional prerequisite for the initiating and maintaining HIV risk reduction behavior. Finally, HIV prevention behavioral skills for taking HIV preventive actions are a third prerequisite for engaging in HIV risk reduction behavior, and determine whether even a well-informed and well-motivated individual is able to skillfully initiate and maintain HIV risk reduction behavior (see Figure below).

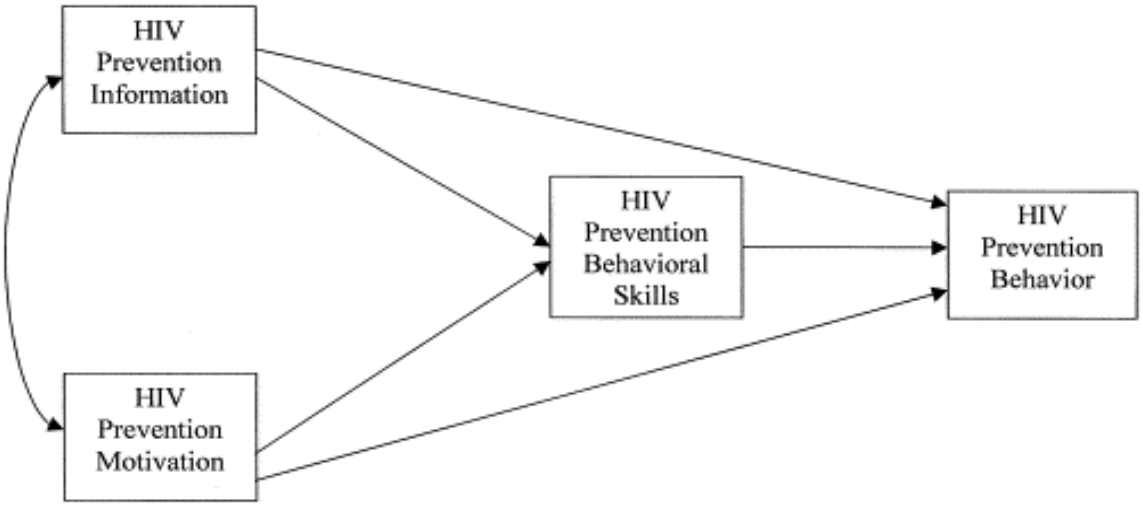

Figure 3: IMB MODEL

Examples of drug- and sex-related HIV-risk reduction knowledge are "If an HIV positive person only has sex with another HIV positive person, they don't need to use condom." and ''If an HIV positive person shared needles with another HIV positive person, they don't need to clean the needles.'' Examples of drug use personal and social

motivation incorporated in the CHRP intervention are “in the next 6 months do you plan (intend) to stop using heroine completely?” and “how important is being drug free to most of the people in your social network?” Examples of sex risk self-efficacy and reported behavior questions are “how confident are you that you would bring up the issue of condoms or safer sex in a conversation when sober” and “how many sexual partners have you had in the past 30 days?”

Based on research to date, access to proven risk reduction behavioral interventions, and also continued research activities to develop optimal interventions for high risk population in the U.S. is crucial. The purpose of the current study was to examine NCI in a sample of HIV-negative methadone-maintained patients participating in an HIV prevention intervention study and to explore the association between NCI and HIV risk reduction intervention outcomes. The subjects were participants in a NIH-funded randomized controlled trial testing the CHRP for HIV-negative drug users participating in drug treatment in New Haven, Connecticut.

OBJECTIVES AND HYPOTHESIS

Objective:

1-To examine whether there is a significant association between neurocognitive impairment and HIV risk reduction intervention outcomes among high-risk HIV-negative drug users seeking drug treatment in a community based methadone program.

Hypothesis:

H1: There is a significant association between neurocognitive impairment and HIV risk reduction intervention outcomes among high-risk HIV-negative drug users seeking drug treatment in a community based methadone program.

METHOD

Design: It should be noted that the parent study was a randomized clinical trial of a community-friendly HIV-risk reduction behavioral intervention designed to reduce HIV risk behavior among high risk drug dependent individuals who were in drug treatment. The current study was a secondary analysis of a subset of data collected from the parent study. Specifically, correlational analysis was used to evaluate the association between HIV risk reduction intervention outcomes and NCI measured using the neuropsychological impairment scale (NIS) (O'Donnell, Reynolds, & De Soto, 1983).

Participants: Two hundred and eighty high-risk HIV-negative opioid dependent drug users who were receiving MMT in a community based organization located in New Haven, Connecticut were recruited. Forty six percent of participants were male and a majority of them were Caucasian (73.9%), never married (65.7%), English speaking (94.6%), had a significant other (70%), with a median age of 33, and with 12 years of education. From those who recruited first, 178 remained until the end of the study. There was no significant difference between the demographic characteristics of those who remained in the study with those who first were recruited ($p > .30$). Participants reported having a similar numbers of children (median = 1, $p = .36$) and had similar rates of living with their children (27.5%, $p = .46$).

High-risk opioid dependent drug users were defined as those patients who reported having unprotected sex or sharing needles (or other unsterilized injection equipment) within the past 6 months.

Inclusion and exclusion criteria for this study were: being at least 18 years of age, meeting DSM-IV criteria for opioid-dependence, seeking MMT, reporting drug- or sex-related HIV risk behavior in the previous 6 months, being able to read and understand the audio computer assisted self-interview (ACASI) questions, being available for the full duration of the study with no anticipated participation limitation and not being actively suicidal, homicidal, or psychotic. Informed consent was obtained from participants and any potential risks to confidentiality were explained to them.

Procedure: Participants were randomly assigned to either the CHRP intervention group (n=136, 63 males) or the active control group (n=144, 66 males). Until the end of the study, only 87 participants remained in the intervention group and 91 participants remained in the control group. Participants in the intervention group received standard of care plus four 45-minute weekly group-sessions of CHRP intervention and participants in control group received standard of care plus a time- and attention-matched control condition that focused on social support.

Study Groups: Subjects in the experimental condition participated in the CHRP intervention, which is a manual-guided and adapted behavioral intervention for optimal use within drug treatment community based organizations. The CHRP intervention sessions consisted of general information on HIV/AIDS and HIV-related risk behaviors. Participants were also taught harm reduction skills, such as how to properly

use male and female condoms and how to properly sterilize needles. The intervention content was delivered by two trained bachelor's level facilitators using cognitive remediation strategies designed to accommodate the mild to moderate cognitive difficulties that are common among this population (M. Copenhaver et al., 2003). The sessions were held at the APT Foundation's methadone maintenance program in New Haven, CT.

Subjects in the control condition participated in standard of care group meetings, which addressed psychological service needs (e.g., housing, employment and childcare) and referral resources in the community.

Measures: Assessments of participants were done at baseline, immediately post-intervention, and at 3-, 6-, and 12-month post-intervention follow-up points through ACASI. Regarding self-reported drug- and sex-related HIV risk behavior, HIV/AIDS knowledge, risk reduction motivation and risk reduction behavioral skills were framed by the IMB skill model of health behavior change (Fisher & Fisher, 1992). Based on the IMB model of health behavior change, upon which the CHRP intervention is based, participants completed an assessment that covered the following domains: drug- and sex-related HIV-risk reduction knowledge (Information component), personal and social motivation to reduce HIV risk behavior (Motivation component), and self-efficacy about reducing HIV risk behavior (Behavioral skills component). Four items were used to assess knowledge about safer sex and safer injection drug use (e.g., "If an HIV+ person shared needles with another HIV+ person, they don't need to clean the needles.''). Six items examined participants' motivation to use condoms and clean needles, intentions to

engage in safer sexual activity and safer injection drug use practices, and their perception of significant others' beliefs about the importance of using condoms and using clean needles (e.g., "in the next 6 months do you plan to stop using heroine completely?" for measuring the personal motivation component). Four items assessed participants' behavioral skills in the form of their self-efficacy about abstaining from sexual activity and using a condom and about abstaining from injecting drugs and using clean needles (e.g., "how confident are you that you would bring up the issue of condoms or safer sex in a conversation when sober" for measuring Behavioral skills component). This assessment approach has been used in a randomized controlled trial of an evidence-based intervention (Fisher et al., 2004, M. M. Copenhaver et al., 2007) in order to inform intervention clinicians about HIV-related information, motivation, and behavioral skills deficits among participants entering treatment.

The NIS was also completed at the same assessment points. The NIS is a 95-item self-report questionnaire (O'Donnell et al., 1983) used to measure NCI. Participants responded to each item using a 5-point response scale (0= not at all to 4= extremely). The NIS includes 7 subscale scores and 3 summary scores, which were computed, based on participant responses. There are also four validity checks contained in the NIS. The NIS is generally used as a screening instrument and not a diagnostic tool. This assessment instrument has been written at a fifth-grade reading level and the respondents have to be at least 18 years of age. Evidence shows that the sensitivity of NIS is 91% and its specificity is 76% using the Halstead Impairment Index (HII), which is a standard, more comprehensive neuropsychological battery (O'Donnell, De Soto, & Reynolds, 1984).

The NIS subscales which show impairment in the different cognitive domains including:

1-Critical Items (CRIT): Assesses the patient's history of neurological illness or injury.

2-Cognitive Efficiency (COG): Assesses general symptoms of NCI.

3-Attention (ATT): Assesses the patient's ability to pay attention and concentrate.

4-Memory (MEM): Assesses the patient's memory.

5-Frustration Tolerance (FRU): Assesses irritability, anger and temper.

6- Learning Verbal (LV): Assesses learning and expressive speech.

7-Academic Skills (ACD): Assesses ability to carry out daily activities involving computing and reading.

Summary scores which are designed to evaluate overall cognitive functioning include:

1-Global Measure of Impairment (GMI) which provides an overall measure of impairment is calculated through total of responses to 80 items on the instrument (excluding Defensiveness Scale and Affective Disturbance items).

2-Total Items Circled (TIC) is defined as total number of items with non-zero responses (excluding Defensiveness Scale and Affective Disturbance items).

3-Symptom Intensity Measure (SIM) is computed by dividing the GMI by the TIC.

NIS scores are usually expressed as T-scores. T-scores are standardized scores on each dimension for each type. A score of 50 represents the mean. A difference of 10 from the mean indicates a difference of one standard deviation (SD). Thus, a score of 60 is one standard deviation above the mean, while a score of 30 is two standard deviations below the mean. High levels in any of these scores indicate NCI but low scores can also indicate problems. For the purpose of this study NIS scores <30T were considered low,

scores >30T and <50T were considered average, a high score was >50T and < 60T, and any score above 60T was considered very high.

The validity scores, which provide a foundation for the interpretation of the other scores, include:

1-Defensiveness (DEF): Indicates the test takers attitude.

2-Affective Disturbance (AFF): Indicates emotional state of the subject at the time of the test.

3- Response Inconsistency (INC): Identifies inconsistent response pairs.

4- The Subjective Distortion Check: tells whether the client is under- or over-reporting symptoms.

Twice weekly urine toxicology screens were also taken from participants during the 4-week intervention period. Urine toxicology screens differentiated between methadone and other opioids and showed the degree to which participants were still using illicit drugs including opiates and cocaine during the intervention period. In addition, a weekly self-report of illicit drug use and other high risk behaviors was obtained, which included self-reported: (a) quantity, frequency, and route of administration of illicit drugs, including heroin and cocaine; (b) frequency and type of other HIV risk behaviors, including needle sharing, unsafe needle cleaning, and unsafe sexual practices, and (c) frequency of harm reduction practices, such as use of needle exchange programs and purchase of needles and condoms. In addition, following each risk reduction group session, a quiz was administered to assess acquisition of intervention content.

All subjects were reimbursed for the time and effort needed to participate in the study. They were paid $50 for each assessment session (at pre-intervention, post-

intervention, and at a 3-, 6-, and 12-month post-intervention follow-ups) and $10 weekly for brief weekly assessments of substance use and HIV risk behaviors during the four week intervention phase.

Data Analysis: Data from pre-intervention and post-intervention were included in the secondary analysis. Simple correlations were carried out between all NIS scale and subscale scores (described above) and treatment outcome scores. P values were set at <.001, <.01 and <.05 and SPSS software was used for all statistical analyses.

RESULTS

Overall, outcomes of the parent study showed significant differences between the intervention and control groups with regard to key drug-risk reduction (i.e., safer drug use behavior, improved drug-risk reduction skills) and sex-risk reduction (i.e., obtaining condoms, self-efficacy in using condoms) variables. Support was also found for the IMB model of health behavior change. Participants in the CHRP group showed significantly improved HIV risk reduction outcomes in terms of changes in demonstrated sex- and drug-risk reduction (i.e., male and female condom application and properly cleaning injection equipment) versus those in the control group.

There were no significant differences between the control and intervention group participants with regard to drug use or drug risk behavior while enrolled in the study. With regard to the NIS scores, the results of the current study show that there was no significant difference between the NIS scores of intervention and control groups from pre- to post-intervention. The NIS scores ranged from approximately 40T (1 SD below

the mean) on the symptom intensity measure subscale to 57T (0.8 SD above the mean) for affective disturbance subscales.

Significant differences were found between NIS scores of male and female participants. Females showed higher scores in global measure of impairment (GMI) - indicating greater overall NCI- compared to males. Females also showed higher scores in subscales of affective disturbance, cognitive efficiency, attention, frustration tolerance, and academic skills (Table 1).

	Control		**Intervention**		**Gender**	
Predictor	Mean	SE	Mean	SE	Male	Female
Validity Scores						
- Response Inconsistency	53.29	.71	52.29	.73	52.01	53.58
- Defensiveness Scale	39.61	.52	40.34	.53	39.86	40.09
- Affective Disturbance	57.79	.82	57.45	.83	55.38***	59.87***
Summary Scores						
- Global Measure	55.07	0.98	55.33	1.00	52.77***	57.63***
- Total Items Circled						
- Symptom Intensity Measure	39.12	0.90	40.78	0.91	38.81	41.09
Impairment Subscales						
- Critical Items	56.55	0.93	56.25	0.95	55.45	57.34
- Cognitive Efficiency	53.75	0.90	55.23	0.92	52.54**	56.53**
- Attention	54.67	0.96	54.67	0.98	51.86***	57.47***
- Memory	52.48	0.95	52.46	0.97	51.32	53.62
- Frustration Tolerance	57.39	0.86	56.84	0.87	54.90***	59.33***
- Learning-Verbal	51.59	0.92	52.46	0.93	51.47	52.58
- Academic Skills	53.40	0.90	53.24	0.91	51.46**	55.18**

Table1. Descriptive results of NIS scale (*p<.05; **p<.01; ***p<.001)

Importantly, the analyses also indicated that intervention group participants with higher levels of NCI tended to benefit less from the intervention content in terms of: (1) learning drug-risk reduction skills (i.e., safer drug use behavior, improved drug-risk reduction skills) and (2) learning sex-risk reduction skills (i.e., obtaining condoms, self-efficacy in using condoms) that were taught during the group sessions compared with participants with lower levels of cognitive impairment. HIV risk reduction skills were not taught in the control group sessions and – as might be expected - this pattern of associations was not observed among control group participants.

For the intervention group, negative relationships were found between most of NIS subscales and improvement in drug-risk reduction skills from pre- to post-intervention compared to those in the control group. This pattern of results indicates that higher scores on the NIS subscales were significantly associated with less improvement in drug-risk reduction skills. For the intervention group, higher scores on the global measure of impairment – indicating greater overall NCI – were associated with less improvement in drug-risk reduction skills from pre- to post-intervention compared with those in the control group. The same results were seen with regard to subscales of cognitive efficiency, attention, memory, frustration tolerance; learning-verbal, academic skill, affective disturbance, and symptom intensity measure (see table2).

For the control group, higher scores on the global measure of impairment – indicating greater overall NCI – were associated with less reported drug use from Pre to Post compared with those in the intervention group. The same results were seen with regard to subscales of cognitive efficiency, response inconsistency, critical items,

attention, frustration tolerance; learning-verbal, academic skill, affective disturbance, and symptom intensity measure (Table 2).

NIS items	Social motivation	Knowledge	Drug RR Skills	Drug information	Drug use	Self-esteem	Personal motivation
Validity Scores:							
Response Inconsistency					x/-.30***		
Defensiveness Scale			x / x	-.16+/x		x /-.18*	x /-.14+
Affective Disturbance			-.22** / x		x / -.23**		
Summary Scores:							
Global Measure			-.19* / x		x / -.24**		
Total Items Circled							
Symptom Intensity Measure			-.20* / x		-.16+ / -.20*	x / .17*	
Impairment Subscales:							
Critical Items					x/ -.29***		
Cognitive Efficiency			-.23** / x		x / -.20*		
Attention			-.15+ / x		x / -.18*		
Memory			-.19* / x				
Frustration Tolerance			-.17+ / x		-.15+ / -.19*		
Learning-Verbal			-.24**/-.18*		-.24**/-.18*		
Academic Skills			-.15+ / x		x / -.21*		

Table2. Significant associations between NIS scores and drug-risk reduction skills from pre to post intervention (intervention / control). *p<.05; **p<.01; ***p<.001

For the intervention group, higher scores on the global measure of impairment – indicating greater overall NCI – were associated with less sex risk reduction (condom use) from pre- to post-intervention compared with those in the control group. The same results were seen with regard to subscales of cognitive efficiency, critical items, memory, academic skill, and symptom intensity measure (Table 3).

NIS items	Social motivation	Knowledge	Self-esteem	Purchasing condoms	Safe sex
Validity Scores:					
Response Inconsistency				x / .15+	x / .18*
Defensiveness Scale				-.28** / x	x / -.16+
Affective Disturbance				x / .18*	
Summary Scores:					
Global Measure				-.18+ / x	
Total Items Circled					
Symptom Intensity Measure				-.29** / x	
Impairment Subscales:					
Critical Items				-.19* / x	
Cognitive Efficiency				-.17+ / x	
Attention					
Memory				-.22* / x	
Frustration Tolerance				x / .19*	
Learning-Verbal					
Academic Skills				-.20* / x	

Table3. Significant associations between NIS scores and sex-risk reduction skills from pre to post intervention (intervention / control). *p<.05; **p<.01; ***p<.001

Discussion

The parent study provided evidence of efficacy of the CHRP intervention, as significant enhancements were demonstrated in participants' behaviors including participants' demonstration of drug- and sex-related HIV risk reduction skills. Consistent with other studies with this target population of HIV-negative chronic drug users indicating deficits in different tasks of neuropsychological tests (Rapeli et al., 2006; Gould, 2010; Gillen et al., 1998; Fernandez-Serrano et al., 2010; Fishbein et al., 2007) in the current study, also moderate to severe cognitive impairment was evident among the participants as indicated by generally low scores on the NIS as well as relatively lower scores across specific subscales. The current study appears to be the first study assessing the potential association between neurocognitive impairment with risk reduction intervention outcomes among HIV-negative chronic drug users. Following the intervention, improvements in drug- and sex-related HIV risk reduction outcomes were negatively associated with NCI among the intervention group participants.

The results of the current study also show that there is no significant difference between the intervention and control groups with regard to the NCI from pre- to post-intervention. This finding supports the concept of positive effects stemming from behavioral interventions in terms of reducing HIV risk behaviors. As this effect was not seen among the control group participants knowing that the only difference between control and intervention groups participants was in having access to the intervention content, therefore, the results of the parent study regarding the efficacy of the CHRP intervention is strongly supported as those participants with lower levels of NCI who specifically receive the CHRP intervention demonstrate more HIV risk reduction skill

development while, less improvement from the intervention content was seen among the intervention group participants with higher levels of NCI.

On the other hand, NCI was associated with lower self-efficacy not involving in drug and sex related risk behaviors and more difficulty learning drug- and sex-risk reduction skills. For example, participants with higher NCI showed less sex-risk reduction (purchased condoms less frequently) and showed less improvement in drug-risk reduction skills.

Type of variable	Constructs
Drug use	Information Personal motivation, Social motivation Self-efficacy/difficulty, Reported behavior
Sex behavior	Information Personal motivation, Social motivation Self-efficacy/difficulty, Reported behavior

Table 4: Variables used and IMB constructs

Moreover, looking at validity scores of NIS, the mean value for defensiveness suggests that participants did not have a wrong attitude towards the test. On the other hand, the mean affective disturbance score was suggestive of some degree of emotional stress at the time of the test which was not a surprising finding considering the nature of the sample and the fact that drug involved individuals are typically socio-economically disadvantaged. The mean response inconsistency score also indicates some inconsistent answers to questions on the NIS.

The current study had a number of limitations. First, the sample size included in this secondary analysis was small. It was not sufficiently large to generate enough

power in the statistical analyses to adequately examine all the variables of interest. And it is strongly recommended for future studies to evaluate a larger number of HIV-negative drug involved patients with more complex analytical tests. Secondly, the NIS does not provide a comprehensive assessment of NCI and does not measure all possible cognitive domains although it is a very user-friendly test. Thirdly, the components of IMB skill model of health behavior change are highly correlated with one another and also the questions used for assessing each component could be understandable for a group of people while at the same time they could be misleading for some other participants. It is possible that, with a larger sample, a multivariate analysis could be carried out which would allow us to control for such associations. Fourthly, almost all data were provided through self-report assessments, and self-reported assessments are always a challenge to the integrity of the responses provided, especially because the study seeks to examine mostly socially unacceptable behaviors. This may have been moderated, however, by the use of ACASI systems, which provided participants with a high level of privacy in addition to the assurance of anonymity. Finally, subjects with poor scores on the validity checks score (e.g. defensiveness, affective disturbance and response inconsistency) should have been excluded from this analysis for more accurate interpretation of results. However, already having a relatively small sample size would have further reduced statistical power.

There was also an unexpected pattern of outcomes to find that, for the control group, reported drug use was negatively associated with NCI from pre- to post-intervention compared with those in the intervention group. This indicates that participants in the control group with higher NCI tended to report less drug use. This

pattern of association was not seen among intervention group participants. The control group participants received more information focused on drug prevention and treatment which could explain why this pattern of association was only seen among control group participants. But, this finding is surprising as we had hypothesized that better HIV risk reduction intervention outcomes such as less drug use would be observed in participants with lower NCI. In fact, participants with higher NCI have been found to show more improvements.

This puzzling finding could have happened as a result of some possible confounding factors that correlate with both the NCI and different items of IMB skill model of health behavior change and subsequently these confounding factors could cause surprising results. In the current study we tried to control for some of these confounding variables as the results show that there were no significant differences between the control and intervention group participants with regard to drug use or drug risk behavior while enrolled in the study. However, due to the inability to control for variability of human studies, confounding is a particular challenge and for future studies, it is important to control for some more important confounding variables like alcohol dependency to isolate the effect of NCI on HIV risk reduction intervention outcomes. For these reasons, future studies could also offer to test confounders in a complex mixed effects or structural equation model. For example it is recommended to test different components of IMB skill model of health behavior change (information, motivation and behavioral skills) among control and intervention group participants with lower and higher NCI.

As NCI apparently has an important role on intervention outcomes targeting sex- and drug-related risk behaviors and considering that these interventions typically

place a high demand on several cognitive domains such as memory, learning, and attention so, NCI may be a potential confounding variable with regard to treatment outcomes. Adequate attention should be paid to NCI when designing and implementing interventions for this population like what Copenhaver et al. done in their study in 2003. This is particularly important where NCI symptoms are mostly mild and can very easily be ignored or be mistaken for other effects of active drug use such as hangovers or being 'high'.

Conclusion

Results of this study suggest that screening for NCI in this population, and potentially accommodating mild to moderate levels of NCI in the delivery of interventions maybe helpful to be applied in all future behavioral risk reduction interventions for this target population as implied in prior work (Copenhaver et al., 2003). Moreover, controlling for confounding factors that correlate NCI may provide more accurate interpretation of study results among this patient population. It may also be necessary to assess the associations of NCI and intervention outcome variables at follow up points. NCI may account for drop outs and may also explain some of the relapse often experienced in behavioral interventions. Moreover, future studies should use more comprehensive and sensitive screening instruments for NCI and also increase the sample size and objectively assess the contributions of cognitive remediation strategies. On the other hand, greater NCI in female participants compared to male participants was an unexpected result and it is recommended that future studies utilize a larger sample, to assess the possible relationship between gender and greater NCI. Relatively high scores

on affective disturbance observed were not unexpected in this sample considering the social and economic challenges faced by this population. It however suggests that those who administer neuropsychological test ought to be careful not to have activities that could add any more emotional strain to participants coinciding with test taking as this could potentially affect the reliability of test results. Although the CHRP intervention has been shown to be efficacious in this target population of HIV-negative chronic drug users, such interventions may not be the first line of treatment for patients with cognitive difficulties, and it may still be necessary to explore other intervention approaches to improve sex- and drug-related risk behaviors in this population. Substance use treatment such as methadone maintenance treatment has been shown to play a helpful role to address drug risk behavior. This study also suggests that there could be sub groups of patients within the larger group of HIV-negative chronic drug users based on neurocognitive status. Recognizing this and tailoring treatment to meet their needs seems to be valuable in order to have an effective intervention targeting this population.

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