Neurocognitive, psychiatric, and substance use characteristics in opioid dependent adults

Franchesca Arias, Julia H. Arnsten, Chinazo O. Cunningham, Kelly Coulehan, Abigail Batchelder, Mia Brisbane, Katie Segal, Monica Rivera-Mindt

PII: S0306-4603(16)30120-4
DOI: doi: 10.1016/j.addbeh.2016.03.018
Reference: AB 4798

To appear in: *Addictive Behaviors*

Received date: 1 September 2015
Revised date: 26 January 2016
Accepted date: 29 March 2016

Please cite this article as: Arias, F., Arnsten, J.H., Cunningham, C.O., Coulehan, K., Batchelder, A., Brisbane, M., Segal, K. & Rivera-Mindt, M., Neurocognitive, psychiatric, and substance use characteristics in opioid dependent adults, *Addictive Behaviors* (2016), doi: 10.1016/j.addbeh.2016.03.018

Declaration of interest: None

Neurocognitive, Psychiatric, and Substance Use Characteristics in Opioid Dependent Adults

Franchesca Arias[1], Julia H. Arnsten[2], Chinazo O. Cunningham[2],

Kelly Coulehan[1], Abigail Batchelder[2], Mia Brisbane[2], Katie Segal[2], and Monica Rivera-Mindt[1,3]

[1] Psychology Department, Fordham University, US

[2] Division of General Internal Medicine, Department of Medicine, Albert Einstein College of Medicine and Montefiore Medical Center, US

[3] Mount Sinai School of Medicine, Departments of Neurology and Psychiatry, US

Address correspondence to Franchesca Arias, MS, Clinical Psychology Department, Fordham University, NY.

Email:farias2@fordham.edu

Short title: Neurocognitive Characteristics of Treatment-Seeking Opioid Dependent Adults

Abstract

Aims: To describe neurocognitive function among opioid-dependent adults seeking buprenorphine treatment and to explore the impact of lifetime psychiatric conditions on neurocognitive function. To explore the additive interaction of patient-based characteristics that may help to inform treatment.

Design: Cross-sectional assessment of neurocognitive function, substance use, and psychiatric characteristics of adults seeking buprenorphine treatment within substance use treatment centers in New York City.

Participants: Thirty-eight opioid-dependent adults seeking buprenorphine treatment.

Measurements: A comprehensive battery, which included measures of executive functioning, learning, memory, verbal fluency, attention, processing speed, and motor functioning were administered. The Wide Range Achievement Test-Third Edition, the Composite International Diagnostic Interview, and an audio computer assisted structured interview were also completed. Correlations and independent sample t-tests were used to ascertain group differences.

Findings: Thirty-nine percent of participants were impaired in global neurocognitive function (*n*=15). Over one third were impaired in either: learning (*n*=28), memory (*n*=26), executive functioning (*n*=17), motor functioning (*n*=17), attention/working memory (*n*=14) or verbal fluency (*n*=12). Lifetime history of alcohol dependence was associated with impairment in global neurocognitive, executive functioning, and motor functioning. Lifetime history of cocaine dependence was associated with impairment in executive functioning and motor functioning (all *p*'s <0.05). Major depressive disorder history was not associated with neurocognitive impairment.

Conclusions: Among this sample of opioid-dependent adults, there were high rates of global and domain-specific neurocognitive impairment, with severe impairment in learning and memory. Lifetime alcohol and cocaine dependence were associated with greater neurocognitive impairment, particularly in executive functioning. Because executive functioning is critical for decision-making and learning/memory dysfunction may interfere with information encoding, these findings suggest that opioid-dependent adults may require enhanced support for medical decision-making.

Key words: opioid dependence; neurocognitive performance; buprenorphine treatment; depression; substance use disorders

1. Introduction

The emerging opioid epidemic constitutes a significant public health problem in the United States (US) (Beletsky et al., 2012; C. M. Jones, 2013; C. M. Jones et al., 2013; Manchikanti et al., 2012). In addition to the estimated 517,000 people currently living with heroin abuse or dependence, approximately 1.9 million Americans abuse or depend on opioid analgesics (Substance Abuse and Mental Health Administration [SAMHSA], 2014). This surge in opioid-related conditions has had significant social, health, and economic repercussions. In the US, women, young adults, and non-Hispanic whites are increasingly affected by opioid dependence (Heil et al., 2011; McCabe et al., 2005; McCabe et al., 2012; SAMHSA, 2014).

Adults with opioid use disorders are at elevated risk for infectious diseases such as HIV and hepatitis C (C. M. Jones, 2013; Meade et al., 2014; Meade et al., 2009). Increased mortality is also associated to opioid-related disorders. In 2010, opioid analgesic overdoses comprised 60% of all fatalities related to prescription drugs in the US (Miech et al., 2013; C.M. Jones et al., 2013) and it is a leading cause of premature death among non-Hispanic whites, middle-aged men, and young adults (Calcaterra et al., 2013; C. M. Jones et al., 2013; Paulozzi, 2011; Paulozzi et al., 2011). Finally, costs associated to illicit opioid consumptions are exorbitant. Estimates suggest that in the US lost productivity, medical expenses, and criminality resulting from illicit opioid consumption cost approximately $40 billion dollars each year (Ghate et al., 2010; Hansen et al., 2011). In light of the changing demographic and the social and economic consequences characterizing the opioid epidemic in America, research in this area is relevant and necessary.

Methadone maintenance therapy (MMT) has been the gold standard intervention for opioid use disorders in the US (Amato et al., 2013; Mayet et al., 2005). In 2002, the US Food and Drug Administration (FDA) introduced buprenorphine maintenance therapy (BMT) as an alternative treatment option (Fiellin et al., 2004; Fudala et al., 2003). BMT confers similar benefits as MMT (Kamien et al., 2008; Mattick et al., 2014), but has lower potential for lethality (Walsh et al.,1994), offers a more flexible medication schedule, is available via prescription; (Gryczynski et al., 2013; Mauger et al., 2014), and is less stigmatizing (Boatwright, 2002; O'Connor et al., 1996). Treatment of opioid use disorders with BMT increased steadily in the US in the last

decade (Turner et al., 2014). For example, BMT was the treatment of choice for opioid dependence in less than 100,000 ambulatory visits in 2003. By 2013, over 2 million ambulatory visits for opioid dependence were treated with BMT (Turner et al., 2014).

Despite the recent increase in the use of BMT to treat opioid dependence, there is a paucity of research characterizing the neurocognitive and psychiatric profiles of adults seeking BMT in the US (Dreifuss et al., 2013; Weiss et al., 2011). For example, a PubMed search using the term “neuropsychological performance and buprenorphine treatment” produced only 12 results, 6 of which were focused on issues extraneous to the topic at hand (i.e., cognitive functioning in adults receiving BMT). Of the remaining, none were conducted on US-based samples. An additional PubMed search using the term “cognitive functioning and buprenorphine treatment” produced only 17 results, eight of which were opinion articles. Of the remaining 12 studies, over 90% were conducted on non-US based samples. In total, our literature review revealed a single US-based study characterizing the neurocognitive profile of adults seeking BMT. Mintzer et al. (2004) examined executive functioning, processing speed, memory, and working memory in community-dwelling African American and non-Hispanic white adults with an active diagnosis of opioid dependence (*N* = 8). Participants ranged in age (6 to 41 years old) and in level of education (10 to 14 years). Results revealed mild cognitive impairment in long-term memory (Mintzer et al., 2004). Despite the novelty of their research design and its scientific relevance, the low sample size limited the generalizability of the findings.

The dearth of research examining neurocognitive characteristics in adults receiving or seeking BMT is particularly troublesome. Baseline cognitive abilities may impact engagement in, and adherence to, substance use treatment (Hinkin et al., 2004; Ornstein et al., 2000; Passetti et al., 2008). Furthermore, a growing body of evidence suggests that patient-specific characteristic (e.g., cognitive abilities, psychiatric presentation) can be used to tailor treatment for opioid dependence. This, in turn, may help to maximize treatment outcomes (Bart, 2012; Gruber et al., 2007; Nosyk et al., 2013; Okie, 2010). Explicitly, examining patients’ neurocognitive profiles may serve an important role in informing clinical decision-making throughout the treatment process.

Co-occurring psychiatric conditions of adults seeking BMT in the US have not been carefully examined in the context of cognitive characteristics. For example, while Mintzer et al. (2004) evaluated the cognitive profile of adults receiving BMT across several domains, they did not examine associations between neurocognitive functioning and either psychiatric or substance use histories. Conversely, while Weiss et al. (2011) used the Composite International Diagnostic Interview (CIDI) to assess psychiatric and substance use characteristics of adults receiving BMT (N = 653), they did not examine neurocognitive functioning. Moreover, Weiss et al. (2011) did not report the prevalence of mood- and anxiety- related conditions in their sample. Like Mintzer et al. (2004), Weiss et al. (2011) studied a group comprised of employed (over 60%), non-Hispanic white adults (over 90%), who had completed an average of 13 years of education. Hence, the neurocognitive, psychiatric, and substance characteristics of more ethnically diverse opioid dependent adults seeking BMT have yet to be well characterized.

The aim of the current study was to examine the neurocognitive, psychiatric, and substance use characteristics of an ethnically diverse US sample of adults seeking BMT. We evaluated global and domain-specific neurocognitive function in opioid-dependent adults presenting for BMT. In addition, we examined rates of current and lifetime psychiatric and substance use diagnoses, and explored associations between neurocognitive function and comorbid lifetime diagnoses of depressive disorder, alcohol dependence, and cocaine dependence. We hypothesized that rates of global and domain-specific impairment would be high. Additionally, we hypothesized that those participants with comorbid lifetime diagnoses of depressive disorder, alcohol dependence, and/or cocaine dependence would have significantly higher rates of neurocognitive impairment compared to those without these comorbidities.

2. Material and Methods

We examined baseline data from an ongoing study (ClincalTrials.gov Identifier: NCT01108679). The goal of the Neurocognitive Effects of Buprenorphine Among HIV+ and HIV- Opioid Users (NEB) study was to examine the effect of buprenorphine treatment on neurocognitive (NC) functioning over a 6-month period. A subset of the data collected as part of the NEB study is presented in this manuscript.

2.1. *Setting*

Participants were recruited from clinics affiliated with Montefiore Medical Center and Albert Einstein College of Medicine. Recruitment was targeted to a Montefiore community health center with a large buprenorphine treatment program and to a network of drug treatment clinics comprising Einstein's Division of Substance Abuse. Recruitment occurred through word of mouth, flyers, and health care providers. Research visits were conducted at the Clinical Research Center of the Einstein-Montefiore Institute for Clinical and Translational Research.

2.2. *Participants*

Eligibility criteria for study participation included: 1) current diagnosis of opioid dependence; 2) no buprenorphine use for 15 consecutive days prior to enrollment; 3) anticipated initiation of buprenorphine treatment within 30 days; 4) 18-68 years of age; 5) proficiency in English or Spanish; 6) at least 6 years of formal education; 7) documented HIV status; 8) capacity to consent to study participation. Participants were excluded if they had: 1) serious medical illness (e.g. severe liver or end stage renal disease); 2) seizure disorder; 3) psychotic or bipolar disorders; 4) current comorbid alcohol or benzodiazepine dependence; or 5) history of head trauma with loss of consciousness longer than 12 hours. Of the 141 participants who were screened for the study, 41 met our inclusion/exclusion criteria and were enrolled, and 38 completed the baseline assessment. This study was approved by Institutional Review Boards at the Albert Einstein College of Medicine and Fordham University. All study participants provided written informed consent.

2.3. Procedures

After a 15-minute screening interview over the phone, eligible participants were invited for an in-person baseline interview. The baseline interview included a comprehensive neuropsychological evaluation, a structured clinical interview, and several computerized assessments. Overall, interviews lasted 4 to 4.5 hours and all measures were completed in a single visit. Participants were alerted about the nature of the visit during the telephone screener and reminded via telephone 24 hours prior to the visit. Participants were scheduled for their baseline within the first 10 days prior to starting buprenorphine treatment. Verbal consent was obtained

prior to completing the telephone screener. Additionally, informed consent was obtained in person, during the initial phase of the visit, and participants were given ample time to make an informed decision about participating. Participants who appeared intoxicated or who reported recent substance use were re-scheduled for another time.

Unobserved urine was collected to determine active use of opioids (heroin, oxycodone, methadone, and buprenorphine) at a 300ng/ml cutoff, benzodiazepines, amphetamines, and/or cocaine. Results were taken into consideration when interpreting the neuropsychological data. Information was collected using the methods described below.

2.4. Measures

Sociodemographic and clinical information (e.g., income, years of education, occupation, and developmental history) was ascertained using both staff-administered questionnaires and audio computerized-assisted self-interviews (R. Jones, 2003)

Current and lifetime history of psychiatric and substance use diagnoses were ascertained using the Composite Diagnostic Interview (Robins et al., 1988), a structured clinical interview. Current diagnoses were assigned to participants who met diagnostic criteria in the 12-month period preceding the interview; lifetime (past) diagnoses were assigned to participants who met diagnostic criteria at any point in their life. Depressive symptoms were assessed using the Beck Depression Inventory-Second Edition (BDI-II) (Beck et al.,1996), which was administered using audio computer assisted structured interviews (ACASI) technology. Substance use patterns were assessed using the Addiction Severity Index (ASI) (McLellan et al., 1980). Hazardous alcohol use was also measured using the Alcohol Use Disorder Identification Test (AUDIT) (Saunders et al., 1993). Urine was collected (unobserved) to assess opioid use (heroin, oxycodone, methadone, and buprenorphine) at a 300ng/ml cutoff, as well as use of benzodiazepines, amphetamines, or cocaine.

Neurocognitive (NC) data were collected in seven domains: executive functioning, learning, memory, verbal fluency, attention/working memory, processing speed, and motor functioning. The reading subtest from the Wide Range Achievement Test-Third Edition (WRAT-III) (Wilkinson, 1993) was administered to estimate

premorbid level of intelligence. Although Spanish-speaking bilingual individuals could opt to complete the evaluation in Spanish, all instruments were administered in English by trained psychometrists using standardized procedures. Table 1 lists measures and references for normative data. Of note, norms that controlled for sociodemographic factors known to impact neurocognitive performance (e.g., age, education, race/ethnicity) were used when available (Heaton, 1993; Heaton et al., 2004). Explicitly, 10 out of 12 of the instruments used to assess neurocognitive abilities in this sample used demographically corrected norms. Table 1 indicates which demographic characteristics each instrument corrected for. Neurocognitive impairment was operationalized as one standard deviation below the mean (i.e., average T-scores < 40). Psychometrists in the study were supervised by an experienced clinical neuropsychologist. Quality assurance strategies included double scoring all charts and double data entry.

Insert Table 1

2.5. Analysis

Raw scores for neurocognitive data were converted to demographically-corrected *T*-scores using the best published normative data (See Table 1). Mean domain *T*-scores were then calculated by averaging the *T*-scores of all tests within a domain, and global NC *T*-scores were calculated by averaging *T*-scores for all tests. Dichotomous variables were created to calculate proportion of neurocognitive impairment. Domain *T*-scores that were one standard deviation below the mean considered impaired (Heaton et al., 2004; See Table 4).

Independent sample *t*-tests tests were used to compare differences in neurocognitive performance between pre-defined groups: lifetime alcohol dependence versus no alcohol dependence, lifetime cocaine dependence versus no cocaine dependence, and lifetime Major depressive disorder (MDD) versus no MDD. Current depressive symptoms were categorized as: minimal (BDI-II 0-13), mild (14-19), moderate (20-28), or severe (>29). Alcohol use disorder identification test (AUDIT) total scores greater than 8 indicated harmful or hazardous drinking.

3. Results

Table 2 summarizes demographic and clinical characteristics. The mean age was 46.4(*SD*=9.6) years and

the mean number of years of education was 11.6(*SD*= 2.6), with 55% having completed at least 12 years of education. Approximately 55% of the sample self-identified as Hispanic/Latino (*n*=21), 26% as non-Hispanic black (*n*=10), 13% as non-Hispanic white (*n*=5) and 5% as non-Hispanic other (*n*=2). Sixty-nine percent were men (*n*=26) and 18% were HIV-seropositive (*n*=7). Over 50 percent of the participants endorsed minimal depressive symptoms (*n*=22). Major depressive disorder (MDD) was the most prevalent lifetime psychiatric diagnosis (31%; *n*=12), followed by dysthymia (7%; *n*=3).

Insert Table 2

Table 3 summarizes substance use diagnoses. Forty-seven percent endorsed lifetime cocaine dependence (*n*=18); 34% lifetime alcohol dependence (*n*=13); 18% lifetime cannabis dependence (*n=7*); and 5% lifetime benzodiazepine dependence (*n*=2). Lifetime diagnoses of substance abuse followed a similar pattern: cocaine was the most commonly abused substance (63%; *n*=24), followed by alcohol (50%; *n*=19), cannabis (47%; *n*=18), and benzodiazepines (15%; *n*=6). In the 30 days prior to the study visit, 94% of the sample reported using opioids (*n*=36), 36% cocaine (*n*=14), 47% alcohol (*n*=18), 31% reported using cannabis (*n*=12), and 15% reported using benzodiazepines (*n*=6).

Insert Table 3

Table 4 summarizes neurocognitive scores and percent impaired. Overall, average global NC and domain *T*-scores were mostly in the low average-to-borderline range, with learning and memory domain *T*-scores in the mild-to-moderately impaired range (*M*=33.9, *SD*=10.2; *M=34.8*, *SD*=11.1, respectively). More than 60% scored in the impaired range in learning and memory (Learning *n*=28; Memory *n*=26). Though *T*-scores for global neurocognitive (global NC) function, executive function (EF), verbal fluency, attention/working memory, processing speed domain, and motor functioning were in the normal range, 39% demonstrated global NC impairment (*n*=15), and over 30% scored in the impaired range in EF (*n*=17), verbal fluency (*n*=12), attention/working memory (*n*=14), and motor functioning (*n*=17) were also noted.

Insert Table 4

Table 5 summarizes differences in rates of NC impairment between study participants with history of

lifetime alcohol dependence versus no alcohol dependence; lifetime cocaine dependence versus no cocaine dependence; and lifetime MDD versus no MDD. Participants with lifetime alcohol dependence demonstrated worse impairment in global NC functioning ($t(36)=2.4$, $p<0.05$) and performed worse in EF ($t(36)=2.9$, $p<0.05$), motor functioning ($t(33)=3.4$, $p<0.05$), and processing speed ($t(36)=2.8$, $p<0.05$) compared to those without lifetime alcohol dependence; effect sizes for these comparisons were large (Cohen's d =0.97 to 1.19). Participants with a history of lifetime cocaine dependence performed worse in tasks assessing EF ($t(36)=2.3$, $p<0.05$) and motor functioning ($t(33)=2.4$, $p<0.05$) compared to those without lifetime cocaine dependence; effect sizes for these comparisons were also large (Cohen's d = 0.75 and 0.81). Current or lifetime cannabis or benzodiazepines diagnoses were not significantly associated with NC impairment (p's>0.05). Participants with a history of lifetime MDD performed worse across all NC domains than those without MDD, but none of the differences reached statistical significance. Small to large effect sizes were observed in global NC function, processing speed, and motor functioning (Cohen's $d \leq .70$). In analyses comparing HIV seropositive to HIV negative participants, no significant differences were observed in any neurocognitive domain (all p's >0.10).

Insert Tables 5

4. Discussion

We observed significant global and domain-specific neurocognitive impairment in this sample of opioid-dependent adults seeking treatment with buprenorphine. Forty-two percent demonstrated global NC impairment and one-third demonstrated impaired EF, attention/working memory, or motor functioning. Most notably, approximately three-quarters of the sample had impaired learning and memory with domain *T*-scores in the mild-to-moderately impaired range. Lifetime (i.e., past) alcohol and cocaine dependence were common, and participants with these comorbidities had greater neurocognitive impairment than those without. Major depressive disorder (MDD) was also common, but lifetime MDD diagnosis was not significantly associated with worse neurocognitive function.

Findings on animal models document the role of opioids in the modulation of neuronal excitability in the hippocampus (Derrick & Martinez, 1994) and link spatial learning and memory deficits to decreased

hippocampal functioning (Meilandt et al., 2004; Simmons & Chavkin, 1996). The human literature, though equivocal, reports neurocognitive impairment in cognitive flexibility, inhibitory control, and working memory (Baldacchino et al., 2012; Mitrovic et al., 2011), as well as impaired processing and psychomotor speed, verbal learning, and verbal fluency (Loeber et al., 2012; Soyka et al., 2008) in former and current opioid users. The current study provides support for these results, as we found that approximately 70% of treatment-seeking opioid-dependent adults demonstrated impaired learning and memory. This risk is critically important for treatment providers to consider, as impaired learning and memory may translate into difficulties retaining treatment-related information and subsequently to suboptimal treatment adherence. To avoid this and enhance treatment engagement and adherence, clinical providers should consider tailoring treatment-related information for individuals at high risk for learning and memory impairment.

The complex clinical presentations that characterize opioid-dependent adults who seek treatment often include psychiatric and other substance use comorbidity (Brooner et al., 1997; Highfield et al., 2007; Schäfer et al., 2011). In the current study, comorbid lifetime alcohol and cocaine dependence diagnoses were common, and were significantly associated with deficits in EF. These findings extend prior research on the prevalence of executive dysfunction among opioid users with current substance-related diagnoses (Fishbein et al., 2007; Pau et al., 2002) by documenting that high risk of impaired EF is also present among opioid-dependent adults with lifetime (past) substance-related diagnoses. Impaired EF functioning can result in poor goal-oriented behavior and difficulty managing complex treatment regimens (Fishbein et al., 2007), and is crucial to recognize among persons with complex medical and psychiatric comorbidity. Our study is also unique in that it addresses gaps in the literature examining the synergistic effect of multiple substance-related comorbidities on neurocognitive functioning. Specifically, a lifetime diagnosis of cocaine or alcohol dependence impacts cognitive functioning in adults with opioid-dependence, which may results in functional implications.

Lifetime diagnosis of MDD was also relatively common (34%) in this sample. Previous studies on opioid-dependent adults report that current MDD diagnosis negatively affects neurocognitive performance and reduces treatment gains (Loeber et al., 2012; Schäfer et al., 2011). Although our analysis did not reveal a

significant association between lifetime MDD diagnosis and neurocognitive functioning, those with lifetime MDD comorbidity performed worse in all domains than those without MDD. The impact of comorbid lifetime MDD was most pronounced in processing speed and motor functioning, with small to medium effect sizes respectively. In contrast to prior studies, we examined lifetime MDD rather than current MDD. Hence, our analysis was limited and did not capture the impact of current MDD on NC functioning.

As buprenorphine treatment gains popularity in the US, research on the neurocognitive characteristics of opioid-dependent adults seeking BMT may help treatment providers make more informed decisions in regards to treatment delivery. Additional research in this area may help elucidate the role of NC functioning in treatment success. Our findings have the potential to foster interdisciplinary collaboration among clinicians treating adults for opioid dependence. Specifically, neuropsychological evaluation may help optimize treatment outcome by offering medical providers information that may help tailor treatment interventions. Similarly, providers may opt to monitor selected patients more closely based on their neurocognitive characteristics.

Despite its strengths, this study has limitations. Of the 141 adults screened for this study, only 41 met our inclusion/exclusion criteria and were enrolled. Of note, 93% of those who met inclusion/exclusion criteria (*N* = 38) successfully completed our baseline evaluation. Our small sample size likely reflects two issues. First, successfully recruiting opioid dependent adults into research is challenging, (Galea & Tracy, 2007; Verdejo-García et al., 2004) particularly in ethnically diverse, low SES area such as the Bronx, NY. However, it is notable that our study was able to retain 93% of enrolled participants to complete an exhaustive baseline evaluation. The second issue is that our relatively stringent exclusion of individuals with non-substance use related neurologic and medical confounding conditions narrowed our pool of eligible participants, but were necessary to strengthen the validity of our neurocognitive findings.

Due to our relatively small sample size, we had limited power to conduct analyses to further examine our data. For instance, we did not have sufficient power to examine the multiplicative influence of co-occurring substance use on neurocognitive functioning. Future studies would benefit from larger sample sizes to investigate potential mechanisms underlying why individuals with comorbid alcohol and/or substance

dependence have poorer neurocognitive function in comparison to those without such co-occurring conditions. In addition, within the current study, we may not have been able to observe the true impact of MDD, because we focused on lifetime rather than current MDD. Moreover, we did not assess anxiety disorders, including post-traumatic stress disorder, which is highly prevalent among US adults receiving opioid agonist therapy (OATs) (Brooner et al., 1997; Schäfer et al., 2011). Finally, the nature of our research design (i.e., observational, cross-sectional, single sample design) limits our ability to establish a causal association between addiction to multiple substances and NC impairment. Hence, these findings do not establish the etiology of the neurocognitive deficits observed. Additional research in this area, particularly prospective cohort studies, will help to elucidate the direction of the association between substance use disorder and neurocognitive deficits.

Additionally, given that our study did not have a comparison group, it is remains to be seen if the current findings are exclusive to a buprenorphine-seeking group or more generally applicable to those seeking other types of treatment for opioid dependence. In general, this study aimed to characterize the NC, substance use, and psychiatric profiles of community dwelling adults seeking buprenorphine treatment. Future research would benefit from more fine-grained analysis of current and past psychiatric comorbid diagnoses, as well as acute symptomology, larger samples, and more rigorous methodologies (including treatment comparison groups) to clarify the current findings. Our findings are specific to an ethnically diverse, urban population seeking buprenorphine treatment; thus caution should be exercised when generalizing these findings to other groups.

In sum, we observed high rates of neurocognitive impairment among treatment-seeking opioid-dependent adults, with three-quarters of study subjects demonstrating impaired learning and memory, and notable impairments in EF, attention/working memory, and motor functioning. Lifetime comorbid alcohol and cocaine dependence were both associated with greater neurocognitive impairment. These findings are important for treatment providers to be aware of, and should inform treatment decisions with opioid-dependent adults.

Acknowledgements

The authors wish to thank our participants for their contributions to this research. This research was supported by P20 DA026149 (Julia Arnsten), K23 MH07971801 (Monica Rivera Mindt), R25 DA023021 (Julia Arnsten), and the Einstein-Montefiore Center for AIDS Research (NIH AI-51519).

References

Amato, L., Davoli, M., Minozzi, S., Ali, R., & Ferri, M. (2013). Methadone at tapered doses for the management of opioid withdrawal. Chochrane Database of Systematic Reviews. 3, CD003409.

Baldacchino, A., Balfour, D. J., Passetti, F., Humphris, G., & Matthews, K. (2012). Neuropsychological consequences of chronic opioid use: A quantitative review and meta-analysis. Neurosci Biobehav R. 36, 2056-2068. doi: 10.1016/j.neubiorev.2012.06.006

Bart, G. (2012). Maintenance medication for opiate addiction: The foundation of recovery. J Addict Dis. 31, 207-225. doi: 10.1080/10550887.2012.694598

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Beck Depression Inventory, second ed.* The psychological corporation, San Antonio.

Beletsky, L., Rich, J. D., & Walley, A. Y. (2012). Prevention of fatal opioid overdose. J Amer Med Assoc. 308, 1863-1864. doi: 10.1001/jama.2012.14205

Benedict, R. H. B., Schretlen, D., Groninger, L., & Brandt, J. (1998). Hopkins Verbal Learning Test–Revised: Normative data and analysis of inter-form and test-retest reliability. Clin Neuropsychol. 12, 43-55.

Benedict, R. H., Schretlen, D., Groninger, L., Dobraski, M., & Shpritz, B. (1996). Revision of the Brief Visuospatial Memory Test: Studies of normal performance, reliability, and validity. Psychol Assess. 8, 145.

Boatwright, D. E. (2002). Buprenorphine and addiction: Challenges for the pharmacist. J Am Pharm Assoc. 42, 432-438.

Brooner, R. K., King, V. L., Kidorf, M., Schmidt, C. W., Jr., & Bigelow, G. E. (1997). Psychiatric and substance use comorbidity among treatment-seeking opioid abusers. Arch Gen Psychiatry. 54, 71-80.

Calcaterra, S., Glanz, J., & Binswanger, I. A. (2013). National trends in pharmaceutical opioid related overdose deaths compared to other substance related overdose deaths: 1999-2009. Drug Alcohol Depen. 131, 263-270. doi: 10.1016/j.drugalcdep.2012.11.018

Derrick, B. E., & Martinez, J. L., Jr. (1994). Opioid receptor activation is one factor underlying the frequency dependence of mossy fiber LTP induction. J Neurosci. 14, 4359-4367.

Dreifuss, J. A., Griffin, M. L., Frost, K., Fitzmaurice, G. M., Potter, J. S., Fiellin, D. A., Selzer J. A., Hatch-Maillette, M. A., Sonne, S.C., & Weiss, R. D. (2013). Patient characteristics associated with buprenorphine/naloxone treatment outcome for prescription opioid dependence: Results from a multisite study. Drug Alcohol Depen. 131, 112-118.

Fiellin, D. A., Kleber, H., Trumble-Hejduk, J. G., McLellan, A. T., & Kosten, T. R. (2004). Consensus statement on office-based treatment of opioid dependence using buprenorphine. J Subst Abuse Treat. 27, 153-159.

Fishbein, D. H., Flannery, B., Krupitsky, E., Langevin, D., Bobashev, G. V., Verbitskaya, E., Bland, C. R., Bolla, K., Zvartau, E., Egorova, V., Bushara, N., & Tsoy M. (2007). Neurocognitive characterizations of Russian heroin addicts without a significant history of other drug use. Drug Alcohol Depen. 90, 25-38.

Fudala, P. J., Bridge, T. P., Herbert, S., Williford, W. O., Chiang, C. N., Jones, K., Collins, J., Raisch, D., Casadonte, P., Goldsmith, R. J., Ling, W., Malkerneker, U., McNicholas, L., Renner, J., Stine, S., Tusel, D., & the Buprenorphine/Naloxone Collaborative Study Group. (2003). Office-based treatment of opiate addiction with a sublingual-tablet formulation of buprenorphine and naloxone. New Engl J Med. 349, 949-958. doi: 10.1056/NEJMoa022164

Galea, S., & Tracy, M. (2007). Participation rates in epidemiologic studies. Ann Epidemiol. 17, 643-653.

Ghate, S. R., Haroutiunian, S., Winslow, R., & McAdam-Marx, C. (2010). Cost and comorbidities associated with opioid abuse in managed care and Medicaid patients in the United Stated: A comparison of two recently published studies. J Pain Palliat Care Pharmacother. 24, 251-258. doi: 10.3109/15360288.2010.501851

Gruber, S. A., Silveri, M. M., & Yurgelun-Todd, D. A. (2007). Neuropsychological consequences of opiate use. Neuropsychol Rev. 17, 299-315. doi: 10.1007/s11065-007-9041-y

Gryczynski, J., Jaffe, J. H., Schwartz, R. P., Dušek, K. A., Gugsa, N., Monroe, C. L., O'Grady, K. E., Olsen, Y. K., & Mitchell, S. G. (2013). Patient perspectives on choosing buprenorphine over methadone in an urban, equal- access system. Am J Addict. 22, 285-291.

Hansen, R. N., Oster, G., Edelsberg, J., Woody, G. E., & Sullivan, S. D. (2011). Economic costs of nonmedical use of prescription opioids. Clin J Pain. 27, 194-202. doi: 10.1097/AJP.0b013e3181ff04ca

Heaton, R. K. (1993). Wisconsin card sorting test: Computer version 2. Psychological Assessment Resources, Odessa.

Heaton, R. K., Taylor, M. J., & Manly, J. (2003). Demographic effects and use of demographically corrected norms for with the WAIS-III and WMS-III. In D. Tulsky (Ed.), *Clinical interpretation of the WAIS-III and WMS-III* (pp. *181-209)*. Orlando, FL: Academic Press.

Heaton, R. K., Miller, S. W., Taylor, M. J., & Grant, I. (2004). Revised comprehensive norms for an expanded Halstead-Reitan Battery: Demographically adjusted norms for African American and Caucasian adults. Psychological Assessment Resources, Lutz.

Heil, S. H., Jones, H., Arria, A., Kaltenbach, K., Coyle, M., Fischer, G., Stine, S., Selby, P., & Martin, P. (2011). Unintended pregnancy in opioid-abusing women. J Subst Abuse Treat. 40, 199-202. doi: 10.1016/j.jsat.2010.08.011

Highfield, D. A., Schwartz, R. P., Jaffe, J. H., & O'Grady, K. E. (2007). Intravenous and intranasal heroin-dependent treatment-seekers: Characteristics and treatment outcome. J Addic Med. 102, 1816-1823. doi: 10.1111/j.1360-0443.2007.01998.x

Hinkin, C. H., Hardy, D. J., Mason, K. I., Castellon, S. A., Durvasula, R. S., Lam, M. N., & Stefaniak, M. (2004). Medication adherence in HIV-infected adults: Effect of patient age, cognitive status, and substance abuse. AIDS. 18, S19.

Jones, C. M. (2013). Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers - United States, 2002-2004 and 2008-2010. Drug Alcohol Depen. 132, 95-100. doi: 10.1016/j.drugalcdep.2013.01.007

Jones, C. M., Mack, K. A., & Paulozzi, L. J. (2013). Pharmaceutical overdose deaths, United States, 2010. JAMA. 309, 657-659.

Jones, R. (2003). Survey data collection using audio computer assisted self-interview. Western J Nurs Res. 25, 349-358.

Kamien, J. B., Branstetter, S. A., & Amass, L. (2008). Buprenorphine-naloxone versus methadone maintenance therapy: A randomised double-blind trial with opioid-dependent patients. Heroin Addict Rel Clin. 10, 5-18.

Lawton, M. P., & Brody, E. M. (1969). Assessment of older people: Self-maintaining and instrumental activities of daily living. Gerontologist. 9, 179-186.

Loeber, S., Nakovics, H., Kniest, A., Kiefer, F., Mann, K., & Croissant, B. (2012). Factors affecting cognitive function of opiate-dependent patients. Drug Alcohol Depen. 120, 81-87. doi: 10.1016/j.drugalcdep.2011.07.001

Manchikanti, L., Helm, S., 2nd, Fellows, B., Janata, J. W., Pampati, V., Grider, J. S., & Boswell, M. V. (2012). Opioid epidemic in the United States. Pain Physician. 15, ES9-38.

Mattick, R. P., Breen, C., Kimber, J., & Davoli, M. (2014). Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database of Systematic Reviews. 2, CD002207. doi: 10.1002/14651858.CD002207.pub4

Mauger, S., Fraser, R., & Gill, K. (2014). Utilizing buprenorphine–naloxone to treat illicit and prescription-opioid dependence. Neuropsychiatr Dis Treat. 10, 587.

Mayet, S., Farrell, M., Ferri, M., Amato, L., & Davoli, M. (2005). Psychosocial treatment for opiate abuse and dependence. Cochrane Database of Systematic Reviews. 1, CD004330. doi: 10.1002/14651858.CD004330.pub2

McCabe, S. E., Teter, C. J., Boyd, C. J., Knight, J. R., & Wechsler, H. (2005). Nonmedical use of prescription opioidsamong U.S. college students: Prevalence and correlates from a national survey. J Addict Behav Ther Rehabil. 30, 789-805. doi: 10.1016/j.addbeh.2004.08.024

McCabe, S. E., West, B., Teter, C. J., & Boyd, C. J. (2012). Medical and nonmedical use of prescription opioids among high school seniors in the United States. Arch Pediatr Adolesc Med. 166, 797-802.

McLellan, A. T., Luborsky, L., Woody, G. E., & O'Brien, C. P. (1980). An improved diagnostic evaluation instrument for substance abuse patients: The Addiction Severity Index. J Nerv Ment Dis. 168, 26-33.

Meade, C. S., Bevilacqua, L. A., Moore, E. D., Griffin, M. L., Gardin, J. G., 2nd, Potter, J. S., Hatch-Maillette, M., & Weiss, R. D. (2014). Concurrent substance abuse is associated with sexual risk behavior among adults seeking treatment for prescription opioid dependence. Am J Addiction. 23, 27-33. doi: 10.1111/j.1521-0391.2013.12057.x

Meade, C. S., McDonald, L. J., & Weiss, R. D. (2009). HIV risk behavior in opioid dependent adults seeking detoxification treatment: An exploratory comparison of heroin and oxycodone users. Am J Addiction. 18, 289-293. doi: 10.1080/10550490902925821

Meilandt, W. J., Barea-Rodriguez, E., Harvey, S. A., & Martinez, J. L., Jr. (2004). Role of hippocampal CA3 mu-opioid receptors in spatial learning and memory. J Neurosci. 24, 2953-2962. doi: 10.1523/jneurosci.5569-03.2004

Mintzer, M. Z., Correia, C. J., & Strain, E. C. (2004). A dose-effect study of repeated administration of bupe/naloxone or performance in opioid-dependent volunteers. Drug Alcohol Depen. 74, 205-209.

Miech, R., Koester, S., & Holliman, B. D. (2013). Towards an explanation of the recent increase in drug-related mortality. In Crime, HIV and Health: Intersections of Criminal Justice and Public Health Concerns (pp. 129-149). Springer, Netherlands.

Mitrovic, S. M., Dickov, A., Vuckovic, N., Mitrovic, D., & Budisa, D. (2011). The effect of heroin on verbal memory. *Psychiatr Danub, 23*, 53-59.

Nosyk, B., Anglin, M. D., Brissette, S., Kerr, T., Marsh, D. C., Schackman, B. R., Wood, E., & Montaner, J. S. (2013). A call for evidence-based medical treatment of opioid dependence in the United States and Canada. Health Affair. 32, 1462-1469. doi: 10.1377/hlthaff.2012.0846

O'Connor, P. G., Oliveto, A. H., Shi, J. M., Triffleman, E., Carroll, K., Kosten, T., & Rounsaville, B. (1996). A pilot study of primary-care-based buprenorphine maintenance for heroin dependence. Am J Drug Alcohol Abuse. 22, 523-531.

Okie, S. (2010). A flood of opioids, a rising tide of deaths. New Engl J Med. 363, 1981-1985. doi: 10.1056/NEJMp1011512

Ornstein, T. J., Iddon, J. L., Baldacchino, A. M., Sahakian, B. J., London, M., Everitt, B. J., & Robbins, T. (2000). Profiles of cognitive dysfunction in chronic amphetamine and heroin abusers. Neuropsychopharmacol. 23, 113-126.

Passetti, F., Clark, L., Mehta, M. A., Joyce, E., & King, M. (2008). Neuropsychological predictors of clinical outcome in opiate addiction. Drug Alcohol Depen. 94, 82-91.

Pau, C. W., Lee, T. M. , & Shui-fun, F. C. (2002). The impact of heroin on frontal executive functions. Arch Clin Neuropsychol. 17, 663-670.

Paulozzi, L. J. (2011). *Drug-induced deaths - United States, 2003-2007*. (1545-8636 (Electronic) 0892-3787 (Linking)). C Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/21430623.

Paulozzi, L. J., Weisler, R. H., & Patkar, A. A. (2011). A national epidemic of unintentional prescription opioid overdose deaths: how physicians can help control it. J Clin Psychiatry. 72, 589-592. doi: 10.4088/JCP.10com06560

Robins, L. N., Wing, J., Wittchen, H. U., Helzer, J. E., Babor, T. F., Burke, J., Farmer, A., Jablenski, A., Pickens, R., Regier, D. A., Sartorius, N., & Towle, L. H. (1988). The Composite International Diagnostic Interview: An epidemiologic instrument suitable for use in conjunction with different diagnostic systems and in different cultures. Arch Gen Psychiatry. 45, 1069-1077.

Saunders, J. B., Aasland, O. G., Babor, T. F., De la Fuente, J. R., & Grant, M. (1993). Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. J Addict Med. 88, 791-804.

Schäfer, I., Fischer, M., Reimer, J., Karow, A., & Haasen, C. (2011). Significance of psychiatric comorbidity for the outcome of maintenance treatment–a review of the literature. Ment Health Subs Use. 4, 62-71.

Simmons, M. L., & Chavkin, C. (1996). Endogenous opioid regulation of hippocampal function. Int Rev Neurobiol. 39, 145-196.

Soyka, M., Lieb, M., Kagerer, S., Zingg, C., Koller, G., Lehnert, P., . . . Hennig-Fast, K. (2008). Cognitive functioning during methadone and buprenorphine treatment: Results of a randomized clinical trial. J Clin Psychopharm. 28, 699-703. doi: 10.1097/JCP.0b013e31818a6d38

Substance Abuse and Mental Health Administration, SAMHSA. (2014). *Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings*. (NSDUH Series H-48, HHS Publication No. (SMA) 14-4863). Rockville, MD: Retrieved from http://www.samhsa.gov/data/sites/default/files/NSDUHresultsPDFWHTML2013/Web/NSDUHresults2013.pdf.

Turner, L., Kruszewski, S. P., & Alexander, G. C. (2014). Trends in the use of buprenorphine by office-based physicians in the United States, 2003–2013. Am J Addiction. n/a-n/a. doi: 10.1111/j.1521-0391.2014.12174.x

Verdejo-García, A., López-Torrecillas, F., Giménez, C. O., & Pérez-García, M. (2004). Clinical implications and methodological challenges in the study of the neuropsychological correlates of cannabis, stimulant, and opioid abuse. Neuropsychol Rev. 14, 1-41.

Walsh, S. L., Preston, K. L., Stitzer, M. L., Cone, E. J., & Bigelow, G. E. (1994). Clinical pharmacology of buprenorphine: Ceiling effects at high doses. Clin Pharmacol Ther. 55, 569-580. doi: 10.1038/clpt.1994.71

Weiss, R. D., Potter, J. S., Fiellin, D. A., Byrne, M., Connery, H. S., Dickinson, W., Gardin, J., Griffin, M. L., Gourevitch, M. N., Haller, D. L., Hasson, A. L., Huang, Z., Jacobs, P., Kosinski, A. S., Lindblad, R., McCance-Katz, E. F., Provost, S. E., Selzer, J., Somoza, E. C., Sonne, S. C., Ling, W. (2011). Adjunctive counseling during brief and extended buprenorphine-naloxone treatment for prescription opioid dependence: A 2-phase randomized controlled trial. Arch Gen Psychiatry. 68, 1238-1246.

Wilkinson, G. S. (1993). WRAT-3: Wide range achievement test administration manual, third edition Wide Range, Inc., Wilmington.

Table 1. Neurocognitive (NC) and Other Measures

NC Domains and Tests	Normative Data Sources
Executive Function	
Wisconsin Card Sorting Task-64 Item Version	Heaton et al. (1993)[1,2,3,4]
Trail Making Test (Part B)	Heaton et al. (2004)[1, 2,3,4]
Attention/Working Memory	
WAIS-III Letter Number Sequencing	Heaton, Taylor, & Manly (2003)[1,2,3,4]
PASAT Total Correct	Heaton et al. (2004)[1, 2,3,4]
Learning	
Hopkins Verbal Learning Test-Revised (Total Recall)	Benedict et al. (1998)[1]
Brief Visuospatial Memory Test-Revised (Total Recall)	Benedict (1996)[1]
Memory (Delayed Recall)	
Hopkins Verbal Learning Test (Delayed Recall Trial)	Benedict et al. (1998)[1]
Brief Visuospatial Memory Test-Revised (Delayed Recall Trial)	Benedict (1997)[1]
Motor	
Grooved Pegboard Time (dominant hand)	Heaton et al. (2004)[1,2,3,4]
Grooved Pegboard Time (non-dominant hand)	Heaton et al. (2004)[1,2,3,4]
Processing Speed	
WAIS-III Digit Symbol	Heaton, Taylor, & Manly (2003)[1,2,3,4]
WAIS-III Symbol Search	Heaton, Taylor, & Manly (2003)[1,2,3,4]
Trail Making Test (Part A)	Heaton et al. (2004)[1, 2,3,4]
Verbal Functioning	
Controlled Oral Word Association Test (F-A-S)	Heaton et al. (2004)[1,2,3,4]
Semantic (Animal) Fluency	Heaton et al. (2004)[1,2,3,4]

Note. WAIS-III =Wechsler Adult Intelligence Scale; PASAT=Paced Auditory Serial Arithmetic Test (PASAT); Norms corrected for the indicated demographic characteristics: 1 =Age; 2 =Education; 3 =Gender; 4 =Ethnicity.

Table 2. Demographic and Clinical Characteristics (*N*=38)	
	Male
Demographic Characteristics	*M* (*SD*)/% (*n*)
Age (yrs)	46.4 (9.6)
Education (yrs)	11.6 (2.6)
Gender	
Male	69% (26)
Race/Ethnicity	
Hispanic	55% (21)
Non-Hispanic black	26% (10)
Non-Hispanic white	13% (5)
Non-Hispanic other	5% (2)
Clinical Characteristics	*M* (*SD*)/(*n*)
BDI-II Total Score:	13.6 (10.8)
Minimal Total Score <13	57% (22)
Mild Total Score between 14-19	13% (5)
Moderate Total Score between 20-28	23% (9)
Severe Total Score between 29-63	5% (2)
CIDI Diagnosis:	
Major Depressive Disorder	31% (12)
Dysthymia	7% (3)
HIV Status:	
HIV+	18% (7)
CD4 count < 200*	15% (1)

Note. BDI-II =Beck Depression Inventory-II; CIDI =Composite International Diagnostic Interview. *% based on HIV+ participants

Table 3. Current and Lifetime Substance Use and Diagnoses (*N*=38)

Substance	Percent (*n*)
Alcohol	
Positive urine toxicology at baseline	NA
Current use per ASI	47% (18)
Lifetime Dependence	34% (13)
Lifetime Abuse	50% (19)
Hazardous Drinking (AUDIT)	18% (7)
Opioids	
Positive urine toxicology at baseline	97% (37)
Current use per ASI	94% (36)
Lifetime Dependence	100% (38)
Lifetime Abuse	97% (37)
Cocaine	
Positive urine toxicology at baseline	34% (13)
Current use per ASI	36% (14)
Lifetime Dependence	47% (18)
Lifetime Abuse	63% (24)
Cannabis	
Positive urine toxicology at baseline	31% (12)
Current use per ASI	31% (12)
Lifetime Dependence	18% (7)
Lifetime Abuse	47% (18)
Benzodiazepines	
Positive urine toxicology at baseline	15% (6)
Current use as per ASI	15% (6)
Lifetime Dependence	5% (2)
Lifetime Abuse	15% (6)

Note. CIDI =Composite International Diagnostic Interview; ASI =Addiction Severity Index; Urine toxicology results obtained from sample collected on interview day; AUDIT =Alcohol Use Disorder Identification Test.

Table 4. Neurocognitive (NC) Characteristics based on average T-scores and rates of impairment (*N*=38)

	M (SD)	***NC impaired %(n)***
WRAT-3 Standard Score	86.2 (13.6)*	-
Global NC Function	41.2 (6.5)	39% (15)
Learning	33.9 (10.2)	73% (28)
Memory	34.8 (11.1)	68% (26)
Executive Function	42.7 (9.4)	44% (17)
Motor	40.2 (9.3)	44% (17)
Attention/Working Memory	42.8 (8.1)	36% (14)
Verbal Fluency	44.9 (9.5)	31% (12)
Processing Speed	48.1 (8.5)	15% (6)

Note. Scores for the WRAT-3, used to ascertain premorbid functioning is presented in Standard Score (M=100, SD=15). T-Scores <40 = NC impairment.

Table 5. Mean comparisons based on alcohol dependence, cocaine dependence, and depression with neurocognitive (NC) functioning *(N*=38*)*.

	Diagnosis of Alcohol Dependence				Diagnosis of Cocaine Dependence				Lifetime Diagnosis of Depression			
	Dependent (*n*=13)	Non-Dependent (*n*=25)			Dependent (*n*=17)	Non-Dependent (*n*=21)			Depressed *(n*=13*)*	Non-Depressed *(n*=25*)*		
Neurocognitive Domain	***M* (*SD*)**	***M* (*SD*)**	***t*-test**	**Cohen's *d***	***M* (*SD*)**	***M* (*SD*)**	***t*-test**	**Cohen's *d***	***M* (*SD*)**	***M* (*SD*)**	***t*-test**	**Cohen's *d***
Global NC Functioning	37.9(6.5)	42.9(5.8)	2.4*	.68	39.6(6.8)	42.5(6.0)	1.4	.46	39.8(8.8)	41.9(4.9)	.82	.32
Learning	33.1(12.2)	34.4(9.2)	0.4	.06	34.6(10.8)	33.4(9.8)	-0.4	.05	33.9(13.5)	34.0(8.3)	.03	.00
Memory	32.3(12.0)	36.1(10.6)	1.0	.17	34.3(11.8)	35.2(10.8)	0.3	.04	34.4(13.7)	35.0(9.8)	.16	.03
Executive Functioning	37.2(5.9)	44.5(6.7)	2.9*	1.13	38.6(6.7)	43.6(6.6)	2.3*	.75	40.6(7.4)	41.8(6.9)	.44	.17
Motor	34.2(9.0)	43.8(7.6)	3.4*	1.19	36.4(9.6)	43.5(8.0)	2.4*	.81	36.3(8.6)	42.6(9.2)	1.9	.70
Attention/Working Memory	40.4(7.3)	44.0(8.3)	1.3	.45	40.8(8.3)	44.3(7.7)	1.3	.44	43.0(8.8)	42.9(7.8)	.12	.01
Verbal Fluency	44.5(8.7)	45.0(9.9)	.18	.05	45.3(8.7)	45.3(10.2)	0.3	.00	43.7(12.8)	45.4(7.6)	.53	.18
Processing Speed	43.2(5.8)	50.7(8.5)	2.8*	.97	45.7(9.3)	50.1(7.3)	1.6	.53	46.8(11.6)	48.8(6.4)	.72	.24

Note. Mean and Standard Deviations (M, SD) based on average T Scores; T-Scores<40 = NC impairment; Diagnosis assessed using the Composite Diagnostic Interview (CIDI); *= *p*< .05, **p*<.001.

Role of Funding Source

This research was supported by P20 DA026149 (Julia Arnsten), K23 MH07971801 (Monica Rivera Mindt), R25 DA023021 (Julia Arnsten), and the Einstein-Montefiore Center for AIDS Research (NIH AI-51519). Funding sources had no role in the study design, collection, analysis or interpretation of the data. Moreover, these sources had no role in the writing of the manuscript or the decision to submit the paper for publication.

Contributors

Julia H. Arnsten, Chinazo O. Cunningham, and Monica Rivera-Mindt designed the study and wrote the protocol. Mia Brisbane and Katie Segal recruited, screened, and scheduled all participants. Abigail Batchelder, Kelly Coulehan, and Franchesca Arias evaluated all participants and entered collected data. Franchesca Arias conducted literature searches, provided summaries of previous research studies, and conducted the statistical analysis, and wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of Interest

Through this letter we confirm that there are no known conflicts of interest associated with this publication. Explicitly, there has been no significant financial support for this work, or any of its authors, that could comprise the objectivity its conclusions. Should you have any questions regarding this manuscript, do not hesitate to call me at 917-771-3161.

Highlights

- We recruited community-dwelling adults, of diverse socio-economic status, seeking buprenorphine treatment.
- We used a comprehensive neurocognitive battery to evaluate baseline cognitive functioning in adults seeking buprenorphine treatment
- We examined psychiatric, functional, and psychological factors.
- We interpreted overall performance within a biopsychosocial framework, emphasizing the effect of multiple factors on neurocognitive performance.
- Generally, adults diagnosed with opioid dependence who present for opioid agonist treatment with buprenorphine, on average, exhibit diminished neurocognitive functioning. In this population, preexisting alcohol and cocaine use disorders are associated with poorer scores.