HHS Public Access

Author manuscript

Subst Abus. Author manuscript; available in PMC 2019 January 02.

Published in final edited form as:

Subst Abus. 2018 January 02; 39(1): 116–123. doi:10.1080/08897077.2017.1391925.

Lifetime Marijuana and Alcohol Use, and Cognitive Dysfunction in People with Human Immunodeficiency Virus Infection

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Abstract

Background—Substance use is common among people with HIV infection. Alcohol, marijuana, and HIV can have negative effects on cognition. We examined associations between current and lifetime marijuana and alcohol use, and cognitive dysfunction in people with HIV infection.

Methods—We studied a cohort of 215 HIV-infected adults with Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) substance dependence or ever injection drug use. In adjusted cross-sectional regression analyses we tested the associations between current marijuana use, current heavy alcohol use, lifetime marijuana use, lifetime alcohol use, duration of heavy alcohol use (the independent variables), and three measures of cognitive dysfunction (dependent variables): both the i) memory and ii) attention domains from the Montreal Cognitive Assessment (MoCA), and iii) the 4-item cognitive function scale (CF4) from

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The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

SAL and RS conceived the study question. ASV was the project manager and led data collection. Both MRW and TCH conducted statistical analyses and supported interpretation of results. Both AYW and MS provided HIV clinical expertise and facilitated clinic access. RS was the Principal Investigator of the Boston ARCH Cohort study and JHS was the Principal Investigator of the URBAN ARCH Consortium. SAL wrote the first draft of the manuscript. All authors provided considerable editing, revisions and content review of the initial manuscript draft. All authors read and approved the final draft of the manuscript.

the Medical Outcomes Study HIV Health Survey (MOS-HIV). Analyses were adjusted for demographics, primary language, depressive symptoms, anxiety, comorbidities, antiretroviral therapy, hepatitis C virus (ever), duration of HIV infection (years), HIV-viral load (log copies/mL), CD4 cell count, lifetime and recent cocaine use, and recent illicit and prescribed opioid use.

Results—Current marijuana use was significantly and negatively associated with the MOS-HIV CF4 score (adjusted mean difference = −0.40, p = 0.01). Current marijuana use was not significantly associated with either MoCA score. Lifetime marijuana use and current heavy and lifetime alcohol use and duration of heavy alcohol use were not associated with any measure of cognitive dysfunction.

Conclusion—Current marijuana use was associated with one measure of cognitive dysfunction, but there was not a consistent pattern of association with lifetime marijuana use or alcohol use and measures of cognitive dysfunction. Understanding the mechanism by which marijuana, with and without alcohol, are associated with worse cognition warrants larger, longer studies with more precise and diverse measurements of cognitive function.

Keywords

cannabis; marijuana; alcohol; ethanol; cognitive function; lifetime; HIV infection

INTRODUCTION

The prevalence of alcohol and marijuana use among people living with human immunodeficiency virus (HIV) infection (PLWH) is disproportionately high, with substance use and substance use disorders thought to affect 40–74%.[1] Half of PLWH report the use of “recreational” marijuana and approximately one-third report marijuana use to relieve symptoms.[2] Those who use marijuana are more likely to drink alcohol, and the prevalence of unhealthy alcohol use (the spectrum from risky use through disorder) in PLWH is twice that in the general population.[3]

HIV infection has deleterious effects on the brain and cognition. HIV preferentially targets the brain, with the central nervous system thought to be an important reservoir for the virus.[4,5] If left untreated, a triad of motor, behavioral, and cognitive symptoms manifest.[5,6] A spectrum of HIV associated neurocognitive disorders (HAND) is well-recognized.[5,7–10] While the use of suppressive combination antiretroviral therapy (ART) has decreased severe forms of HAND, virologically suppressed individuals continue to experience varying degrees of neurocognitive dysfunction.[11–13]

Marijuana use and heavy alcohol use can negatively alter brain activity and cognitive function. Acute and long-term effects of delta-9-tetrahydrocannabinol (Δ^9-THC) include altered brain metabolism and changes in neuronal networks, respectively, and pro-inflammatory states as well as frontal cortical atrophy are often seen in individuals with alcohol use disorders [14–17, 21,22] Deficits in memory, specifically delayed recall, are most often observed due to acute and chronic marijuana use, but these deficits are often absent after several weeks of abstinence.[14–16,18,19] In people with symptomatic HIV infection, marijuana use is associated with greater cognitive dysfunction compared to asymptomatic or

uninfected individuals, indicating a potential negative, synergistic effect of comorbid marijuana use and HIV infection.[20] Alcohol affects cognition on a continuum, ranging from mild cognitive impairment to more severe conditions such as Wernike-Korsakoff's syndrome and alcohol-related dementia.[23,24] In the presence of HIV infection, alcohol increases the risk of cognitive dysfunction across all ages. Minor or sub-clinical cognitive deficits caused by marijuana use or heavy alcohol use may be exacerbated and manifest in the presence of HIV infection.[20, 25,26]

The combination of marijuana use, alcohol use, and HIV infection may produce additional, negative synergistic effects on the brain resulting in decreased cognition and related daily functioning. For example, memory and executive function pertaining to real-world tasks are important for adherence to complicated medication regimens critical for viral suppression, prevention of HIV disease progression, and maximizing quality of life.[27] Because marijuana use and alcohol use are both common in PLWH, and PLWH are at risk for cognitive impairment, it is important to understand how both substances affect cognitive function in this population. Few, if any, studies have examined the combined effects that alcohol use and marijuana use may have on cognition in PLWH. Such an understanding could contribute to efforts to reduce harmful substance use and prevent clinical consequences, particularly in an era in which "moderate" drinking is at times discussed in terms of possible beneficial effects, and in which marijuana is discussed as a relatively safe and even therapeutic substance.

Past studies of the effects of alcohol and drug use in PLWH tend to assess current use only, often with assessments that are not very detailed. Clearly current, particularly very recent use (e.g. intoxication) can have effects on cognition. However, chronic organ system effects, such as cognitive impairment due to brain damage, are often the result of long-term, repeated, high dose exposure to toxins (such as alcohol). Thus, the aim of this study was to test the associations between current and lifetime marijuana and alcohol use on cognitive function in HIV-infected adults.

METHODS

Study Design

This study is a cross-sectional analysis of data collected from adults with HIV infection and substance use disorder (current Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) dependence or ever injection drug use) who were enrolled in a prospective cohort study between December 2012 and November 2014. The Institutional Review Board of the Boston University medical campus reviewed and approved all study procedures.

Participants

Participants were part of the Boston Alcohol Research Collaboration on HIV/AIDS (ARCH) Cohort, one of three cohorts that make up the Uganda Russia Boston Alcohol Network for Alcohol Research Collaboration on HIV/AIDS (URBAN ARCH) Consortium. Participants were recruited from clinical sites for HIV care in Boston, Massachusetts: the Center for

Infectious Disease at Boston Medical Center and the Boston Healthcare for the Homeless Program. Inclusion criteria were the following: documentation of HIV infection in any medical record; current (past 12-month) Diagnostic and Statistical Manual Fourth Edition[28] drug or alcohol dependence determined by the Mini International Neuropsychiatric Interview (MINI 6.0)[29] or ever injection drug use; fluency in English; 18 years or older; willingness to provide contact information for one person knowledgeable of whereabouts to assist with follow up; and completion of the Lifetime Drinking History and lifetime items from the Addiction Severity Index (ASI)[30,31] at a follow-up assessment 6–12 months after study entry. The data set in this analysis was closed after 215 participants completed both lifetime assessments. Exclusion criteria were pregnancy, plans to leave the area within the year, and cognitive impairment that would interfere with informed consent or understanding the interview questions as determined by the research interviewer. Of note, no one was excluded due to cognitive impairment. All participants provided written informed consent and were compensated for their time.

Assessments

Data collection methods included: trained research assistant administered interviews, medical record review, and collection of blood samples by trained phlebotomists.

Main Independent Variables

The five main independent variables were current and lifetime marijuana use (2 measures), current heavy alcohol use, lifetime alcohol use, and duration of heavy alcohol use (3 measures). Current marijuana use was defined as the number of days marijuana was used in the past 30, measured using questions adapted from the validated ASI.[31] Current heavy alcohol use was defined as the number of heavy drinking days in the past 30 measured using a validated 30-day Timeline Follow Back (TLFB) method.[32] A heavy drinking day was defined as four or more standard drinks (14g ethanol) for women and five or more standard drinks for men in 24 hours. Lifetime marijuana use was defined as the number of years marijuana was used 3 or more times per week, measured by lifetime questions from the ASI. Lifetime alcohol use was summarized in two ways: (i) total amount of alcohol consumed in kilograms from initiation of regular drinking (1 or more drink per month) until the time of the assessment, and (ii) duration of heavy alcohol use defined as the number of years of daily use of > 6 drinks per day (84g ethanol). Both measures of lifetime alcohol use were assessed using the Lifetime Drinking History, a validated, semi-structured interview. [30]

Covariates

The following covariates were also assessed: age; sex; race; education (completed high school or equivalent); employment; non-English primary language; depressive symptoms defined as score of >2 on the Patient Health Questionnaire-2 (PHQ-2)[33]; anxiety disorder defined a score of ≥8 on the Overall Anxiety Severity and Impairment Scale (OASIS).[34] Other covariates included: comorbidities measured using the Charlson Comorbidity Index[35]; currently taking antitretroviral therapy; hepatitis C virus infection ever (defined as detectable antibody or viral RNA)[49,50]; duration of HIV infection (years since first test); HIV viral load (log copies/mL); CD4 cell count (<200/mm^3, 200–500/mm^3, >500/mm^3); years of regular cocaine use (3 or more times per week, or 2 binges per week) measured by lifetime ASI

questions; any cocaine use in the past 30 days measured by ASI; any sedative or opioid use in the past 30 days measured by ASI; and any current opioid prescription by self-report.

Dependent Variables

Dependent variables were three measures of cognitive dysfunction: both the i) memory and ii) attention domains from the Montreal Cognitive Assessment (MoCA) and (iii) the Medical Outcomes Study HIV Health Survey 4-item cognitive function scale (MOS-HIV CF4) score. Both the MoCA memory score (range 0–5) and MOS-HIV CF4 score (0–100) were analyzed as continuous variables, while the MoCA attention score was dichotomized at 2 versus 0 or 1 (lower values in all cases indicate worse cognitive dysfunction). The MoCA is a rapid screening measure that assesses various domains of cognition.[36,37] For the present study, the domains of memory, specifically delayed recall, and attention, were assessed. In the MoCA memory section, interviewers read participants a list of five words, which participants were asked to recall directly after the words were presented in two consecutive trials and then again approximately five minutes later. Participants scored one point for each word recalled for a total of five points. The MoCA attention section tested participants' ability to repeat a sequence of numbers forward and backward in two consecutive trials. Participants scored one point each if they repeated each sequence of numbers correctly and zero points if the sequences were repeated incorrectly for a maximum of two points. The MOS-HIV measures the health related quality of life of HIV-infected individuals and consists of 35 questions in 11 different domains.[38] For the present study, the cognitive function domain (CF4) was used, comprising four questions related to overall self-reported cognitive function.

Statistical Analysis

Unadjusted and adjusted multivariable linear and logistic regression models were fit to test the association between the five independent and three dependent variables. Unadjusted models were fit including each predictor variable separately as well as unadjusted models fit to include both current and lifetime marijuana use, current heavy alcohol use, and either lifetime alcohol use (kg) or duration of heavy alcohol use. Results of these models did not differ substantially. Adjusted models included all covariates listed previously that were chosen based on factors known to impact cognitive function. Collinearity between all covariates and independent variables was assessed using a Spearman correlation matrix. For pairs of variables with a Spearman's rho greater than 0.40, only one variable was included in the model. Only lifetime alcohol use (kg) and duration of heavy alcohol use were highly correlated (Spearman's rho= 0.86); therefore these two variables were not included in the same multivariable model. In all final models collinearity diagnostics (tolerance and variance inflation factor estimates) were conducted and they revealed no evidence for collinearity.

Logistic regression models were used for dichotomous (MoCA Attention Score) outcomes and linear regression models were used for continuous (MoCA Memory Score and MOS-HIV CF4 scores) outcomes. Duration of heavy drinking was highly correlated with lifetime alcohol use (kg); we present results for the latter herein, and for the former in the Appendix. We also fit two additional models testing the interaction between current marijuana and

heavy alcohol use for each cognitive outcome and the interaction between lifetime marijuana and alcohol use (kg) for each cognitive outcome. To illustrate differences in outcomes associated with current marijuana use, predicted mean outcome scores were calculated from adjusted models for those with zero and 10 days of marijuana use in the past 30 days (10 days was the median number of days used for those using marijuana). Data analyses were conducted using SAS/STAT software, Version 9.3 of the SAS System for Microsoft Windows (SAS Institute Inc., Cary, NC, USA).

RESULTS

Participant characteristics are shown in Table 1. Over half (65%) of the 215 participants were male, the mean age was 49 years, and most were unemployed and of non-white race. The mean number of days of marijuana use in the past 30 days was 6.5 and the mean number of years of regular marijuana use was 9.8 years. The mean number of heavy drinking days in the past 30 days was 4.8, mean lifetime alcohol use was 720.7 kg, and mean number of heavy drinking years was 6.4. One third (34%) of participants scored a 0 or 1 on the MoCA attention test and the mean score on the MoCA memory test was 3.2. The mean score on the MOS-HIV CF4 was 68.8.

Associations between current and lifetime marijuana and alcohol use and cognitive dysfunction

Although current marijuana use was not significantly associated with lower cognitive function (MOS-HIV CF4 score) in the unadjusted model ($\beta = -0.21$ $p = 0.20$), it was in the adjusted model ($\beta = -0.40$ $p = 0.01$)(Table 2). No significant associations were found between lifetime marijuana use, current heavy alcohol use, or lifetime alcohol use and cognitive function (MOS-HIV CF4 score). Similarly, there were no significant associations between any of the 5 independent variables and MoCA memory score or MoCA attention score (Tables 3 and 4). For illustrative purposes, predicted mean scores for the outcome variables were generated based on zero days of marijuana use in the past 30 days, and 10 days of marijuana use in the past 30 days (the median among marijuana users) using fully adjusted models including current and lifetime marijuana use, current heavy alcohol use, and lifetime alcohol use (kg) as independent variables. The mean MOS-HIV CF4 score for zero days of use was 70.17, while the mean MOS-HIV CF4 score for the median number of days of use was 67.67. The mean MoCA memory scores for those with zero and 10 days of use were 3.22 and 3.18, respectively, and the mean MoCA attention scores were 0.69 and 0.68, respectively.

Interactions between current marijuana and current heavy alcohol use were not statistically significant in any of the models for each measure of cognitive dysfunction ($p = 0.88$ for MOS HIV CF4 score, $p = 0.61$ for MoCA attention score, $p = 0.95$ for MoCA memory score). Interactions between lifetime marijuana use and lifetime alcohol use (kg) were also not significant in any of the models fit for each of the three measure of cognitive dysfunction ($p = 0.82$ for MOS HIV CF4 score, $p = 0.59$ for MoCA attention score, $p = 0.82$ for MoCA memory score). Similar results as those shown above in Tables 2–4 were found in the models in which we replaced lifetime alcohol use measured in kg with number of heavy

drinking years as detailed in the Appendix. A significant, negative association was found between current marijuana use and the MOS-HIV CF4 score ($\beta = -0.36$, $p = 0.01$).

DISCUSSION

We examined the effects of marijuana and alcohol use on cognitive function in a cohort of 215 adults with HIV infection and substance use disorder (current dependence or ever injection drug use). Regression analyses revealed a significant, negative association between current marijuana use and the MOS-HIV CF4 score. No other significant associations were found between lifetime marijuana use, lifetime alcohol use (kg), or duration of heavy alcohol use (years) and any measure of cognitive dysfunction. There were also no interactions found between current marijuana and heavy alcohol use or lifetime marijuana and alcohol use and any measure of cognitive dysfunction. Current heavy alcohol use was associated with improved cognition in one of many statistical analyses uncorrected for multiple comparisons, but because it was not in the hypothesized direction nor are we aware of any mechanisms by which this could be the case, we do not think this association is causal.

Since the MOS-HIV assesses overall functional status and well-being in those with HIV infection, our findings suggest that current marijuana use may contribute to deficits in cognitive function as well as overall health. For every additional day (in the past 30 days) an individual used marijuana, their MOS-HIV CF4 score decreased by approximately 0.4 points. This may be clinically significant since daily functioning pertaining to real world tasks such as medication adherence is necessary for HIV suppression. A significant, negative association between current marijuana use and cognitive function is consistent with other reports in the literature that acute use of marijuana has negative effects on the cognitive domains of memory, executive function, and attention.[14–16] Ramaekers et al. examined neuropsychological function after participants smoked varying concentrations of THC.[39] They found that acute THC exposure impairs executive function and worsens as THC concentration is increased.[39] In another study of current, heavy marijuana use, Pope et al. found that on zero, one, and seven days after smoking marijuana, memory was impaired in the form of recalling word lists.[19]

The result that current, but not lifetime, marijuana use is associated with cognitive dysfunction is also consistent with the literature in that the effects of marijuana use are diminished or absent after approximately one month of abstinence.[18,19] According to Schreiner and Dunn, residual effects of cannabis subside after 25 days.[40] Similarly, Jager et al. reported that there are no cognitive deficits in marijuana users after one week of abstinence.[18] In the Coronary Artery Risk Development In Young Adults (CARDIA) study Auer et al. gathered lifetime self-report marijuana use data in a cohort followed for over 25 years[41]. A significant association was found between cumulative lifetime exposure to marijuana and worse verbal memory in participants reporting prior marijuana use with no current use in the past 30 days.

It is well documented that marijuana causes deficits in recall.[14,39,42,43] We hypothesized that current and lifetime marijuana use would be significantly associated with the MoCA

memory score since this section of the measure directly tests recall by requiring participants to repeat a list of words directly after hearing them and again five minutes later. No significant association was found. One reason for this, and a potential limitation of our study, may have been that only the MoCA memory and attention subtests were administered, rather than the entire MoCA assessment. The MoCA in its entirety has been validated in HIV-infected populations while individual MoCA subtests have not. The subtests assessing attention and memory individually (and the MOS HIV CF4) may not be sensitive enough to detect mild cognitive dysfunction in PLWH and comorbid substance use and may explain in part why no association was found between the MoCA attention score and current marijuana use. Other studies reporting attentional dysfunction due to acute marijuana use used the MoCA in its entirety as well as more extensive neuropsychological batteries (e.g. the Stroop Test, Wisconsin Card Sorting Test, Symbol Digit Modalities Test) to screen for neurocognitive impairment [15,36] Further, our findings that current marijuana use was not significantly associated with either MoCA score, but was significantly associated with the MOS-HIV CF4 score may be reflective of the MOS-HIV being sensitive to executive function impairment and global cognitive dysfunction in general. Executive function measured using validated neuropsychological assessments (e.g. the Tower of London Task, Iowa Gambling Task, Inspection Time Task) has been shown to be affected by both HIV infection and marijuana use.[6,10,15,39,44]

It is also well documented that exposure to heavy alcohol use over long periods of time can lead to cognitive dysfunction.[23,24] In a review of cognitive function among individuals who use alcohol without alcohol use disorders, Parsons and Nixon suggested that 5–6 standard drinks per occasion on 5–7 days per week over the span of one year or more increases risk for cognitive deficits.[45] These levels of drinking are consistent with heavy drinking as defined in the present study. It is unclear why we did not find any negative, significant associations between current or lifetime alcohol use and cognitive function. One reason may be that that our cohort was exposed to multiple substances as well as HIV infection, and the effect of alcohol was not detectable among such competing risks. However, a recent study examining lifetime history of alcohol use also found no association with cognitive performance among older adults in adjusted analyses, hypothesizing that prior study results finding associations may be due to uncontrolled confounding.[46]

Marijuana use, alcohol use, and HIV infection are known to affect similar brain regions. specifically the basal ganglia and frontal lobes which are involved in executive function. [6,10,14,15,21,47] HIV as well as the cannabinoid-1 (CB1) receptor which binds Δ^9-THC in the brain, are found in highest concentration in the basal ganglia, and increases in inflammation markers in the basal ganglia of individuals with alcohol use disorders have been documented.[6,10,14,47] Hippocampal damage in people with alcohol use disorder, and evidence supporting CB1 receptor induced hippocampal cell death also suggest a synergistic effect of alcohol use and marijuana use on memory function.[14,21] Despite these overlaps, we did not find synergistic effects.

A strength of this study was that we thoroughly evaluated many variables known to influence cognition and added them into the analyses as covariates to adjust for potential confounders.[1,5,42,48,49] Also, the main independent and dependent variables were assessed

using validated instruments, which is another strength of this study. Specifically, self-report cognitive dysfunction measured by the MOS-HIV CF4 has been validated against the Reitan Trail Making Test.[38] The main limitation of this study in addition to possible limitations in the selected outcome measures, is the inability to attribute causality, or a lack thereof, to the tested associations. Although we used validated tools, self-report substance use measures are subject to recall and social desirability biases and inaccuracy. Those with cognitive dysfunction reporting less lifetime substance use could bias analyses towards the null hypothesis. It is also possible that the one significant association we identified is the result of Type I error (multiple testing), though there was only one test of the association between current use and overall cognitive function. Another limitation of this study is that our results may not apply to people with severe enough cognitive impairment that they would have been excluded from the study or may not have enrolled in the first place, potentially limiting the external validity of these findings. Although we did not have any screening tests to exclude people based on cognitive function, one individual was excluded by the research interviewer because they were not “mentally fit.”

In summary, current marijuana use appears to be associated with lower self-reported cognitive function. We did not detect significant associations between lifetime marijuana use and any measure of cognitive dysfunction, nor did we detect significant associations between lifetime alcohol use and any measure of cognitive dysfunction. No interactions were detected between current marijuana use and heavy alcohol use and cognitive function or between lifetime marijuana use and alcohol use and cognitive function. Future research should utilize measures specific to HIV infected people as well as measures sensitive to more subtle forms of cognitive dysfunction and possibly a wider range of cognitive domains in addition to memory and attention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors would like to thank the Boston ARCH Cohort study participants for the time and effort they have dedicated to this research. We also wish to thank all staff at Boston University and Boston Medical Center who supported this project. Specifically, we want to acknowledge Margo Godersky, Kate Haworth, Keshia Toussaint and Laura Vercammen for their work in recruitment, data collection and participant retention; and Seville Meli for her leadership and assistance with study management.

FUNDING

Funding for this study was provided through a collaborative agreement with the National Institute of Alcohol Abuse and Alcoholism (NIAAA), National Institutes of Health (grant numbers: U01AA020784, U24AA020778, U24AA020779). NIAAA was not involved in the collection, analysis or interpretation of data and was also not involved in writing this manuscript or the decision to submit it for publication. Funding was also provided from the National Center for Advancing Translational Science, National Institutes of Health to the Boston University Clinical and Translation Science Institute (grant number UL1TR001430) which supplemented the cost of study visits conducted at the Boston University General Clinical Research Unit. The National Center for Advancing Translational Science was not involved in the collection, analysis or interpretation of data and was also not involved in writing this manuscript or the decision to submit it for publication.

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Table 1

Characteristics of 215 adults with HIV infection and substance dependence or injection drug use

Characteristic	
Age *Mean±SD*	48.6±9.5
Male *n*(%)	140(65)
White *n*(%)	43(20)
Completed high school *n*(%)	143(66)
Primary language English *n*(%)	184(86)
Employed *n*(%)	37(17)
Depressive symptoms[a] *n*(%)	60(28)
Anxiety symptoms[b] *n*(%)	96(45)
Duration of HIV infection (years)[c] *Mean±SD*	16±8.4
HIV viral load (log copies/mL) *Mean±SD*	1.6±1.7
CD4 cell count <200 cells/mL *n*(%)	22(1)
Currently on antiretroviral medication *n*(%)	187(87)
Charlson comorbidity index score *Mean±SD*	2.9±2.5
Hepatitis C virus infection (ever)[d, e] *n*(%)	126(59)
Current marijuana use (days in past 30) *Mean±SD*	6.5±10.5
Current heavy alcohol use (days in past 30) *Mean±SD*	4.8±8.1
Lifetime marijuana use (years)[f] *Mean±SD*	9.8±11.8
Lifetime alcohol use (kg) *Mean±SD*	720.7±1,079.8
Duration of heavy alcohol use (years) *Mean±SD*	6.4±9.5
Cocaine use (any, past 30 days) *n(%)*	66 (31%)
Lifetime cocaine use (years)[g] *Mean±SD*	9.3±9.8
Opioid use (any illicit, past 30 days) *n(%)*	55 (26%)
Current opioid prescription (yes or no) *n(%)*	84 (39%)

HIV=Human immunodeficiency virus, SD=standard deviation, kg=kilogram

[a]Depressive symptoms defined as a score of ≥ 3 on the 2-item Patient Health Questionnaire (PHQ-2)(n=214)

[b]Anxiety symptoms defined as a score of ≥ 8 on the Overall Anxiety Severity and Impairment Scale (OASIS)

[c]n=213

[d]n=213

[e]Defined as detectable antibody or viral RNA

[f]n=214

[g]Number of years cocaine was used ≥ 3 times per week or any 2 day binges in one week occurred

Table 2

Associations between current marijuana and heavy alcohol use, lifetime marijuana and alcohol use, and cognitive function

	Cognitive function MOS-HIV CF4[a] Score Unadjusted model		Cognitive function MOS-HIV CF4 Score Adjusted[b] model	
Independent variable	**β CI (95%)**	**p**	**β CI (95%)**	**p**
Current marijuana use (days in past 30)	−0.2063 (−0.5059, 0.0933)	0.18	**−0.3573 (−0.6426, −0.0721)**	**0.01**
Current heavy alcohol use (days in past 30)	0.1391 (−0.2035, 0.4817)	0.42	0.3177 (−0.0063, 0.6417)	0.05
Lifetime marijuana use (years)	0.1142 (−0.1488, 0.3772)	0.39	0.0331 (−0.2197, 0.2859)	0.80
Lifetime alcohol use (kg)	−0.0008 (−0.0033, 0.0018)	0.54	−0.0008 (−0.0032, 0.0016)	0.51

[a] MOS-HIV CF4=Medical Outcomes Study HIV Health Survey 4-item cognitive function

[b] Adjusted for age, sex, race, education, employment, primary language, depressive symptoms, anxiety symptoms, comorbidities, antiretroviral therapy, hepatitis C virus infection (ever), duration of HIV infection (years), HIV viral load (log copies/mL), CD4 cell count, lifetime and recent cocaine use, and recent illicit or prescribed opioid use

CI=confidence interval, kg=kilogram

Table 3

Associations between current marijuana and heavy alcohol use, lifetime marijuana and alcohol use, and memory

	MoCA[a] memory score Unadjusted model		MoCA memory score Adjusted[b] model	
Independent variable	**β CI (95%)**	**p**	**β CI (95%)**	**p**
Current marijuana use (days in past 30)	0.0026 (−0.0184, 0.0235))	0.81	−0.0047 (−0.0268, 0.0174)	0.67
Current heavy alcohol use (days in past 30)	−0.0169 (−0.0409, 0.0071)	0.17	−0.0118 (−0.0370, 0.0133)	0.35
Lifetime marijuana use (years)	0.0112 (−0.0072, 0.0296)	0.23	0.0129 (−0.0067, 0.0325)	0.19
Lifetime alcohol use (kg)	0.0001 (−0.0001, 0.0003)	0.37	0.0001 (−0.0001, 0.0003)	0.25

[a]MoCA=Montreal Cognitive Assessment

[b]Adjusted for age, sex, race, education, employment, primary language, depressive symptoms, anxiety symptoms, comorbidities, antiretroviral therapy, hepatitis C virus infection (ever), duration of HIV infection (years), HIV viral load (log copies/mL), CD4 cell count, lifetime and recent cocaine use, and recent illicit or prescribed opioid use

CI=confidence interval, kg=kilogram

Table 4

Associations between current marijuana and heavy alcohol use, lifetime marijuana and alcohol use, and attention

	MoCA[a] attention score Unadjusted model		MoCA attention score Adjusted[b] model	
Independent variable	**Odds Ratio CI (95%)**	**p**	**Odds Ratio CI (95%)**	**p**
Current marijuana use (days in past 30)	1.00 (0.97, 1.05)	0.95	1.00 (0.96, 1.06)	0.87
Current heavy alcohol use (days in past 30)	1.01 (0.97, 1.04)	0.68	1.01 (0.96, 1.05)	0.67
Lifetime marijuana use (years)	1.02 (0.99, 1.05)	0.32	1.02 (0.98, 1.06)	0.31
Lifetime alcohol use (kg)	1.00 (1.00, 1.00)	0.62	1.00 (1.00, 1.00)	0.71

[a]MoCA=Montreal Cognitive Assessment

[b]Adjusted for age, sex, race, education, employment, primary language, depressive symptoms, anxiety symptoms, comorbidities, antiretroviral therapy, hepatitis C virus infection (ever), duration of HIV infection (years), HIV viral load (log copies/mL), CD4 cell count, lifetime and recent cocaine use, and recent illicit or prescribed opioid use

CI=confidence interval, kg=kilogram