Published in final edited form as:
Am J Addict. 2014 September ; 23(5): 431–439. doi:10.1111/j.1521-0391.2014.12124.x.

Cognitive Performance Profiles by Latent Classes of Drug Use

PT Harrell[1], **B Mancha**[2], **SS Martins**[3], **PM Mauro**[4], **JH Kuo**[5], **M Scherer**[4], **KI Bolla**[6], and **WW Latimer**[2]

[1]Department of Health Outcomes and Behavior, Moffitt Cancer Center, Tampa, FL, USA

[2]Department of Clinical and Health Psychology, College of Public Health and Health Professions, University of Florida, Gainesville, FL, USA

[3]Department of Epidemiology, Columbia University Mailman School of Public Health, USA

[4]Department of Mental Health, Johns Hopkins School of Public Health, Baltimore, MD, USA

[5]Department of Epidemiology, Johns Hopkins School of Public Health, Baltimore, MD, USA

[6]Department of Neurology, Johns Hopkins School of Medicine, Baltimore, MD, USA

Abstract

Background and Objectives—The relationship between substance use and cognitive deficits is complex and requires innovative methods to enhance understanding. The present study is the first to use LCA to examine associations of drug use patterns with cognitive performance.

Methods—Cocaine/heroin users (N=552) completed questionnaires, and cognitive measures. LCA identified classes based on past-month drug use and adjusted for probabilities of group membership when examining cognitive performance. Latent indicators were: alcohol (ALC), cigarettes (CIG), marijuana (MJ), crack smoking (CS), nasal heroin (NH), injection cocaine (IC), injection heroin (IH), and injection speedball (IS). Age and education were included as covariates in model creation.

Results—Bootstrap Likelihood Ratio Test (BLRT) supported a 5-class model. Prevalent indicators (estimated probability of over 50%) for each class are as follows: "Older Nasal Heroin/ Crack Smokers" (*ONH/CS*, n=166.9): ALC, CIG, NH, CS; "Older, Less Educated Polysubstance" (*OLEP*, n=54.8): ALC, CIG, CS, IH, IC, and IS; "Younger Multi-Injectors" (*MI*, n=128.7): ALC, CIG, MJ, IH, IC, and IS; "Less Educated Heroin Injectors" (*LEHI*, n=87.4): CIG, IH; and "More Educated Nasal Heroin" users (*MENH*, n = ALC, CIG, NH). In general, all classes performed worse than established norms and older, less educated classes performed worse, with the exception that *MENH* demonstrated worse cognitive flexibility than *YMI*.

Discussion and Conclusions—This study demonstrated novel applications of a methodology for examining complicated relationships between polysubstance use and cognitive performance.

Correspondence to: Dr. Paul T. Harrell, Ph.D., JHSPH, Dept. of MH, 895 Hampton House, 624 North Broadway Baltimore, MD 21295, (443) 287-8271, pharrell@jhsph.edu.

DECLARATION OF INTEREST The authors Paul Harrell, Brent Mancha, Michael Scherer, Julie Kuo, Pia Mauro, Silvia Martins, Karen Bolla, and William Latimer declare no conflict of interest. The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

NIH-PA Author Manuscript
NIH-PA Author Manuscript

Scientific Significance—Education and/or nasal heroin use are associated with reduced cognitive flexibility in this sample of inner city drug users.

Keywords

Cognition; cocaine; heroin; polydrug; latent class analysis; injection

INTRODUCTION

The relationship between substance use and cognitive deficits is complex and requires innovative methods to enhance understanding. Cognitive deficits, particularly disinhibition, may lead to the development of substance dependence [1, 2]. Further, drugs themselves can cause cognitive deficits. This contributes to the chronic nature of substance dependence [3-6]. Most evidence suggests associations with neuropsychological deficits for both cocaine dependence [7, 8] and opioid dependence [9-13]. However, due to the high prevalence of polydrug use among cocaine and heroin users [14], it is difficult to discriminate which drugs may be most associated with the deficits.

Previous research has attempted to examine deficits associated with polydrug use by various methodological means. Ornstein and colleagues examined set-shifting, i.e., shifting between relevant/irrelevant stimuli, among non-drug users compared to amphetamine users and heroin users after withdrawal symptoms had been resolved [13]. This intra/extra-dimensional set-shift is similar to the set-shifting in the Wisconsin Card Sorting Task. Though both groups demonstrated memory impaiments, heroin users performed worse in identifying the initial relevant stimuli, while amphetamine users demonstrated deficits with relevant stimuli [13].

Verdejo-Garcia and colleagues examined groups of polysubstance cocaine and opioid users on tasks measuring cognitive impulsivity. Though polysubstance use among opioid users was greater than cocaine users, cocaine users performed significantly worse on selective attention, impulsivity, response inhibition, and cognitive flexibility [15, 16]. Both groups of polysubstance users performed worse than controls on decision-making, impulsivity, working memory and reasoning. This is of particular concern as impulsivity and disinhibition may lead to more severe substance use and possible substance dependence [1, 2]. However, it is difficult to discern which patterns of substance use are associated with which deficits.

In addition, most research ignores drug routes of administration (ROAs), e.g., smoking, nasal, injection, despite associations with unique health consequences for different ROAs [17-19]. For example, smoking is linked with greater medical complaints, higher mortality rates, and greater risk of injection drug use (IDU) [19-23]. Smoking crack cocaine, as opposed to nasal use, is associated with increased risk of dependence [24]. Injection is associated with increased risk for drug dependence [25, 26], overdose [27], and HIV and hepatitis C infection [28, 29].

Although research in this area is limited, there are reasons to believe ROAs may be differentially associated with cognitive functioning for both cocaine and heroin. Injection or smoking produces larger highs and greater pain reduction than nasal or oral use [30-32], suggesting that cognitive performance may be differentially impacted as well. Further, given that injection is associated with well-known negative consequences, injection drug users may be particularly impulsive and severe [33, 34]. Indeed, academic failure is associated with heroin injection severity [35] and impaired planning ability is associated with increased cocaine and heroin injection practices [36]. Thus, there is some limited evidence to suggest cognitive functioning and ROAs are differentially associated, but further research is needed.

Very little research has used latent variables to examine complicated questions regarding drug use and cognitive performance. Latent modeling – a technique that infers unobserved, "latent" variables from observed variables –is a promising tool to assess cognitive performance and enhance understanding of effects of multiple drug use. For example, item-centered analyses, such as Principal Component Analysis (PCA) provided useful information on identifying cognitive domains that are damaged in substance abuse [16] and Exploratory Factor Analysis (EFA) provided information on beliefs about substance use and relationship to executive deficits [37]. However, only one paper used person-centered analyses, such as Latent Profile Analysis (LPA). This recent paper used LPA to examine cognitive performance profiles, finding three levels of intellectual and executive functioning, viz., impaired, intact, and high [38]. However, it appears no one has used person-centered analyses, such as Latent Class Analysis (LCA), to address associations between polydrug use and cognitive performance.. Effective use of LCA has allowed for furthering our understanding of the development of drug dependence [20, 39-46] . Although LCA has been used in increasing frequency, the present study is the first to use LCA to examine associations of drug use patterns with cognitive performance. More extreme drug use patterns (e.g., injection drug use, polysubstance use) are expected to be associated with poorer executive functioning.

MATERIALS AND METHODS

Participants

The present study sample consisted of 552 Black and White drug users in Baltimore, Maryland, from the NEURO-HIV Epidemiologic study [21, 47, 48]. Upon arrival, participants provided informed consent, blood and urine samples, completed the HIV-Risk Behavior Interview – a semi-structured interview about drug use and sexual practices – and performed cognitive assessments described below. The study was approved by the Institutional Review Board at the University of Florida.

Assessments

Latent class indicators included all routes of administration (ROAs) and substances used in the past month by 20% or more of the sample. Self-report results of prior 30-day drug use were consistent with urinalysis drug results [20]. The eight binary substance use indicators included in the analyses were: alcohol, cigarettes, smoking marijuana, smoking crack, snorting heroin, injecting heroin, injecting cocaine, and injecting "speedball" (cocaine and heroin mixed). In addition, since age and education appeared to be important variables (see Table 1), dichotomous median-split variables for age (33) and education (highest grade completed, 11) were included in model creation using the “c on” command in M-plus. Other variables included in separate analyses were race (Caucasian or African-American), gender, current participation in drug treatment, and lifetime history of regular drug use for all indicators except cigarette smoking.

Cognitive measures were selected to assess major domains implicated in substance abuse. These tests included measures of intelligence, memory, and three measures of executive functioning. Executive functioning refers to cognitive processing of the initiation and maintenance of actions. It is believed to be critical for the initiation, maintenance, and cessation of substance abuse behavior [1-6]. The cognitive measures used included measures of general intelligence, viz., the Shipley Institute of Living Scale (SILS) [49], working memory, viz., the Digit-span subtest of the WAIS-R [50], attention, viz., the Trail Making Test [51], behavioral inhibition, viz., the Stroop test [52], and cognitive flexibility, viz., the Wisconsin Card Sorting Task [53]. .

The cessation of substance abuse behavior theoretically requires adequate intelligence to understand the problematic nature of the behavior and to gain value from instructions from others [54]. To measure overall intelligence, we used the Shipley Institute of Living Scale (SILS). The SILS consists of a vocabulary subtest and an abstraction subtest. For the verbal subtest of the SILS, participants were given 20 minutes to complete 40 multiple choice vocabulary questions. For the abstraction section of the SILS, participants were given 20 minutes to complete 20 abstract reasoning questions. Raw scores were calculated according to the number of questions answered correctly in the allotted time. Adjusted total T-scores controlling for age/education were used in the present analysis [49]. As SILS scores are sometimes used as a proxy for pre-morbid intellectual functioning among substance using samples [55], we further report predicted IQ based on the Wechsler Adult Intelligence Scale – Revised [50]. This provides a full scale IQ using the SILS age-stratified raw score [49].

To cease substance use behavior, adequate working memory is needed to continually work towards goals [56]. Working memory was assessed using the Digit Span subtest of the WAIS-R [50]. Participants were asked to repeat a list of numbers read aloud by the administrator either in the same order (forward) or in reverse (backward) order. Individuals’ ability to manipulate increasingly long strings of numbers, reversing the order of two to seven digits, reflects their ability to retain information and manipulate it [57]. The Digit Span subtest is commonly used in studies of cognitive functioning and substance use [58-61].

Attention is another domain theoretically important in the reduction of substance use behavior [62]. Two sections of the Trail Making Test were included in this study. In the first trial (Part A), the time to connect the dots with incremental numbers was recorded. In the second trial (Part B), the time to connect the dots from numbers to letters, both increasing by one digit or letter was recorded. While the first test largely examines psychomotor speed, the second test requires careful attention due to its relatively higher level of complexity and novelty. Participants were asked to connect the dots as fast as they could in each of the trials [51]. The Trailmaking Test is commonly used to assess cognitive impairment amongst substance users [63]. The scores in the table reported here reflect the time spent on the task and thus, higher scores are indicative of worse performance. However, for the sake of clarity, the scores in the figure are reversed z-scores and thus, similar to the other measures reported, higher scores are indicative of better performance.

Behavioral inhibition seems to be critically important in the reduction of substance use. Individuals in recovery must inhibit drug abuse, a highly rewarding behavior [64]. The Stroop test is a widely used measure of behavioral inhibition [65]. The Stroop test was administered in three parts in this study [52]. Participants were first asked to read words printed in black, and second name colors printed without words as fast as they could. Third, participants were asked to name the color of the word printed, while ignoring the word that was printed. “Interference” scores report the number of correct answers in the third trial adjusted for the number of correct answers on the first two trials [66]. Thus, higher interference scores represent better performance. The Stroop appears to be associated with an inability to inhibit behavior amongst substance abusers [11, 67].

Finally, cognitive flexibility is needed to reduce substance use [68]. When substance use is no longer available as a coping strategy, recovering individuals need to learn a new set of rules for their behavior. We used a computerized version of the WCST to measure cognitive flexibility. In the WCST, participants must match 128 cards; after 10 correct matches, the rules for matching change without alerting the participant [53]. The number of times the participant continues using the previous matching rules are called “perseverative errors”; this has been described as the most sensitive executive function score in the WCST [69]. Perseverative error scores were standardized for age and education [53]. These standard scores are also reversed so that higher scores indicate better performance.

Statistical Analyses

Mplus version six was used for the Latent Class Analysis (LCA) modeling, which assumes that “latent classes”, i.e., an underlying grouping of individuals, exist and can explain the patterns of reporting by individuals [70]. Eight drug use indicator variables were entered into the LCA model. Starting with a one class model and incrementally increasing the number of classes, a series of LCA models were fit to the data. As part of LCA, Mplus begins with a random value, i.e, a “random start”, and then performs several iterations until it reaches ideal values, i.e., “maxima”. However, any set of maxima determined after several iterations of a random start could potentially be missing a superior set of maxima on a more global level. As suggested in the M-plus manual, we used a minimum of 500 random starts to ensure that global, rather than local, maxima were reached [70]. If the log likelihood was not replicated at least five times, the number of starts was increased until the log likelihood was replicated a minimum of five times.

Multiple fit statistics were used to determine the best-fitting, most parsimonious model, including the Bayesian Information Criteria (BIC) [71], the parametric bootstrap likelihood ratio test (BLRT) [72], and the Lo-Mendell-Rubin adjusted likelihood ratio test (LMR) [73]. The value and utility of the resultant classes was assessed using entropy [74, 75]. Entropy uses individual estimated posterior probabilities to summarize the degree to which the latent classes are distinguishable and the precision of assignment of individuals into classes. Entropy ranges from 0 to 1; with higher values indicating better class separation. Finally, the choice of latent class solution presented was also informed by a priori substantive criteria, such as meaningfulness in terms of the current epidemiology of drug use. Higher class models were preferred to increase specificity and understanding of the relationships with specific drugs and cognitive dysfunction. Mplus uses a full information maximum likelihood estimation with the assumption the data is missing at random [76], a widely accepted approach [77], so participants were not removed due to missing data on latent class indicators. There were no more than 2 participants with missing data on any of the latent class indicators. Covariance coverage ranged from 0.993-1.0, well over minimum thresholds for adequate coverage, e.g., 0.10 [78].

The *n* reported in each class is a total based on individual probabilities of class membership, i.e., a number ranging from 0.0, or no chance of membership in that specific class for that specific individual, and 1.0, or 100% certainty of class membership. Thus, these numbers are decimals, rather than whole numbers. However, in order to compare groups on categorical demographic variables, such as race, we used Most Likely Class Membership to add group assignment to IBM SPSS 19.0 and then conducted chi-square analyses. Similar methodology has been used elsewhere [46].

After deciding on the appropriate number of classes that best fit the data, we examined the association between class membership and several demographic, predictor and outcome variables utilizing the auxiliary option [79-81]. This option was used to study the association of classes with cognitive performance measures without changing the unconditional latent class model [70]. The AUXILIARY (e) option was used to examine the extent to which cognitive variables and continuous demographic variables varied as a function of latent class membership by testing the equality of means across latent classes using posterior probability-based multiple imputations. LCA was used to identify classes based on past-month drug use and adjust for probabilities of group membership when examining cognitive performance. Results obtained are reported with standard errors based on probabilities of class membership. The inclusion of auxiliary information in mixture analysis helps us to understand and evaluate the fidelity and utility of the resultant profiles [82], as well as providing useful information for understanding relationships between drug use and cognitive performance.

RESULTS

Lo-Mendel Rubin (LMR) test supported a 5-class model. Monte carlo simulations support the LMR and Bootstrap Likelihood Ratio Test (BLRT) over other fit statistics [83]. However, according to the BLRT, all 6 models were superior to the models with less classes. Since a large number of classes generally decreases the usefulness of the model, we used the LMR-supported 5-class model. Although in prior research we chose a three class model [20], we chose to use a five class model in the present study so as to provide further information above and beyond prior research and increase specificity when looking at associations between drugs and cognitive factors. LCA assumes local independence. This assumption holds if bivariate residuals are all less than 3.84 [84, 85]. In the 5-class model presented here, bivariate residuals ranged from 0.000-0.039. Entropy was relatively high (0.759) indicating good class separation.

As can be seen in figure 1a, prevalent indicators (having an estimated probability of over 50%) for each class are as follows: “Nasal Heroin/Crack Smokers” (n=166.9): cigarettes, alcohol, nasal heroin, and crack smoking; “Polysubstance” (n=54.8): cigarettes, alcohol, crack smoking, injection heroin, injection cocaine, and injection speedball; “Multi-Injectors” (n=128.7): cigarettes, alcohol, marijuana, injection heroin, injection cocaine, and injection speedball; “Heroin Injectors” (n=135.7): cigarettes and injection heroin; and “Nasal Heroin” (n=62.9): cigarettes, alcohol, and nasal heroin.

The groups differed on demographic characteristics (Table 2). “Crack Smoke/Nasal Heroin” and “Polysubstance” were both significantly older than “Nasal Heroin” users and “Heroin Injectors”. “Multi-Injectors” were significantly younger than the other four groups. “Polysubstance” users and “Heroin Injectors” were significantly less educated than “Crack Smoke/Nasal Heroin” and “Multi-Injectors”, whereas “Nasal Heroin” users were significantly more educated. Since age and education were included in model creation, these variables were used in class naming. There were also significant differences in gender, race, and current drug treatment.

In addition, there were significant differences in lifetime history of drug use (Table 2). These differences were in the anticipated directions. For example, more individuals in the “More Educated Nasal Heroin” group had a lifetime history of regularly snorting heroin (65.7%) than members of the “Less Educated Heroin Injectors” group (44.7%). This demonstrates that for most individuals, the past-month drug use was similar to their lifetime history of drug use, although there is some important variability. For example, a majority of “Older, Less Educated Polysubstance” users, “Older Crack Smoke / Nasal Heroin” users, “Younger Multi-injectors”, and “More Educated Nasal Heroin” users reported drinking alcohol regularly, compared to a minority of “Less Educated Heroin Injectors”

Cognitive performance results are presented on Table 3 and graphically, using z-scores, in Figure 1b. The results indicated profound impairment among this sample of cocaine and heroin users in comparison to published norms [61, 86-89]. In general, younger and more educated groups out-performed older and less educated groups, but with some notable variations discussed further below.

DISCUSSION

This is the first study of which we are aware to use latent classes to elucidate the complex relationship between polydrug use and cognitive performance. Five classes were found: Older-Less-Educated-Polysubstance, Older-Crack-Smoke/Nasal-Heroin, Less-Educated-Heroin-Injectors, More-Educated-Nasal-Heroin, and Younger-Multi-Injectors (YMI). These classes are largely consistent with similar latent class analyses [40, 44, 46] and clinician reports [14]. The associations with age and education are novel and may be due to cohort/demographic effects, as suggested by significant differences in race and gender.

Although a non-drug user control group was not available for comparison in this data set, there was evidence to suggest that substance use in itself was associated with worse cognition. Cognitive performance on nearly all tests was substantially worse than published normative values. Though age- and education-matched mean time on the Trail-Making Test Part A was comparable, Part B time was considerably higher in our study population, with a range of 80.7 – 92.9 seconds, compared to the normative time of 50.7 seconds [90]. This finding is consistent with the different degree of difficulty on these two tasks, as Part B is a more difficult cognitive task due to its increase in visually interfering stimuli and consequent increased demands in psychomotor speed and visual search [91]. Similarly, the Stroop Color and Word Test Manual reports predicted word and color scores for age 30-35, with 11 years of education to be approximately 99 and 75 points, respectively, which indicates a far greater number of items correctly completed than the scores of our study population [52]. Similar differences are seen in the Wisconsin Card Sorting Task (WCST) [53].

This study demonstrated novel applications of a methodology for examining the complicated relationships between polysubstance use and cognitive performance. The analysis found associations between age, education, and polydrug patterns. In general, younger classes performed better on cognitive measures. Age-related decrements in cognitive performance, including executive functioning, are documented for those 55 years and older [69] and many argue that cognitive decline begins when individuals are in their 20's or 30's [92].

More educated classes performed better on intelligence and memory, but not significantly so on attention. Further, the More-Educated-Nasal-Heroin class performed significantly worse than Young-Multi-Injectors on both behavioral inhibition and cognitive flexibility and did not differ significantly from Less-Educated-Heroin-Injectors. This is difficult to interpret, but some interesting and important possibilities exist. It is possible that education and/or nasal heroin use are particularly associated with lower cognitive flexibility. Either of these possibilities deserve further research. If education received by this sample of inner-city drug users did not enhance, and perhaps even impaired, cognitive flexibility, other interventions may be needed [93-95]. If nasal heroin use is associated with more extreme decrements in cognitive performance than injection use, this is important for clinicians to understand for purposes of addressing limitations in particular subpopulations and for harm reduction efforts. Alternatively, as the multi-injectors were the youngest class, it is possible that age overcame effects of education or other drug use, which would have important implications for understanding changes in drug dependence as users age.

There are some limitations to this study. Although these classes were different with respect to specific cognitive measures, this may only be a result of in-group variabilities. The sample consisted of a population that had varying times of last drug use. This introduces a type of random error into the analysis, which may make finding significant differences difficult. Further, as with all cross-sectional studies, no causal relationships can be established from the data presented. Experimental or longitudinal research is needed to address these issues.

LCA provides a novel method for exploring the relationships between polydrug use and cognitive function. This is necessary as polydrug use is the norm among illicit drug users [14]. As all human cognitive functioning data is contaminated by confounders, it is anticipated that latent modeling will become more common and more sophisticated so as to address these difficult issues. Future research should develop this potential to further refine and explore this methodology in different populations and gain deeper insights into associations between executive functioning and drug use.

Acknowledgments

This research was funded by a grant awarded to William Latimer, currently at University of Florida in Gainesville, FL, from the National Institute on Drug Abuse (NIDA-R01 DA14498), by the Behavioral Oncology Training Grant (R25CA090314) at Moffitt Cancer Center in Tampa, FL, awarded to Director Paul Jacobsen, and by the Drug Dependence Epidemiology Training Grant (NIDA T32 DA007292), at the Johns Hopkins Bloomberg School of Public Health in Baltimore, MD, awarded to Director Debra Furr-Holden. Neither NIDA nor NCI had any further role in the study design; in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit for publication.

The authors wish to acknowledge the help and support of the researchers who gathered this data including Jonathan Rose, Eugene Dunn, and April Lawson.

REFERENCES

1. Belin D, et al. High impulsivity predicts the switch to compulsive cocaine-taking. Science. 2008; 320(5881):1352–5. [PubMed: 18535246]
2. Verdejo-Garcia A, Lawrence AJ, Clark L. Impulsivity as a vulnerability marker for substance-use disorders: review of findings from high-risk research, problem gamblers and genetic association studies. Neurosci Biobehav Rev. 2008; 32(4):777–810. [PubMed: 18295884]
3. Bechara A. Decision making, impulse control and loss of willpower to resist drugs: a neurocognitive perspective. Nat Neurosci. 2005; 8(11):1458–63. [PubMed: 16251988]
4. Goldstein RZ, Volkow ND. Drug addiction and its underlying neurobiological basis: neuroimaging evidence for the involvement of the frontal cortex. Am J Psychiatry. 2002; 159(10):1642–52. [PubMed: 12359667]
5. Verdejo-Garcia A, Bechara A. A somatic marker theory of addiction. Neuropharmacology. 2009; 56(Suppl 1):48–62. [PubMed: 18722390]
6. Fernandez-Serrano MJ, Perez-Garcia M, Verdejo-Garcia A. What are the specific vs. generalized effects of drugs of abuse on neuropsychological performance? Neurosci Biobehav Rev. 2011; 35(3): 377–406. [PubMed: 20451551]
7. Camchong J, et al. Frontal hyperconnectivity related to discounting and reversal learning in cocaine subjects. Biol Psychiatry. 2011; 69(11):1117–23. [PubMed: 21371689]
8. Ersche KD, et al. Abnormal structure of frontostriatal brain systems is associated with aspects of impulsivity and compulsivity in cocaine dependence. Brain. 2011; 134(Pt 7):2013–24. [PubMed: 21690575]
9. Brand M, et al. Executive functions and risky decision-making in patients with opiate dependence. Drug Alcohol Depend. 2008; 97(1-2):64–72. [PubMed: 18485620]
10. Ersche KD, et al. Differences in orbitofrontal activation during decision-making between methadone-maintained opiate users, heroin users and healthy volunteers. Psychopharmacology (Berl). 2006; 188(3):364–73. [PubMed: 16953385]
11. Fishbein DH, et al. Neurocognitive characterizations of Russian heroin addicts without a significant history of other drug use. Drug Alcohol Depend. 2007; 90(1):25–38. [PubMed: 17382488]
12. Forman SD, et al. Opiate addicts lack error-dependent activation of rostral anterior cingulate. Biol Psychiatry. 2004; 55(5):531–7. [PubMed: 15023582]
13. Ornstein TJ, et al. Profiles of cognitive dysfunction in chronic amphetamine and heroin abusers. Neuropsychopharmacology. 2000; 23(2):113–26. [PubMed: 10882838]
14. Leri F, Bruneau J, Stewart J. Understanding polydrug use: review of heroin and cocaine co-use. Addiction. 2003; 98(1):7–22. [PubMed: 12492751]
15. Verdejo-Garcia AJ, Perales JC, Perez-Garcia M. Cognitive impulsivity in cocaine and heroin polysubstance abusers. Addict Behav. 2007; 32(5):950–66. [PubMed: 16876962]

16. Verdejo-Garcia A, Perez-Garcia M. Profile of executive deficits in cocaine and heroin polysubstance users: common and differential effects on separate executive components. Psychopharmacology (Berl). 2007; 190(4):517–30. [PubMed: 17136401]
17. Gossop M, et al. Severity of dependence and route of administration of heroin, cocaine and amphetamines. British Journal of Addiction. 1992; 87(11):1527–36. [PubMed: 1458032]
18. Strang J, et al. Route of drug use and its implications for drug effect, risk of dependence and health consequences. Drug Alcohol Rev. 1998; 17(2):197–211. [PubMed: 16203485]
19. Patkar AA, et al. Medical symptoms associated with tobacco smoking with and without marijuana abuse among crack cocaine-dependent patients. American Journal on Addictions. 2005; 14(1):43–53. [PubMed: 15804876]
20. Harrell PT, et al. Latent classes of heroin and cocaine users predict unique HIV/HCV risk factors. Drug and Alcohol Dependence. 2012; 122(3):220–227. [PubMed: 22030276]
21. Harrell PT, et al. Cigarette smoking, illicit drug use, and routes of administration among heroin and cocaine users. Addictive Behaviors. 2012; 37(5):678–681. [PubMed: 22305644]
22. Hser YI, McCarthy WJ, Anglin MD. Tobacco use as a distal predictor of mortality among long-term narcotics addicts. Preventive Medicine. 1994; 23(1):61–9. [PubMed: 8016035]
23. Hurt RD, et al. Attitudes toward nicotine dependence among chemical dependence unit staff--before and after a smoking cessation trial. J Subst Abuse Treat. 1995; 12(4):247–52. [PubMed: 8830151]
24. Chen CY, Anthony JC. Epidemiological estimates of risk in the process of becoming dependent upon cocaine: cocaine hydrochloride powder versus crack cocaine. Psychopharmacology (Berl). 2004; 172(1):78–86. [PubMed: 14598014]
25. Gossop M, et al. Cocaine: patterns of use, route of administration, and severity of dependence. Br J Psychiatry. 1994; 164(5):660–4. [PubMed: 7921717]
26. Strang J, et al. Heroin chasers and heroin injectors: differences observed in a community sample in London, UK. Am J Addict. 1999; 8(2):148–60. [PubMed: 10365195]
27. Gossop M, et al. Frequency of non-fatal heroin overdose: survey of heroin users recruited in non-clinical settings. BMJ. 1996; 313(7054):402. [PubMed: 8761230]
28. Chitwood DD, Comerford M, Sanchez J. Prevalence and risk factors for HIV among sniffers, short-term injectors, and long-term injectors of heroin. J Psychoactive Drugs. 2003; 35(4):445–53. [PubMed: 14986873]
29. Nelson KE, et al. HIV infection in young men in northern Thailand, 1991-1998: increasing role of injection drug use. J Acquir Immune Defic Syndr. 2002; 29(1):62–8. [PubMed: 11782592]
30. Ward M, Minto G, Alexander-Williams JM. A comparison of patient-controlled analgesia administered by the intravenous or intranasal route during the early postoperative period. Anaesthesia. 2002; 57(1):48–52. [PubMed: 11843742]
31. Abreu ME, et al. Effect of intravenous injection speed on responses to cocaine and hydromorphone in humans. Psychopharmacology (Berl). 2001; 154(1):76–84. [PubMed: 11292009]
32. Comer SD, et al. Comparison of intravenous and intranasal heroin self-administration by morphine-maintained humans. Psychopharmacology (Berl). 1999; 143(4):327–38. [PubMed: 10367549]
33. Carpenter MJ, Chutuape MA, Stitzer ML. Heroin snorters versus injectors: comparison on drug use and treatment outcome in age-matched samples. Drug Alcohol Depend. 1998; 53(1):11–5. [PubMed: 10933336]
34. Lloyd-Smith E, et al. Incidence and determinants of initiation into cocaine injection and correlates of frequent cocaine injectors. Drug and alcohol dependence. 2009; 99(1):176–182. [PubMed: 18805655]
35. Trenz RC, et al. A Model of School Problems, Academic Failure, Alcohol Initiation, and the Relationship to Adult Heroin Injection. Substance Use & Misuse. 2012; 47(10):1159–1171. [PubMed: 22621313]
36. Severtson SG, et al. The association between planning abilities and sharing injection drug use equipment among injection drug users in Baltimore, MD. Journal of Substance Use. 2009; 14(5): 325–333.

37. Severtson SG, et al. The association between executive functioning and motivation to enter treatment among regular users of heroin and/or cocaine in Baltimore, MD. Addict Behav. 2010; 35(7):717–20. [PubMed: 20226598]
38. Severtson SG, et al. Patterns of Cognitive Impairments Among Heroin and Cocaine Users The Association With Self-Reported Learning Disabilities and Infectious Disease. Journal of learning disabilities. 2012; 45(2):139–150.
39. Agrawal A, et al. A latent class analysis of illicit drug abuse/dependence: results from the National Epidemiological Survey on Alcohol and Related Conditions. Addiction. 2007; 102(1):94–104. [PubMed: 17207127]
40. Monga N, et al. Using latent class analysis (LCA) to analyze patterns of drug use in a population of illegal opioid users. Drug Alcohol Depend. 2007; 88(1):1–8. [PubMed: 17049753]
41. Reboussin BA, et al. A latent class analysis of underage problem drinking: Evidence from a community sample of 16-20 year olds. Drug and Alcohol Dependence. 2006; 83(3):199–209. [PubMed: 16359829]
42. Martins SS, et al. Perceived risk associated with ecstasy use: A latent class analysis approach. Addictive Behaviors. 2011; 36(5):551–554. [PubMed: 21296504]
43. Scheier LA, et al. Tri-city study of Ecstasy use problems: A latent class analysis. Drug and Alcohol Dependence. 2008; 98(3):249–263. [PubMed: 18674872]
44. Patra J, et al. Profiling poly-substance use typologies in a multi-site cohort of illicit opioid and other drug users in Canada-a latent class analysis. Addiction Research & Theory. 2009; 17(2): 168–185.
45. Trenz RC, et al. Latent class analysis of polysubstance use, sexual risk behaviors, and infectious disease among South African drug users. Drug Alcohol Depend. 2013
46. Kuramoto SJ, Bohnert ASB, Latkin CA. Understanding subtypes of inner-city drug users with a latent class approach. Drug and Alcohol Dependence. 2011; 118(2-3):237–243. [PubMed: 21530105]
47. Latimer WW, et al. Prevalence and correlates of hepatitis A among adult drug users: the significance of incarceration and race/ethnicity. Vaccine. 2007; 25(41):7125–31. [PubMed: 17766016]
48. Severtson SG, et al. Patterns of Cognitive Impairments Among Heroin and Cocaine Users: The Association With Self-Reported Learning Disabilities and Infectious Disease. J Learn Disabil. 2010
49. Zachary, RA. Shipley Institute of Living Scale: Revised Manual. Western Psychological Services; Los Angeles: 1986.
50. Wechsler, D. Manual for the Wechsler Adult Intelligence Scale - Revised (WAIS-R). The Psychological Corporation; San Antonio, TX: 1981.
51. Reitan, RM. Trail Making Test: Manual for administration and scoring. Reitan Neuropsychology Laboratory; Tucson: 1992.
52. Golden, CJ. Stroop Color and Word Test: A manual for clinical and experimental uses. Stoeling Company; Wood Dale, IL: 1978.
53. Heaton, RK., et al. Wisconsin Card Sorting Test (WCST) manual, revised and expanded. Psychological Assessment Resources; Odessa, FL: 1993.
54. Goldstein RZ, et al. The neurocircuitry of impaired insight in drug addiction. Trends in cognitive sciences. 2009; 13(9):372–380. [PubMed: 19716751]
55. Bolla KI, et al. Dose-related neurocognitive effects of marijuana use. Neurology. 2002; 59(9): 1337–43. [PubMed: 12427880]
56. Bickel WK, et al. Remember the future: working memory training decreases delay discounting among stimulant addicts. Biological psychiatry. 2011; 69(3):260–265. [PubMed: 20965498]
57. Banken JA. Clinical utility of considering digits forward and digits backward as separate components of the Weschler Adult Intelligence Scale - Revised. Journal of Clinical Psychology. 1985; 41:6.
58. Wagner D, et al. A prospective study of learning, memory, and executive function in new MDMA users. Addiction. 2012

59. Joos L, et al. Age of Onset and Neuropsychological Functioning in Alcohol Dependent Inpatients. Alcohol Clin Exp Res. 2012
60. Nulsen C, Fox A, Hammond G. Electrophysiological indices of altered working memory processes in long-term ecstasy users. Hum Psychopharmacol. 2011; 26(7):488–97. [PubMed: 21953632]
61. Kalapatapu RK, et al. A pilot study of neurocognitive function in older and younger cocaine abusers and controls. Am J Addict. 2011; 20(3):228–39. [PubMed: 21477051]
62. Day AM, et al. Working memory and impulsivity predict marijuana-related problems among frequent users. Drug and alcohol dependence. 2013
63. Horton AM, Roberts C. Demographic effects on the Trail Making Test in a drug abuse treatment sample. Arch Clin Neuropsychol. 2003; 18(1):49–56. [PubMed: 14591477]
64. de Wit H. Impulsivity as a determinant and consequence of drug use: a review of underlying processes. Addiction Biology. 2009; 14(1):22–31. [PubMed: 18855805]
65. Cheung AM, Mitsis EM, Halperin JM. The relationship of behavioral inhibition to executive functions in young adults. Journal of Clinical and Experimental Neuropsychology. 2004; 26(3): 393–404. [PubMed: 15512928]
66. Lezak, MD.; Howieson, D.; Loring, DW. Neuropsychological Assessment. Oxford University Press; New York: 2004.
67. Banich MT, et al. Brain activation during the Stroop task in adolescents with severe substance and conduct problems: A pilot study. Drug Alcohol Depend. 2007; 90(2-3):175–82. [PubMed: 17499456]
68. Giancola PR, Tarter RE. Executive cognitive functioning and risk for substance abuse. Psychological Science. 1999; 10(3):203–205.
69. Rhodes MG. Age-related differences in performance on the Wisconsin card sorting test: a meta-analytic review. Psychol Aging. 2004; 19(3):482–94. [PubMed: 15382998]
70. Muthén, LK.; Muthén, BO. Mplus User's Guide. Seventh Edition. Muthén & Muthén; Los Angeles, CA: 2012.
71. Schwartz G. Estimating the dimension of a model. The Annals of Statistics. 1978; 6:461–464.
72. McLachlan, G.; Peel, D. Finite Mixture Models. John Wiley; New York: 2000.
73. Lo Y, Mendell N, Rubin D. Testing the number of components in a normal mixture. Biometrika. 2001; 88:767–778.
74. Celeux G, Soromenho G. An entropy criterion for assessing the number of clusters in a mixture model. Journal of Classification. 1996; 13(2):195–212.
75. Ramaswamy V, et al. An empirical pooling approach for estimating marketing mix elasticities with PIMS Data. Marketing Science. 1993; 12(1):103–124.
76. Hogan JW, Roy J, Korkontzelou C. Handling drop-out in longitudinal studies. Stat Med. 2004; 23(9):1455–97. [PubMed: 15116353]
77. Schafer JL, Graham JW. Missing data: our view of the state of the art. Psychol Methods. 2002; 7(2):147–77. [PubMed: 12090408]
78. Muthén, LK.; Muthén, BO. Mplus User's Guide. Sixth Edition. Muthén & Muthén; Los Angeles, CA: 2010.
79. Bandeen-Roche K, et al. Latent variable regression for multiple discrete outcomes. Journal of the American Statistical Association. 1997; 92(440):1375–1386.
80. Muthén, BO.; Asparouhov, T. [cited 2011 April 19] Wald test of mean equality for potential latent class predictors in mixture modeling. 2007. [Unpublished Web Note]Available from: www.statmodel.com/download/MeanTest1.pdf
81. Wang CP, Brown CH, Bandeen-Roche K. Residual diagnostics for growth mixture models: Examining the impact of a preventive intervention on multiple trajectories of aggressive behavior. Journal of the American Statistical Association. 2005; 100(471):1054–1076.
82. Petras, H.; Masyn, K. General Growth Mixture Analysis with Antecedents and Consequences of Change. In: Piquero, A.; Weisburd, D., editors. Handbook of Quantitative Criminology. Springer; New York: 2010. p. 69-100.

83. Nylund KL, Asparoutiov T, Muthen BO. Deciding on the number of classes in latent class analysis and growth mixture modeling: A Monte Carlo simulation study. Structural Equation Modeling-a Multidisciplinary Journal. 2007; 14(4):535–569.
84. Ghandour LA, Martins SS, Chilcoat HD. Understanding the patterns and distribution of opioid analgesic dependence symptoms using a latent empirical approach. Int J Methods Psychiatr Res. 2008; 17(2):89–103. [PubMed: 18393262]
85. Vermunt, JK.; Magidson, J. Latent Gold 4.0. User's Guide. 2005.
86. Crawford J, Allan K. Estimating premorbid WAIS-R IQ with demographic variables: Regression equations derived from a UK sample. The Clinical Neuropsychologist. 1997; 11(2):192–197.
87. Lin SH, et al. Performance on the Wisconsin Card Sorting Test in families of schizophrenia patients with different familial loadings. Schizophr Bull. 2013; 39(3):537–46. [PubMed: 23196712]
88. Seidman LJ, et al. Neuropsychological function in adults with attention-deficit hyperactivity disorder. Biol Psychiatry. 1998; 44(4):260–8. [PubMed: 9715357]
89. Tombaugh TN. Trail Making Test A and B: Normative data stratified by age and education. Archives of Clinical Neuropsychology. 2004; 19(2):203–214. [PubMed: 15010086]
90. Tombaugh TN. Trail Making Test A and B: normative data stratified by age and education. Arch Clin Neuropsychol. 2004; 19(2):203–14. [PubMed: 15010086]
91. Gaudino EA, Geisler MW, Squires NK. Construct validity in the Trail Making Test: what makes Part B harder? J Clin Exp Neuropsychol. 1995; 17(4):529–35. [PubMed: 7593473]
92. Salthouse TA. When does age-related cognitive decline begin? Neurobiol Aging. 2009; 30(4):507–14. [PubMed: 19231028]
93. Themanson JR, Pontifex MB, Hillman CH. Fitness and action monitoring: evidence for improved cognitive flexibility in young adults. Neuroscience. 2008; 157(2):319–28. [PubMed: 18845227]
94. Sofuoglu M, Sugarman DE, Carroll KM. Cognitive function as an emerging treatment target for marijuana addiction. Exp Clin Psychopharmacol. 2010; 18(2):109–19. [PubMed: 20384422]
95. Sofuoglu M. Cognitive enhancement as a pharmacotherapy target for stimulant addiction. Addiction. 2010; 105(1):38–48. [PubMed: 20078461]

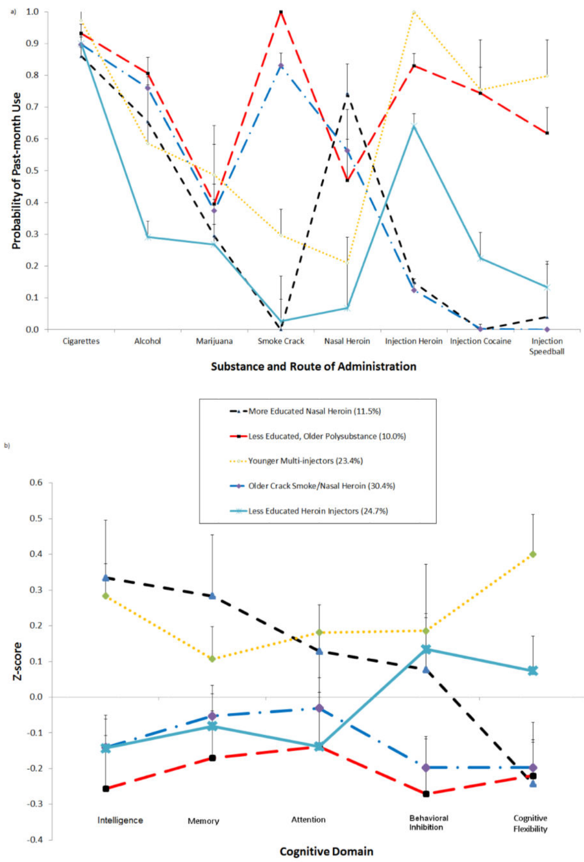

Figure 1.

a) Five class solution of a latent class analysis of 552 users of cocaine and/or heroin in Baltimore, MD. Estimated probabilities for past-month drug use are graphed based on latent class membership. Error bars indicate standard errors of estimated probabilities. b) Cognitive performance by class. Intelligence is based on total t-score from Shipley Institute of Living Scales. Memory is based on total score from Digit Span task. Attention is based on number of seconds to complete Trails B task. Behavioral Inhibition is based on Interference score from the Stroop task. Cognitive Flexibility is based on perseverative errors on Wisconsin Card Sorting Task. For illustrative purposes, z-scores were computed and scores from Trails B and Wisconsin Card Sorting Task were reverse-scored. Thus, higher scores always indicate better performance.

Table 1

Fit statistics and entropy for a latent class analysis of 8 substances used in the past month, controlling for age and education, among 549 users of cocaine and heroin in the past 6 months.

Classes	LL[a]	parameters	LMR[b]	BLRT[c]	s.c. r.f. (f)[d]	Entropy
1	−3482.92	12	NA[e]	NA[e]	NA[e]	NA[e]
2	−2447.87	19	$p < .001$	$p < 0.001$	.48 (266.0)	0.779
3	−2396.44	30	$p=.013$	$p < 0.001$	.22 (120.3)	0.742
4	−2369.49	41	$p = .021$	$p < 0.001$	.10 (55.5)	0.759
5	−2347.95	52	**p<.0500**	$p < 0.001$	.10 (54.8)	0.769
6	−2328.51	63	$p=0.204$	$p<.0001$	.09 (51.4)	0.779

[a]Log Likelihood;

[b]Lo-Mendell-Rubin adjusted likelihood ratio test;

[c]parametric Bootstrap Likelihood Ratio Test;

[d]smallest class relative frequency (frequency);

[e]Not Applicable

Ideal number of classes based on fit statistic shown in bold

Table 2

Demographics and drug use characteristics by latent class.

	Older, Less Educated Polysubstance	Older Crack Smoke / Nasal Heroin	Less Educated Heroin Injectors	More Educated Nasal Heroin	Younger Multi-injectors
	M (SE) / N (%)	**M (SE) / N (%)**	**M (SE) / N (%)**	**M (SE) / N (%)**	**M (SE) / N (%)**
Age***	**36.42 (0.98)** ^{b}	**36.01 (0.48)** ^{a,b}	32.65 (0.75) ^{a}	32.43 (1.04) ^{a}	*28.90 (0.68)* ^{c}
Highest Grade Completed***	*10.17 (0.28)* ^{b}	11.16 (0.15) ^{c}	*10.29 (0.18)* ^{b}	**12.44 (0.16)** ^{a}	10.87 (0.16) ^{c}
Female**	22 (44.0%)	82 (51.2%)	61 (43.3%)	25 (35.7%)	39 (30.5%)
African-American***	31 (62.0%)	125 (78.1%)	47 (33.3%)	49 (70.0%)	22 (17.2%)
Currently in Drug Treatment**	17 (34.0%)	42 (26.6%)	48 (35.3%)	16 (23.9%)	16 (12.6%)
Lifetime History of Regular Use					
Drink Alcohol**	34 (68.0%)	101 (63.5%)	65 (46.4%)	37 (52.9%)	81 (64.3%)
Smoke Marijuana***	29 (58.0%)	92 (57.5%)	66 (48.2%)	34 (49.3%)	94 (73.4%)
Smoke Crack***	22 (44.0%)	106 (66.2%)	20 (14.2%)	11 (15.7%)	36 (28.1%)
Nasal Heroin**	28 (56.0%)	99 (61.9%)	63 (44.7%)	46 (65.7%)	79 (61.7%)
Inject Heroin***	40 (80.0%)	39 (24.4%)	104 (73.8%)	14 (20.0%)	119 (93.0%)
Inject Cocaine***	20 (40.0%)	9 (8.3%)	29 (20.6%)	1 (1.4%)	49 (38.3%)
Inject Speedball***	24 (48.0%)	13 (8.1%)	27 (19.1%)	4 (5.7%)	50 (39.1%)

* Omnibus test (degrees of freedom = 4), $p < .05$

** Omnibus test (df = 4), $p < .01$

*** Omnibus test (df = 4), $p < .001$

Subscripts with same letter are not significantly different at $p < .05$, as revealed by post-hoc pairwise tests (df = 1).

If at least one class is significantly *lower* than another, class(es) with *lowest* number on variable shown in *italics*.

If at least one additional class is significantly **higher** than another, class(es) with **highest** number on variable shown in **bold**.

Table 3

Cognitive performance by class.

	Older, Less Educated Polysubstance	Older Crack Smoke / Nasal Heroin	Less Educated Heroin Injectors	More Educated Nasal Heroin	Younger Multi-injectors	Published Norms
	M (SE)	**M (SE)**	**M (SE)**	**M (SE)**	**M (SE)**	**M (SE)**
Intelligence (Shipley)						
Verbal ***	*36.42 (1.62)* [a]	*36.42 (0.91)* [a]	37.40 (1.05) [a,b]	**41.50 (1.81)** [c]	**41.84 (0.91)** [b,c]	---
Abstract ***	*44.57 (1.35)* [a]	*46.55 (0.73)* [a]	45.77 (0.83) [a]	49.89 (1.35) [b]	49.18 (0.84)b	---
Predicted IQ ***	*83.57 (1.94)* [a]	*85.22 (1.06)* [a]	*84.54 (1.27)* [a]	91.53 (2.13) [b]	90.07 (1.24) [b]	102.5 (0.92)
Memory (Digit Span Task)						
Forward	9.63 (0.30)	9.71 (0.19)	9.68 (0.22)	10.10 (0.37)	10.01 (0.20)	10.2 (0.52)
Backward *	*5.20 (0.29)* [a]	*5.55 (0.19)* [a,b]	*5.41 (0.20)* [a]	6.38 (0.38) [b]	*5.78 (0.20)* [a,b]	7.20 (0.45)
Total †	*14.73 (0.51)* [a]	*15.18 (0.33)* [a,b]	*15.08 (0.35)* [a,b]	16.48 (0.66) [b]	*15.80 (0.35)* [a,b]	---
Attention (Trail Making)						
Trails A (seconds)	27.29 (1.53)	27.55 (0.92)	28.72 (1.15)	27.15 (1.66)	25.95 (0.92)	24.40 (1.52)
Trails B (seconds)*	*92.92 (6.95)* [a,b]	*87.99 (3.89)* [a,b]	*92.91 (4.73)* [b]	*80.64 (6.00)* [a,b]	78.24 (4.00) [a]	50.68 (2.15)
Beh Inhibition (Stroop)						
Word Score	41.26 (1.21)	41.50 (0.69)	40.89 (0.76)	42.21 (1.39)	42.74 (0.77)	---
Color Score	43.72 (1.24)	42.36 (0.70)	42.27 (0.77)	43.13 (1.24)	43.56 (0.75)	---
Interference Score †	*45.95 (1.33)* [a]	*46.55 (0.66)* [a]	49.30 (0.73) [b]	*48.83 (1.31)* [a,b]	49.73 (0.76) [b]	50.7 (1.0)
Cog Flexibility (WCST)						
Categories Completed *	*3.75 (0.33)* [a]	*4.29 (0.17)* [a]	*4.38 (0.20)* [a,b]	*4.47 (0.29)* [a,b]	4.87 (0.20) [b]	5.0 (0.2)
Non-perseverative Errors***	*82.35 (2.82)* [a]	*87.74 (1.33)* [a,b]	89.92 (1.69) b,d	*88.05 (2.04)* [a,d]	**95.60 (1.80)** [c]	---
Perseverative Errors***	*90.98 (3.78)* [a,b]	*91.55 (1.80)* [a]	98.37 (2.44) [b]	*90.41 (3.10)* [a,b]	**106.58 (2.79)** [c]	---

† Omnibus test (degrees of freedom = 4), p < .1

* Omnibus test (df = 4), p < .05

** Omnibus test (df = 4), p < .01

*** Omnibus test (df = 4), p < .001

NIH-PA Author Manuscript
NIH-PA Author Manuscript

Subscripts with same letter are not significantly different at $p < .05$, as revealed by post-hoc pairwise tests ($df = 1$).

If at least one class is significantly *worse* than another, class(es) with *worst* performance on variable shown in *italics*.

If at least one additional class is significantly **better** than another, class(es) with **best** number on variable shown in **bold**.

Note: Higher scores on all tasks, except for Trail Making Task, indicate better performance

Table 4

Cognitive performance by class.

	Older, Less Educated Polysubstance	Older Crack Smoke / Nasal Heroin	Less Educated Heroin Injectors	More Educated Nasal Heroin	Younger Multi-injectors	Published Norms
	M (SE)	M (SE)	M (SE)	M (SE)	M (SE)	M (SE)
Intelligence (Shipley)						
Verbal ***	*36.42 (1.62)* [a]	*36.42 (0.91)* [a]	37.40 (1.05) [a,b]	**41.50 (1.81)** [c]	**41.84 (0.91)** [b,c]	--
Abstract ***	*44.57 (1.35)* [a]	*46.55 (0.73)* [a]	45.77 (0.83) [a]	49.89 (1.35) [b]	49.18 (0.84)[b]	---
Predicted IQ ***	*83.57 (1.94)* [a]	*85.22 (1.06)* [a]	*84.54 (1.27)* [a]	91.53 (2.13) [b]	90.07 (1.24) [b]	102.5 (0.92)
Memory (Digit Span Task)						
Forward	9.63 (0.30)	9.71 (0.19)	9.68 (0.22)	10.10 (0.37)	10.01 (0.20)	10.2 (0.52)
Backward *	*5.20 (0.29)* [a]	*5.55 (0.19)* [a,b]	*5.41 (0.20)* [a]	6.38 (0.38) [b]	*5.78 (0.20)* [a,b]	7.20 (0.45)
Total †	*14.73 (0.51)* [a]	*15.18 (0.33)* [a,b]	*15.08 (0.35)* [a,b]	16.48 (0.66) [b]	*15.80 (0.35)* [a,b]	---
Attention (Trail Making)						
Trails A (seconds)	27.29 (1.53)	27.55 (0.92)	28.72 (1.15)	27.15 (1.66)	25.95 (0.92)	24.40 (1.52)
Trails B (seconds)*	*92.92 (6.95)* [a,b]	*87.99 (3.89)* [a,b]	*92.91 (4.73)* [b]	*80.64 (6.00)* [a,b]	78.24 (4.00) [a]	50.68 (2.15)
Beh Inhibition (Stroop)						
Word Score	41.26 (1.21)	41.50 (0.69)	40.89 (0.76)	42.21 (1.39)	42.74 (0.77)	---
Color Score	43.72 (1.24)	42.36 (0.70)	42.27 (0.77)	43.13 (1.24)	43.56 (0.75)	---
Interference Score †	*45.95 (1.33)* [a]	*46.55 (0.66)* [a]	49.30 (0.73) [b]	*48.83 (1.31)* [a,b]	49.73 (0.76) [b]	50.7 (1.0)
Cog Flexibility (WCST)						
Categories Completed *	*3.75 (0.33)* [a]	*4.29 (0.17)* [a]	*4.38 (0.20)* [a,b]	*4.47 (0.29)* [a,b]	4.87 (0.20) [b]	5.0 (0.2)
Non-perseverative Errors***	*82.35 (2.82)* [a]	*87.74 (1.33)* [a,b]	89.92 (1.69) [b,d]	*88.05 (2.04)* [a,d]	**95.60 (1.80)** [c]	---
Perseverative Errors***	*90.98 (3.78)* [a,b]	*91.55 (1.80)* [a]	98.37 (2.44) [b]	*90.41 (3.10)* [a,b]	**106.58 (2.79)** [c]	---

† Omnibus test (degrees of freedom = 4), p < .1

* Omnibus test (df = 4), p < .05

** Omnibus test (df = 4), p < .01

*** Omnibus test (df = 4), p < .001

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Subscripts with same letter are not significantly different at $p < .05$, as revealed by post-hoc pairwise tests (df = 1).

If at least one class is significantly *worse* than another, class(es) with *worst* performance on variable shown in *italics*.

If at least one additional class is significantly **better** than another, class(es) with best number on variable shown in **bold**.

Note: Higher scores on all tasks, except for Trail Making Task, indicate better performance