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Neurocognitive Profiling of Adult Treatment Seekers Enrolled in a Clinical Trial of a Web-Delivered Intervention for Substance Use Disorders

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Abstract

Objective—This study is a secondary descriptive analysis that explores and compares the cognitive profiles of adults entering treatment at geographically diverse community-based substance use disorder treatment facilities.

Methods—Performance on cognitive measures at baseline was compared across five primary substance subgroups of individuals (alcohol=104, cocaine=102; stimulants=69; opioids=108; marijuana=114) enrolled in a web-based psychosocial treatment study conducted within the National Drug Abuse Treatment Clinical Trials Network. MicroCog™ subtests were used to assess cognitive domains of attention and mental control, reasoning and cognitive flexibility, and spatial processing.

Results—The average age of onset for a substance use disorder was early to mid-20s, with marijuana users reporting the earliest age of onset (Mean=19.9, SD=7.5) and stimulant users reporting the latest (Mean=25.2, SD=9.9). Among the total sample, half (49.7%) demonstrated impairment in cognitive flexibility and reasoning and over one-third (37.3%) had impairment in verbal learning and memory. Stimulant (37.68%) and cocaine (34.31%) users showed significantly greater clinical impairment in attention and mental control compared to alcohol users (17.31%) and opioid (21.30%) users (stimulant subgroup only) ($X^2(4)=10.97$, $p=.027$). Cocaine users showed the greatest overall impairment across total and proficiency subtest scores, although these were not statistically different from other subgroups.

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Conflicts of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the manuscript.

Contribution

Dr. Aharonovich, Dr. Campbell, and Dr. Shulman wrote the initial draft of the manuscript. Dr. Campbell and Dr. Nunes supervised data collection. Dr. Hu completed the statistical analyses. All authors contributed to and have approved the final manuscript.

Conclusions—These findings confirmed previous studies indicating a high prevalence of significant cognitive dysfunction across all substance use categories among treatment-seeking adults, and found that cocaine use appears to be associated with the most impairment. Increasing knowledge of similarities and differences between primary substance subgroups can help guide substance use disorder treatment planning.

Keywords

cognitive performance; substance use disorder; web-based treatment; addiction; eHealth

INTRODUCTION

A growing body of evidence suggests that chronic substance users have higher rates of cognitive impairment than the general population (Tomasí et al., 2007). A substantial amount of research has aimed to investigate the neurocognitive performance of individuals with various substance use disorders; a recent review of the evidence suggests that substance using populations differ with regards to specific cognitive impairments (Ersche et al., 2006). Heavy cannabis use has been associated with impairment in verbal memory (Battisti et al., 2010) and executive functions such as impulse inhibition, cognitive flexibility, and complex information processing (Crean et al., 2011). With regard to individuals suffering from alcohol use disorder, studies indicate that chronic drinkers demonstrate greater rates of impaired memory, abstract reasoning and poor decision making (Le Berre et al., 2010). Learning problems have also been found to be significantly greater in severe drinkers (Ryan & Butters, 1986). In chronic cocaine users, studies have found neurocognitive impairments in the areas of attention, memory, verbal abilities, and executive function (Madoz-Gurpide et al., 2011) and these have persisted even after weeks of abstinence (Bolla et al., 2004).

Research has found that chronic use of addictive substances has been associated with impaired executive function and memory (Fernandez-Serrano et al., 2011). A number of smaller studies have compared groups using different substances (Ersche et al., 2006) but large studies comparing severity and areas of dysfunction across a wide range of substances are more limited. Although there is some support that cognitive profiles differ by type of substance used, this topic has not been adequately investigated.

A better understanding of the cognitive impairments associated with use of specific substances could inform treatment. Multiple studies have found cognitive impairment predicts treatment retention. For example, impaired attention has been found to be related to poor retention in cocaine treatment (Aharonovich et al., 2006), while memory impairments were less common in completers versus non-completers among marijuana users in treatment (Aharonovich et al., 2008). Such findings make sense, given that attention and memory are needed to be successful in many forms of treatment (Carroll et al., 2011).

Recognizing specific impairments in substance users may help better address obstacles to treatment by informing the selection of intervention best suited to each individual's cognitive profile. One study found that among cognitively impaired alcohol users, those in CBT had poorer outcomes than those in supportive group therapy (Cooney et al., 1991). Another study found that compromised verbal learning ability was associated with poor

drinking outcomes in relapse prevention treatment but not in supportive therapy (Jaffe et al., 1996). Other research suggests that differences in cognition may contribute to differences in baseline motivation to change. In a study examining motivation among alcohol users, Blume, Schmalting, and Marlatt (2005) found that verbal memory scores predicted stage of change at baseline; lower scoring individuals were more likely to be in the pre-contemplation phase while higher scoring individuals were more likely to be in the contemplation phase. Similarly, Le Berre et al. (2012) found that impaired memory and executive functioning were associated with low motivation.

The apparent high prevalence between substance use disorders and cognitive impairments gave rise to new approaches aiming to enhance cognitive impairments in the treatments of substance use disorders. There are promising behavioral, cognitive and pharmacological strategies that can target and improve impairments associated with executive control such as response inhibition, working memory, planning and mental flexibility (Brady et al., 2011; Eack et al., 2016; Sofuoglu et al., 2016). The primary objective of our study was to contribute to this growing body of literature by identifying a comprehensive profile of neurocognitive deficits related to five primary substances of abuse (i.e., alcohol, cocaine, stimulants, opioids and marijuana). Further research in this area could provide insight that assists clinicians with appropriately identifying cognitive impairments and tailoring cognitive enhancement interventions to the needs of individuals presenting to substance use treatment. Thus, we present cross-sectional neuropsychiatric data representing a large, diverse sample of individuals newly seeking outpatient substance-related treatment at geographically diverse community-based programs.

METHODS

Study Design and Setting

Data were drawn from a large (N=497) randomized controlled trial evaluating a web-based version of the Community Reinforcement Approach plus prize-based contingency management among participants newly enrolled in 10 outpatient substance use disorder treatment programs across the United States. Full details about study procedures are available elsewhere (Campbell et al., 2014). Participants were eligible if they were in the first thirty days of a treatment episode and if they self-reported using substances within the 30 days prior to screening (or 60 days if recently exiting a controlled environment). Clinics specializing in medication assisted opioid dependence treatment did not participate in the trial. Participants were enrolled between June 2010 and August 2011. Data for this study were collected as part of the baseline assessment.

Measures

Participant Characteristics—Demographic data were collected for all participants. Self-reported physical health was measured using a visual analogue scale (EuroQol Group, 1990).

Primary Substance and Drug/Alcohol Abstinence—Participants self-reported their primary substance, that is, the substance for which they were currently seeking treatment or

considered to be the most problematic. Participants' self-reported primary substance matched closely to their DSM-IV substance use diagnosis; 97%–99% of participants who identified alcohol, cocaine, stimulants, or opioids as the primary substance met diagnostic criteria; 87% of participants who identified marijuana as primary met diagnostic criteria. A semi-structured interview was performed by research staff using the DSM-IV Checklist to determine current substance use diagnosis and age of onset (Hudziak et al., 1993). Abstinence from drugs and alcohol was assessed via self-report using the Timeline Follow-back method (Sobell & Sobell, 1992) and confirmed via biological screening: urine drug (QuickTox® dip card for 10 drugs using standard lateral flow chromatographic immunoassays and temperature and adulterant test strips) and breath alcohol screens.

Neuropsychological Assessment—The MicroCog™ computerized Assessment of Cognitive Functioning is an age and education normed cognitive assessment (Powell et al., 2004). Based on previous work (Aharonovich et al., 2008; Aharonovich et al., 2006), a custom version of the MicroCog (20–25 minutes in length; 8 sub-tests) was used to measure three cognitive domains:

1. Attention and mental control, or the ability to attend to new information and store and mentally manipulate this information short-term, was measured using the *Numbers Forward* and *Numbers Reversed* subtests. These ask participants to recall digit spans either forward or reversed. *Wordlist 1* and *Wordlist 2* subtests were used to test incidental verbal learning or memory for words presented without initially being prompted to recall them.
2. Reasoning and cognitive flexibility were measured via the *Analogies* subtest, which tests individuals' ability to connect new ideas and questions with information they have already learned. *Object Match A* and *Object Match B* subtests measure cognitive flexibility and abstraction, or one's ability to shift patterns of thinking.
3. Spatial processing was measured using the *Clocks* subtest, which shows analog clocks with and without markings and asks subjects to determine the time. *Clocks* examines subjects' ability to interpret visually observed pictures or objects in meaningful ways (Strauss et al., 2006).

A total score was calculated based on number of correct responses. Response time scores were recorded as well. Subtest raw scores were transformed to population based scaled scores (mean = 10.0, sd = 3.0), whereby clinically significant impairment is defined as being less than one standard deviation below the mean (Powell et al., 2004). Proficiency scores were then calculated using a combination of measured accuracy and speed, with higher weight given to accuracy.

Statistical Analysis

Participants were categorized into groups based on their primary substance (i.e., alcohol, cocaine, other stimulants, opioids, or marijuana) (10 participants who identified an “other” drug, nine benzodiazepines and one PCP, as their primary substance were excluded from the analyses due to small numbers). Chi-square (X^2) tests for categorical variables and F-tests

for continuous variables were computed. The Kruskal-Wallis test (non-parametric equivalent of the one-way independent ANOVA) was used when distributions were non-normal. Pairwise comparisons between primary substance subgroups were conducted if the test statistic was $p < .05$. Statistical tests were adjusted for gender, age, race/ethnicity (white vs. nonwhite) and education level (high school graduate or higher vs. less than high school) in ordinal regression models for the scaled scores and logistic regression models for impairment scores. Given the exploratory nature of this analysis, a formal correction for multiple statistical tests was not utilized. *SAS* 9.2 was used for all analyses.

RESULTS

Sample Characteristics

Table 1 displays demographic and clinical characteristics of the sample as a whole and by primary substance. A more detailed description of demographic and clinical characteristics by primary substance has been previously published (Campbell et al., 2013). The sample was 37.7% women with a mean age of 35.0 years ($SD=10.9$). Marijuana users were the youngest subgroup, and were significantly younger than alcohol, cocaine, and stimulant users. About half (47.5%) self-identified as a racial/ethnic minority. The majority of the sample had a high school education or the equivalent (61.4%). The sample was split relatively evenly among the five major categories of primary substance use: 20.9% alcohol; 20.5% cocaine; 13.9% other stimulants; 21.7% opioids; and 22.9% marijuana. Virtually all participants met DSM-IV abuse or dependence criteria for their primary substance (except for marijuana users, where 86.8% met abuse/dependence criteria).

Most individuals reported other drug or alcohol use in addition to their reported primary substance. For example, among those who identified alcohol as their primary substance, 48.1% also met criteria for marijuana abuse or dependence, 41.4% for cocaine abuse or dependence, and 28.9% for opioid abuse or dependence. The average age of onset for substance dependence was early to mid-20s. Marijuana users reported the earliest age of onset ($M=19.9$, $SD=7.5$) and stimulant users reported the latest age of onset ($M=25.2$, $SD=9.9$). Stimulant and cocaine users had significantly older ages of dependence onset than the other subgroups.

Neurocognitive Scaled Subtest Scores

Table 2 shows the normed and scaled mean MicroCog scores for the whole sample and for each primary substance group. Mean scores across primary substance groups were generally within one standard deviation of population based means. However, there were several exceptions. Specifically, nearly all substance category groups were almost a full standard deviation below the mean on reasoning and cognitive flexibility (Analogies). Total scaled scores were also lower for incidental verbal learning and memory (Wordlist 1), as were proficiency scores of attention and mental control (Numbers Reversed) and reasoning and cognitive flexibility (Analogies), and response time scores for spatial processing (Clocks).

Significant differences were found between subgroups on one proficiency subtest (Clocks-spatial processing) and several response time subtests (Numbers Reversed-attention and

mental control; Analogies-reasoning and cognitive flexibility; and Clocks-spatial processing). Marijuana users were least proficient on the spatial processing subtest (Clocks) and significantly less proficient than alcohol or stimulant users ($X^2(4)=10.45$, $p=.034$). Mean response times for all groups were close to population average norms on all subtests, except for spatial processing (Clocks). However, opioid users had the lowest response time for attention and mental control and significantly lower compared to cocaine and marijuana users ($X^2(4)=12.72$, $p=.013$). Alcohol users had the lowest mean response time in reasoning and cognitive flexibility (Analogies), although scores across subgroups were in the normal range. Cocaine users had the lowest mean response time scores on spatial processing (Clocks), however opioid users were significantly lower than alcohol and stimulant users ($X^2(4)=13.92$, $p=.008$). As noted above, a formal correction for multiple statistical tests was not utilized due to the exploratory nature of this analysis.

Clinically Significant Neurocognitive Impairment

Table 3 shows the percentage of each subgroup with clinically significant cognitive impairment, defined as a full standard deviation below population normed average scores of 10.0. The two cognitive domains indicating the most clinical impairment were attention/mental control (Wordlist 1 and Numbers Reversed) and reasoning/cognitive flexibility (Analogies and Object Match B). Among the total sample, almost half (49.70%) demonstrated scores that were more than one standard deviation below the normed average on reasoning and cognitive flexibility (Analogies). A quarter to a third of the sample demonstrated impairment in verbal learning (37.30%, Wordlist 1), cognitive and conceptual flexibility/abstraction (29.3%, Object Match B), and working memory (26.36%, Numbers Reversed).

Significant differences in impairment were found on one subtest of attention and mental control (Numbers Reversed). Stimulant (37.68%) and cocaine (34.31%) users showed greatest impairment. Stimulant users had greater clinically significant impairment compared to alcohol (17.31%) and opioid (21.30%) users, while cocaine users had greater clinically significant impairment compared to alcohol users only ($X^2(4)=10.97$, $p=.027$).

DISCUSSION

This study used a computerized neuropsychological battery to compare the neurocognitive profiles of five substance use subgroups identified as primary by adult treatment seekers. The fair amount of impairment in this diverse sample of substance users is consistent with prior research showing that individuals with substance use disorders have greater cognitive impairment compared with non-drug using counterparts (Tomasi et al., 2007).

Although this cross-sectional study cannot inform the debate regarding causality, the findings can inform clinicians' understanding of the neurocognitive deficits present in treatment-seeking populations. Specifically, most clinical impairments were detected in reasoning and cognitive flexibility (50% and 29%, respectively on Analogies and Object Match subtests), a domain related to executive function. High prevalence of clinical impairment was also found on attention and memory (37% of the sample, Wordlist subtest), which is sensitive to temporal lobe dysfunction. These findings are consistent with the

prefrontal cortical dysfunction thesis in chronic drug users (Goldstein & Volkow, 2011). This is supported by studies indicating high prevalence of executive functional impairment in clinical samples of substance users (Fernandez-Serrano et al., 2010) and in numerous neuroimaging studies with chronic cocaine (Bolla et al., 2004), methamphetamine (Nestor et al., 2011), and cannabis users (Gruber & Yurgelun-Todd, 2005).

Beyond these general patterns of impairment, there were limited significant differences in cognitive functioning between users of specific substances after controlling for demographic variables, but some trends did emerge. Cocaine users demonstrated the lowest scores for most of the total and proficiency subtests, as well as the greatest impairment across total subtest scores. This is consistent with a previous study comparing cocaine and heroin polysubstance users to controls on various measures of executive function. In this study, the cocaine users had more impairment than heroin users and controls on measures of inhibition (Stroop) and cognitive shifting (go/no go and category test) (Verdejo-Garcia et al., 2006). The finding that cocaine users have impairments in attention and reasoning is also consistent with previous studies examining both non-clinical and clinical populations (Aharonovich et al., 2006; Sofuoglu et al., 2013). A meta-analysis by Jovanovski et al. (2005) comparing cocaine users (n=481) with healthy controls (n=586) also reported large effect sizes for attention, moderate effect sizes for visual and working memory and small effect sizes for language and sensory-perceptual functions.

The group identifying marijuana as primary followed in terms of impairment in total scores (cognitive flexibility, verbal learning and memory). The significant dysfunction observed in marijuana users is consistent with studies showing that chronic heavy marijuana use is associated with impairment in sustained attention, verbal learning and memory, and executive functioning (Pope et al., 1995). Impaired attention and memory has also been related to the duration of cannabis use, with greater impairment associated with greater length of use (Solowij et al., 2002). However, other research reported minimal or no effects of chronic cannabis use on overall IQ, attention, working memory, and abstract reasoning (Jager et al., 2006).

The finding that the opioid group was less impaired overall compared to other substance groups in cognitive flexibility and abstraction (although not on several response time subtest scores - mental control and spatial processing) is also supported by previous studies. There is evidence that chronic amphetamine users, but not opioid users, display deficits in decision-making (Rogers et al., 1999). Further, examination of postmortem brains indicate qualitatively more severe neuropathology in amphetamine users than opioid users (Wilson et al., 1996). This conclusion is also supported by results from studies that have failed to detect a difference between opioid users and controls on other measures of neuropsychological functioning thought to correlate with frontal lobe damage (e.g., abstract thinking (Bruhn & Maage, 1975). However, later work (Ornstein et al., 2000) found some indication of impairment in heroin users on tasks assessing executive function. In this study, opioid and amphetamine users were similarly impaired.

The use of proficiency scores and neurocognitive profiling of these substance use subgroups can provide some guidance to clinicians when thinking about treatment planning, as they

highlight areas of cognitive dysfunction that may hamper certain activities or tasks. For example, cocaine users showed significantly worse impairment in total and proficiency scores. In other words, cocaine users tended to respond quickly but erroneously. The proficiency score of cocaine users may reflect a more vigilant, rapid scanning of the environment that leads to faulty decision making. Awareness of the cognitive style of the individual presenting to treatment could inform type and modality of intervention (group vs individual, processing vs educational, in person vs technology-based) in order to promote better treatment outcomes.

Regarding the question of whether impairments such as those observed in this study are the cause or result of substance use, additional research is needed. On one hand, neurocognitive impairment may lead directly to substance use disorders due to failed inhibitory control and impaired error processing, preventing affected individuals from considering negative effects of behaviors. This line of thinking has been reinforced by studies that found that neurocognitive deficits were likely to precede significant substance use and therefore represent premorbid risk factors (Giancola et al., 1996). Other evidence suggests that observed neurocognitive deficits represent permanent or reversible changes in cognitive functioning as a result of substance use itself. For example, heavy cannabis use has been found to alter right prefrontal brain activity and debilitate certain executive functions such as inhibition of impulses, cognitive flexibility, and complex information processing (Crean et al., 2011). In alcohol research, chronic drinkers have greater rates of impaired memory and abstract reasoning (Bates et al., 2006). Reversible neurotoxic effects on cognitive function due to alcohol consumption was implied in a meta-analysis of studies comparing cognitive testing in individuals after short, intermediate, and long term abstinence (Stavro et al., 2013) showing more significant impairment on testing performed in early abstinence. As noted earlier, no conclusions can be drawn regarding causality of the observed impairments, but understanding neurocognitive profiles across substance domains may aid in designing longitudinal studies that might provide better insight into the question of causality versus association.

This is the first study to directly compare cognitive function in a clinical population of alcohol, cocaine, stimulant, opioid, and marijuana users. The sample was large, with over 100 participants per group (except for the stimulant subgroup). Findings add to our understanding of the differences between these main subgroups. However, limitations of the study should be noted. First, given the exploratory nature of this study and the aim to identify possible signals for future research, we did not adjust the analysis for multiple comparisons. Not performing statistical corrections can increase the likelihood of Type I error (i.e., false positives). Second, we did not use a full battery but a subset of neurocognitive tests. In doing so, we hoped to select subtests representative of the range of cognitive function, although use of full batteries may have provided more reliable measures of neurocognitive functions.

The drug and alcohol subgroups were also distinguished based on participants' self-report of primary substance. But as noted in Table 1, participants often met diagnostic criteria for multiple substances. It is possible the effects found in this study could be attributed to the use of multiple substances. This issue may be unavoidable as most substance users do not

limit their consumption to a single substance. The majority of studies examining cognitive profiles of substance users therefore must classify users by a primary substance (Fernandez-Serrano et al., 2011). Further, about half of the participants screened positive for illicit drug use on the urine toxicology screen at baseline. Therefore, we cannot rule out the influence of recent drug taking on the neurocognitive assessment scores. An ideal study testing neurocognitive functioning would ensure that participants were fully detoxified from all substances, but this was beyond the scope of the current trial. The effect of drug taking was minimized as any individual who showed clear signs of intoxication were asked to complete assessment on a later date.

Also, other factors such as sociodemographic and clinical characteristics (e.g., age of substance use onset, psychiatric comorbidity, employment, income level etc.) may show differential effects among subgroups. Future studies should examine the associations of cognition with course of substance use disorders, comorbidity and if these differ by other individual characteristics.

Lastly, it should also be noted that this study's opioid users only represented a subset of this population who were not engaged in medication assisted treatment for opioid use. Those taking medications for opioid use disorder may differ from the study population so conclusions regarding generalizability should be cautious.

CONCLUSION

This secondary analysis of a large and heterogeneous sample of treatment-seeking substance users participating in an effectiveness trial confirmed significant cognitive dysfunction, especially in the domains of reasoning, cognitive flexibility, and memory. It also substantiated previous research showing cocaine use to be particularly deleterious to cognitive functioning. The study used a computerized neuropsychological battery that has been used previously in clinical samples of substance using populations. Some differential impairment between the primary substance subgroups was observed, contributing to and expanding our knowledge of neurocognitive profiling of substance users. Increasing knowledge of the similarities and differences between subgroups of substance users can increase clinicians' awareness of cognitive difficulties patients might experience in treatment as well as assist in the consideration and development of profile-specific behavioral and pharmacological treatment.

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Table 1

Descriptive Characteristics by Primary Substance of Abuse (N=497)¹

	Total N=497	Alcohol N=104	Cocaine N=102	Stimulants N=69	Opioids N=108	Marijuana N=114	X ² / F	p-value
Mean (SD) or %								
Sex (% women)	37.70	37.50	46.53	33.33	31.48	38.60	X ² (4) = 5.74	.2198
Age (yrs)	35.0 (10.9)	37.6 (10.7) ^a	40.4 (10.0) ^a	36.7 (9.8) ^{ab}	31.7 (10.1) ^{bc}	29.9 (10.2) ^c	F(4, 492)=19.44	<.001
Race/Ethnicity							X ² (12) = 144.03	<.001
White	52.52	56.73	40.20	42.03	82.41	37.72		
Black/African American	22.13	20.19	45.10	4.35	5.56	29.82		
Hispanic/Latino	10.87	15.38	7.84	8.70	7.41	14.04		
Multi-racial/Other	14.49	7.69	6.86	44.93	4.63	18.42		
Education							X ² (8) = 10.02	.264
< High School	23.34	20.19	27.45	20.29	27.78	20.18		
High School/GED	61.37	58.65	59.80	65.22	54.63	69.30		
> High School	15.29	21.15	12.75	14.49	17.59	10.53		
Abuse or Dependence								
Alcohol	62.58	97.12 ^a	64.71 ^b	39.13 ^c	54.63 ^{bc}	50.88 ^{bc}	X ² (4) = 78.95	<.001
Cocaine	41.65	41.35 ^a	97.06 ^b	8.70 ^c	38.89 ^a	14.91 ^c	X ² (4) = 193.57	<.001
Stimulants	22.94	13.46 ^a	6.86 ^a	98.55 ^b	12.96 ^a	9.65 ^a	X ² (4) = 260.84	<.001
Opiates	33.40	28.85 ^a	14.71 ^{ab}	7.25 ^b	99.07 ^c	7.89 ^b	X ² (4) = 280.96	<.001
Marijuana	49.70	48.08 ^a	33.33 ^a	34.78 ^a	37.04 ^a	86.84 ^b	X ² (4) = 87.02	<.001
Other	8.47	13.46 ^a	6.86 ^{ab}	1.45 ^b	14.95 ^a	3.51 ^b	X ² (4) = 17.49	.002
Onset age of substance use dependence (any substance) ³	22.3 (8.6)	21.1 (7.7) ^{ab}	24.6 (9.3) ^c	25.2 (9.9) ^c	21.5 (7.7) ^a	19.9 (7.5) ^b	X ² (4) = 25.81 ²	<.001
Abstinent at Baseline (all substances) ⁴	45.45	39.42 ^a	50.00 ^{ab}	69.12 ^c	56.48 ^{bc}	22.12 ^d	X ² (4) = 47.84	<.001

	Total N=497	Alcohol N=104	Cocaine N=102	Stimulants N=69	Opioids N=108	Marijuana N=114	X ² / F	p-value
	Mean (SD) or %							
Abstinent at Baseline (primary) ⁴	64.98	61.54 ^a	70.59 ^{ab}	83.82 ^{bc}	84.26 ^c	33.04 ^d	X ² (4) = 80.43	<.001
Physical Health Status (0–100)	72.8(19.8)	71.7(21.2)	72.0 (20.9)	76.4 (17.9)	72.0 (18.4)	73.3 (19.7)	X ² (4) = 3.32 ²	.506

^{abcd} When the overall test statistic is significant (p<.05, column 8), superscripts within the row (columns 3–7) indicate which primary substance subgroups are statistically different from one another (p<.05). For example, “a” is significantly different from “b” or “c”, but does not differ from other columns with “a” superscripts.

¹ 10 cases whose primary substance was “other” (9 Benzodiazepine and 1 PCP) were excluded in the analyses by substance categories.

² Kruskal-Wallis test (non-parametric equivalent of the one-way independent ANOVA).

³ 43 individuals excluded because they did not meet substance abuse/dependence criteria: 6 alcohol, 5 cocaine, 6 stimulants, 26 marijuana.

⁴ Alcohol Abstinence was defined as no use in the prior 7 days based on self-report.

MicroCog™ subtests scaled scores at baseline for total sample and by primary substance of abuse adjusted by age, sex, race/ethnicity, and education (N=497¹)

Table 2

Scaled Scores [^]	Observed Mean (SD)							Chi-Square (4) ²	P-value
	Total (N=497)	Alcohol (N=104)	Cocaine (N=102)	Stimulants (N=69)	Opioids (N=108)	Marijuana (N=114)			
Total									
Attention and Mental Control									
Numbers Forward	8.59(2.57)	8.59(2.48)	8.10(2.76)	8.70(2.51)	8.87(2.44)	8.72(2.64)	1.85	.763	
Numbers Reversed	8.15(2.70)	8.15(2.24)	7.87(2.95)	8.12(2.78)	8.36(2.73)	8.20(2.83)	3.04	.551	
Wordlist 1	7.53(4.49)	7.60(4.49)	7.08(4.78)	7.94(4.47)	8.31(4.43)	6.89(4.26)	4.78	.310	
Wordlist 2	9.61(3.23)	9.67(3.17)	8.86(3.86)	10.10(2.47)	9.92(2.76)	9.65(3.43)	3.13	.536	
Inductive Reasoning and Cognitive Flexibility									
Analogies	6.70(2.85)	6.63(3.01)	6.04(2.81)	6.78(2.61)	7.06(2.73)	6.96(2.95)	2.86	.581	
Object Match A	8.28(3.90)	8.66(3.38)	8.28(4.31)	8.32(3.74)	8.37(3.82)	7.82(4.14)	0.92	.921	
Object Match B	8.60(3.15)	8.59(3.48)	7.84(3.15)	8.67(2.98)	9.08(3.06)	8.79(2.97)	3.29	.511	
Spatial processing									
Clocks	11.00(1.86)	11.30(1.53)	10.87(1.77)	11.13(2.06)	10.93(1.99)	10.83(1.95)	6.91	.141	
Proficiency									
Attention and Mental Control									
Numbers Forward	8.42(2.32)	8.28(2.36)	7.92(2.53)	8.59(2.60)	8.67(2.12)	8.66(2.05)	1.40	.844	
Numbers Reversed	7.54(2.13)	7.48(1.88)	7.34(2.28)	7.46(2.26)	7.56(1.97)	7.81(2.28)	0.54	.970	
Inductive Reasoning and Cognitive Flexibility									
Analogies	7.76(2.29)	7.60(2.40)	7.27(2.25)	7.71(1.95)	8.08(2.10)	8.06(2.51)	2.17	.705	
Object Match A	8.44(2.94)	8.31(3.08)	8.17(3.31)	8.59(2.91)	8.66(2.64)	8.51(2.78)	5.40	.249	
Object Match B	9.16(3.35)	8.48(3.56)	8.24(3.43)	8.75(3.35)	10.31(2.94)	9.75(3.06)	3.56	.468	
Spatial processing									
Clocks	9.69(1.30)	9.84(1.21) ^{ab}	9.58(1.27) ^{ac}	9.93(1.47) ^a	9.68(1.30) ^c	9.54(1.28) ^{bc}	10.45	.034	
Response Time									

	Total (N=497)	Alcohol (N=104)	Cocaine (N=102)	Stimulants (N=69)	Opioids (N=108)	Marijuana (N=114)	Chi-Square (4) ²	P-value
Scaled Scores [^]	Observed Mean (SD)							
Attention and Mental Control								
Numbers Forward	9.57(2.95)	9.44(3.26)	9.36(2.84)	9.14(2.88)	9.65(2.83)	10.05(2.89)	7.23	.124
Numbers Reversed	9.95(2.76)	9.75(2.84) ^{ab}	10.24(2.59) ^{ac}	9.62(2.90) ^{abc}	9.59(2.80) ^b	10.41(2.69) ^c	12.72	.013
Inductive Reasoning and Cognitive Flexibility								
Analogies	10.53(2.92)	10.10(3.09) ^{ab}	10.56(3.08) ^c	10.39(3.07) ^{acd}	10.44(2.84) ^{ad}	11.05(2.52) ^{bc}	13.57	.009
Object Match A	9.54(2.88)	9.27(2.80)	9.45(3.22)	9.43(3.04)	9.84(2.77)	9.64(2.65)	7.79	.100
Object Match B	10.57(3.06)	9.88(3.06)	10.24(3.24)	9.87(3.31)	11.40(2.69)	11.11(2.82)	9.15	.058
Spatial processing								
Clocks	7.93(2.91)	8.12(2.87) ^{ab}	7.53(3.15) ^{ac}	8.57(2.95) ^a	7.93(2.84) ^c	7.75(2.74) ^{bc}	13.92	.008

¹ 10 cases whose primary substance was "other" (9 Benzodiazepine and 1 PCP) were excluded from analyses.

² Statistic tests were adjusted for gender, age, race/ethnicity (white vs. nonwhite) and education level (high school graduate or higher vs. less than high school) in the ordinal regression models (i.e., cumulative logistic models for ordinal outcomes).

[^] mean=10.0; SD=3.0

^{abcd} When the overall test statistic is significant ($p < .05$, column 8), superscripts within the row (columns 3–7) indicate which primary substance subgroups are statistically different from one another ($p < .05$). For example, "a" is significantly different from "b" or "c", but does not differ from other columns with "a" superscripts.

Table 3

Observed percentage of sample with clinically significant cognitive impairment¹ on MicroCog™ subtests at baseline by primary substance of abuse adjusted by age, sex, race/ethnicity, and education (N=497²)

	Total (N=497)	Alcohol (N=104)	Cocaine (N=102)	Stimulants (N=69)	Opioids (N=108)	Marijuana (N=114)	Chi-Square (4) ³	P-value
Observed Percentage (%) clinically significant cognitive impairments								
Total Subtest								
Attention and Mental Control								
Numbers Forward	19.11	21.15	30.39	17.39	12.04	14.91	7.23	.124
Numbers Reversed	26.36	17.31 ^a	34.31 ^{bc}	37.68 ^b	21.30 ^{abc}	25.44 ^{bc}	10.97	.027
Wordlist 1	37.30	38.46	41.18	32.35	29.63	42.98	4.17	.384
Wordlist 2	13.51	13.46	20.59	5.88	11.11	14.04	7.86	.097
Inductive Reasoning and Cognitive Flexibility								
Analogies	49.70	45.19	58.82	46.38	44.44	52.63	2.38	.666
Object Match A	18.86	10.89	23.76	15.94	16.67	25.44	8.50	.075
Object Match B	29.30	29.70	34.00	26.09	25.93	29.82	1.29	.864
Spatial processing								
Clocks	3.02	0.96	2.94	2.90	3.70	4.39	1.95	.745

¹ cognitive impairment defined as one standard deviation below the general population mean.

² 10 cases whose primary substance was “other” (9 Benzodiazepine and 1 PCP) were excluded from analyses.

³ Statistic tests were adjusted for gender, age, race/ethnicity (white vs. nonwhite) and education level (high school graduate or higher vs. less than high school) in the logistic models.

^{abc} When the overall test statistic is significant (p<.05, column 7), superscripts within the row (columns 3–7) indicate which primary substance subgroups are statistically different from one another (p<.05). For example, “a” is significantly different from “b” or “c”, but does not differ from other columns with “a” superscripts.