Published in final edited form as:

Psychiatry Res. 2012 September 30; 199(2): 102–110. doi:10.1016/j.psychres.2012.05.009.

Selective neurocognitive deficits and poor life functioning are associated with significant depressive symptoms in alcoholism-HIV infection comorbidity

Stephanie A. Sassoon¹, Margaret J. Rosenbloom^{1,2}, Rosemary Fama^{1,2}, Edith V. Sullivan², and Adolf Pfefferbaum^{1,2}

¹Neuroscience Program, SRI International, Menlo Park, CA

²Department of Psychiatry & Behavioral Sciences, Stanford University School of Medicine, Stanford, CA

Abstract

Alcoholism, HIV, and depressive symptoms frequently co-occur and are associated with impairment in cognition and life function. We administered the Beck Depression Inventory-II (BDI-II), measures of life function, and neurocognitive tests to 67 alcoholics, 56 HIV+ patients, 63 HIV+ alcoholics, and 64 controls to examine whether current depressive symptom level (significant, BDI-II ≥ 14 vs. minimal, BDI-II < 14) was associated with poorer cognitive or psychosocial function in alcoholism-HIV comorbidity. Participants with significant depressive symptoms demonstrated slower manual motor speed and poorer visuospatial memory than those with minimal depressive symptoms. HIV patients with depressive symptoms showed impaired manual motor speed. Alcoholics with depressive symptoms showed impaired visuospatial memory. HIV+ alcoholics with depressive symptoms reported the poorest quality of life; alcoholics with depressive symptoms, irrespective of HIV status, had poorest life functioning. Thus, significant depressive symptoms were associated with poorer selective cognitive and life functioning in alcoholism and in HIV infection, even though depressive symptoms had neither synergistic nor additive effects on cognition in alcoholism-HIV comorbidity. The results suggest the relevance of assessing and treating current depressive symptoms to reduce cognitive compromise and functional disability in HIV infection, alcoholism, and their comorbidity.

Keywords

Alcoholism; HIV infection; depressive symptoms; life function; neurocognitive function; comorbidity

1 Introduction

One of the greatest challenges in developing effective treatment for individuals with HIV infection is distinguishing the effects of the disease from the effects of common comorbidities such as alcoholism and depression (Bing et al., 2001, Havlik et al., 2011).

© 2012 Elsevier Ireland Ltd. All rights reserved.

Corresponding Author: Adolf Pfefferbaum, M.D., Neuroscience Program, BN168 SRI International 333 Ravenswood Ave Menlo Park, CA 94025, Phone: (650) 859-2927, FAX: (650) 859-2743, dolf@synapse.sri.com.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Individuals with any one of these conditions (HIV infection, alcoholism, or depression) carry a liability for cognitive impairments, and observed cognitive deficit patterns likely reflect neural pathways affected in each condition. Whether the trimorbidity of HIV infection, alcoholism and depressive symptoms leads to synergistic deficits in any particular cognitive domain remains largely unexplored.

Alcoholism is highly prevalent in the HIV-infected community (Conigliaro et al., 2006, Galvan et al., 2002, Petry, 1999). Not only is excessive alcohol use a significant factor in the acquisition of HIV infection through its role in facilitating risky behaviors (Fritz et al., 2010, Kalichman et al., 2007), but heavy alcohol use can exacerbate susceptibility to HIV infection, induce change in mood (Kelley and Dantzer, 2011), and may impair adherence to antiretroviral medication (Hendershot et al., 2009). Cognitive processes found to be disproportionately affected with chronic, heavy alcoholism and HIV infection include motor and visuomotor speed and coordination (Fama et al., 2007, Rothlind et al., 2005), sustained attention and associative learning (Sassoon et al., 2007), remote semantic memory (Fama et al., 2011), and immediate episodic memory for verbal and visual material (Fama et al., 2009).

Affective disorders, particularly depression, are highly prevalent in individuals with either HIV infection or alcoholism alone (Sullivan et al., 2011, Sullivan et al., 2008). Depression spectrum disorders are the most common psychiatric comorbidity in HIV infection (Dube et al., 2005), with upwards of one-third of HIV-infected individuals having co-occurring mood disorders or significant depressive symptoms (Bing et al., 2001, Morrison et al., 2002). Over the course of their illness, individuals with an alcohol use disorder (AUD) are almost twice as likely as those without an AUD to experience depression (Fergusson et al., 2009).

While cognitive impairment is widely documented in advanced HIV infection, it is increasingly recognized that asymptomatic HIV-positive individuals may also show mild cognitive impairment (Heaton et al., 2011, Maki and Martin-Thormeyer, 2009). Disruption of frontostriatal circuits and other networks depending on these circuits have been implicated in HIV (Heaton et al., 1995, Woods et al., 2009). Some studies suggest that executive and motor skills and information processing speed show the greatest decline from early to later disease stages (Reger et al., 2002) with psychomotor slowing a significant predictor of progression to AIDS, dementia, and death (Sacktor et al., 1996). Impairment in episodic memory for verbal and visual material is also highly prevalent in HIV and also increases with disease progression (Heaton et al., 1995, Martin et al., 2007, Woods et al., 2009).

Long-term, heavy alcohol consumption has deleterious effects on frontal-parietal cortical systems and frontocerebellar circuits, with deficits consistently observed in visuospatial construction, memory, executive functions, and motor abilities including gait and balance (Oscar-Berman and Marinkovic, 2007, Parsons and Nixon, 1998, Smith and Fein, 2011, Sullivan et al., 2002, Sullivan et al., 2000). Some deficits, particularly in visuospatial functioning, mental flexibility, abstract reasoning, short-term memory, and balance may persist even after significant abstinence (for a review, see Fein et al., 1990, Sullivan et al., 2010).

Depressive symptoms have been associated with verbal and visual memory impairments (Austin et al., 2001), executive deficits (e.g., set shifting and verbal fluency), and motor slowing (Beats *et al.*, 1996, Channon and Green, 1999, Purcell *et al.*, 1997). While some studies of asymptomatic HIV positive individuals failed to find a significant effect of depression on neurocognitive function, e.g., (Bornstein *et al.*, 1993), others found that depressive symptoms were related to poorer performance on measures of attention and

executive skills and slower information processing (Baldewicz et al., 2004). Furthermore, depressive symptoms and impairment in executive functioning, learning, attention, working memory, and verbal abilities in persons with HIV predicted failures in everyday functioning (Heaton et al., 2004).

In the social functioning arena, alcoholism and depressive symptoms are associated with greater suicidality (Conner et al., 2007) and greater social and occupational functional impairment (Cornelius et al., 1995). Furthermore, depressive symptoms and poor neurocognitive functioning are predictors of relapse in alcoholics (Parsons, 1998). Likewise, HIV-infected individuals with significant depressive symptoms have poorer adherence to medication (Gonzalez et al., 2011), poorer life functioning (Rabkin, 2008), increased progression to AIDS (Bouhnik et al., 2005), and increased HIV-related mortality (Cook et al., 2004). Patients with alcohol and HIV comorbidity have poorer health-related quality of life than those with either disease alone, with depression symptomatology being the strongest predictor of quality of life (Rosenbloom et al., 2007).

To date, few studies have explicitly addressed the increasingly common disease “trimorbidity” of HIV infection, alcoholism, and depressive symptoms even though HIV-infected patients with this combined disease burden who received no treatment for psychiatric symptoms or substance problems carry the highest risk of mortality (DeLorenze et al., 2010).

The current study used the Beck Depression Inventory-II (BDI-II), a comprehensive questionnaire commonly used in clinical and research settings, to categorize patients as having significant or absent/minimal depressive symptoms (Beck et al., 1996, Coleman et al., 2012, Dutton et al., 2004). We explicitly focused on current depressive symptomatology but also documented whether patients met lifetime DSM-IV criteria for a unipolar mood disorder. We examined whether a significant level of current depressive symptoms, regardless of prior diagnosis of mood disorder, place a greater burden on cognition, life functioning in those with both HIV and alcoholism than in those with either disease alone. We also examined whether a significant level of depressive symptoms affects HIV disease severity as measured by CD4 counts and viral load in HIV positive patients and lifetime alcohol use and length of sobriety in patients with alcohol dependence. Specifically, we tested the hypotheses that, irrespective of DSM-IV diagnosis of past history of a unipolar mood disorder, 1) participants with either HIV infection and current significant depressive symptoms, or alcoholism and current significant depressive symptoms, would show poorer cognitive function and life function, and greater disease severity than their counterparts with minimal depressive symptoms; 2) participants with HIV-alcoholism comorbidity and current significant depressive symptoms (trimorbid patients) would show poorer cognitive function and life function, and greater disease severity than either single disease group with depressive symptoms or than the HIV-alcoholism comorbid participants with absent/minimal depressive symptoms.

2. Methods

2.1 Participants

Data reported here were from initial visits of participants in a longitudinal study investigating CNS sequelae of alcoholism and HIV comorbidity and also from participants in a cross-sectional neuroimaging study examining the effects of alcoholism and aging on brain structure and function. Participants were recruited from the greater San Francisco Bay area between the years 2002 to 2010 through referrals from community treatment centers, clinics, hospitals, flyers, or through word of mouth. Participants ($n = 186$) were grouped in a 2 depressive symptom level (BDI-II score ≥ 14 or < 14) $\times$ 3 disease status (HIV infection,

alcoholism, alcoholism-HIV comorbidity) factorial design: 24 alcohol-dependent HIV-positive participants with significant depressive symptoms (SDS+ALC+HIV), 39 ALC+HIV with minimal depressive symptoms (MDS+ALC+HIV), 19 ALC with significant depressive symptoms (SDS+ALC), 48 ALC with minimal depressive symptoms (MDS+ALC), 22 HIV with significant depressive symptoms (SDS+HIV), and 34 HIV with minimal depressive symptoms (MDS+HIV). In addition to the patient groups, a healthy “normal” comparison (NC) group of 64 individuals with neither HIV, significant depressive symptoms, nor heavy drinking in their lifetime participated in this study.

2.2 Procedure

Studies were reviewed and approved by the institutional review boards at SRI International, Stanford University, and Santa Clara Valley Medical Center. All participants provided written informed consent after receiving a detailed explanation of the study procedures and received a modest stipend for study participation.

Participants were screened to exclude anyone with a history of bipolar disorder or schizophrenia, a medical illness or trauma potentially affecting the central nervous system, loss of consciousness greater than 30 minutes, neurological disease not related to HIV infection or alcohol use, or factors precluding MR scanning. Those who met initial criteria were invited to our laboratory for a more detailed medical and psychiatric assessment. All participants provided a blood sample to confirm HIV and Hepatitis C status. CD4 T-lymphocyte count and plasma viral load were obtained for HIV-positive participants. Blood draws for laboratory tests typically occurred within a month of neuropsychological testing.

To assess psychiatric history and to characterize lifetime alcohol use, experienced clinicians administered the Structured Clinical Interview for DSM-IV (SCID) (First et al., 1998) and a lifetime alcohol use interview (Pfefferbaum et al., 1992, Skinner, 1982, Skinner and Sheu, 1982) to all participants. Participants included in the high-alcohol-consuming groups met DSM-IV criteria for an alcohol use disorder (AUD): either alcohol dependence ($n = 121$) or abuse ($n = 9$) within the past 3 years, did not have any drug abuse/dependence more recently than alcohol dependence, and did not have drug abuse/dependence within the prior three months. In this sample, median for reported sobriety from drugs was > 70 weeks for all groups. Healthy comparison participants had no history of any Axis I disorder.

Current depression symptomatology was assessed using the Beck Depression Inventory, Second Edition (BDI-II) (Beck et al., 1996). This 21-item self-report instrument measures the severity of depressive symptoms. Each item is rated on a scale of 0 to 3. Scores of 0 – 13 are considered indicative of no to minimal depressive symptoms, 14 – 19 mild, 20 – 28 moderate, and 29 – 63 severe depressive symptoms. A cutoff score of 14 or greater is often used to indicate clinically significant depressive symptoms (Beck et al., 1996, Coleman et al., 2012, Dutton et al., 2004), and this cut-off score was used here to differentiate those with and without significant depressive symptoms. The diagnostic interview established that 25% of HIV, 36% of ALC, and 48% of ALC+HIV met formal criteria for a history of lifetime DSM-IV unipolar mood disorder, of whom $< 12\%$ in each group met criteria for a current episode.

Overall level of functioning in the past month was rated by clinicians using the Global Assessment of Functioning scale (Endicott et al., 1976). Scores range from 1–10 (reflecting “persistent danger of hurting self or others” or “gravely disabled”) to 90–100 (reflecting “superior functioning in a wide range of activities”). A score of 50 or below defines “serious mental disorder or serious impairment in functioning” (Kessler et al., 2005). As part of the SCID diagnostic interview, clinicians assessed and categorized the type of current psychosocial and environmental stressors reported by participants as problematic in their

lives (e.g., dissolution of or discord in a relationship, inadequate social support, financial or legal problems, unemployment in the cases where employment was expected, i.e., not by choice or because of documented disability). Participants could have stressors in as many as 10 categories. Quality of life was assessed with the Brief Health and Functioning Questionnaire (Bozzette et al., 1995), which includes a 21-item version of the Medical Outcome Survey Health-Related Quality Of Life instrument, with which participants rate how well they functioned in the past 4 weeks. Responses to each of the 21 items were standardized to a 0–100 scale, and a mean summary score was computed for all items.

Participants completed a neuropsychological test battery of tests previously shown to be especially sensitive to cognitive impairment in depression, HIV infection, and alcoholism. A subset of these participants ($n = 218$) completed the National Adult Reading Test (Nelson, 1982) as an estimator of premorbid IQ.

2.3 Neuropsychological Measures

Fine Finger Movement (Corkin et al., 1986) measured simple motor speed and manual dexterity represented by the summed total number of turns of a knurled dowel made by each hand separately in 30 seconds. A combined mean of each hand separately was obtained.

Alternated Finger Tapping (Reitan and Davison, 1974) required participants to depress a telegraph key with alternating forefingers. This test measure coordinated manual fine motor skills. The average number of taps from three 15-second trials was obtained.

The *Grooved Pegboard Test* (Klove, 1963) assessed manual dexterity, hand-eye coordination, and attention by measuring speed in inserting pegs with a key along one side by rotating the pegs to fit holes in a grooved board. A combined mean of time to complete the board by each hand separately was obtained.

Color Trails-1 (Maj et al., 1993) assessed psychomotor speed, attention, sequencing and visual scanning efficiency; participants connected numbered circles sequentially from 1 to 25. *Color Trails-2* required participants to connect numbered circles in order from 1 to 25 while alternating between two colors (yellow and pink), which additionally assessed set-shifting ability. Color Trails was completed by 161 of the 250 participants because of a protocol change.

The *Controlled Oral Word Association Test (FAS Test)* (Benton and Hamsher, 1976) measured verbal fluency (i.e., a measure of executive functioning). Participants were given 60 seconds to list aloud words beginning with F, then A, and then S. The total number of words produced from each of the three trials was calculated.

The *Rey-Osterrieth Complex Figure (ROCF) Test* (Osterrieth and Rey, 1944, Rey, 1942) assessed visuospatial construction and memory ability. Subjects were asked to reproduce a complex line drawing (*Copy*). Incidental recall of the figure was tested immediately after copy (*Immediate Recall*). Drawing accuracy was scored on a 36-point scale (Meyers and Meyers, 1995, Taylor, 1969). The immediate recall score was expressed as a ratio of the drawing copy score to differentiate the memory component from the visuospatial component of this task.

Demographic characteristics of the 250 participants are presented in Table 1. The three disease groups (ALC, HIV, and ALC+HIV) were comparable in all demographics except ethnicity. ALC had significantly more Caucasian participants than the other groups [$\chi^2(3) = 10.8, p = 0.01$]. The healthy comparison sample was significantly younger than ALC, and had more years of education, higher premorbid IQs, and lower scores on the BDI-II than

each of the three disease groups. BDI-II scores were statistically similar across disease groups, and mean scores among all 4 groups fell within the no to minimal depression category.

2.4 Statistical Analysis

Demographic indices among groups were compared using analyses of variance (ANOVAs) and chi-square tests. A Kruskal-Wallis test compared lifetime alcohol consumption among the groups. Parametric t-tests and nonparametric Mann-Whitney U tests compared approximate age of HIV onset, CD4 cell count, and plasma viral load in the HIV-positive groups, and approximate age of alcoholism onset and number of months of alcoholism remission in the high-alcohol groups. Spearman correlations tested associations between BDI-II total score and dependent variables.

Main study hypotheses regarding group differences in cognitive performance and life functioning were tested with 2X3 analyses of covariance (ANCOVAs), with significant BDI-II depressive symptoms (yes/no) and disease group (ALC, HIV, ALC+HIV) as factors, followed by Bonferroni post hoc tests corrected for multiple comparisons. In the healthy comparison sample, age was associated with tests involving manual motor ability (Fine Finger Movement, Alternated Finger Tapping, and Grooved Pegboard Test) and was thus used as a covariate in these analyses while education correlated with visuospatial, sequencing, and verbal fluency tasks (Rey-Osterrieth Complex Figure Test, Color Trails 1 & 2, and FAS Test) and thus was a covariate in these corresponding analyses. All statistical analyses were conducted with PASW Statistics 18 and statistical significance was set at $p < .05$.

Exploratory analyses of the contribution of antiviral medication and Hepatitis C seropositivity were conducted using t-tests comparing patients in each group with and without the condition.

3. Results

3.1 Demographic characteristics of disease groups by BDI-II symptom level

Demographic characteristics of disease groups, divided by a BDI-II cutoff score of 14 (Beck et al., 1996, Dutton et al., 2004) are shown in Table 2.

The resulting subgroups were demographically similar and the proportion of participants with significant BDI-II depressive symptoms was similar across disease groups (HIV = 39%, ALC = 28%, ALC+HIV = 38%).

It has been suggested that the BDI may artificially inflate depressive symptoms in HIV-infected individuals because somatic symptoms, such as fatigue, sleep difficulties and appetite disturbance, are also commonly reported medical symptoms of HIV infection or side effects of pharmacological treatment for HIV infection (Kalichman et al., 2000). To examine this possible bias, we excluded 8 somatic symptoms (agitation, loss of energy, sleep disturbance, irritability, appetite disturbance, concentration difficulty, fatigue, and loss of sexual interest; (Buckley et al., 2001), and reclassified participants based on a proportional cut off of .9. This somatic-symptom-free classification assigned >90% of individuals to the same depression symptom groups as the full BDI-II score.

3.2 Depressive symptoms and cognitive functioning in HIV, alcoholism, and their comorbidity

ANCOVAs tested the effects of significant BDI-II depressive symptoms (≥ 14 vs <14) and disease (HIV, alcoholism, and their comorbidity) on cognitive function. Age was a covariate

in tests of manual motor ability (Fine Finger Movement, Alternated Finger Tapping, and Grooved Pegboard Test); education was a covariate in visuospatial, sequencing, and verbal fluency tasks (Rey-Osterrieth Complex Figure Test [ROCF], Color Trails 1 & 2, and FAS Test). Mean raw scores and standard errors on individual cognitive tests for disease group separated by BDI-II depressive symptom level are presented in the Figure.

Level of depressive symptoms yielded significant main effects for ROCF immediate recall and Fine Finger Movement but no interaction with diagnostic group. As a whole, patients with significant depressive symptoms performed worse on the Fine Finger Movement test [$F(1, 176) = 4.31, p = 0.039$] and ROCF immediate recall [$F(1, 179) = 4.69, p = 0.046$] than their counterparts with minimal depressive symptoms, supporting our first hypothesis with regard to these tests. On the Fine Finger Movement test, both HIV-infected groups with significant depressive symptoms were particularly impaired relative to the healthy comparison group, [SDS+HIV: $F(1, 83) = 8.03, p = 0.006$; and SDS+ALC+HIV: $F(1, 85) = 10.85, p = 0.001$]. On the ROCF immediate recall, both alcoholic groups with significant depressive symptoms showed impairment relative to the healthy comparison group, [SDS+ALC: $F(1, 80) = 4.71, p = 0.033$; and SDS+ALC+HIV: $F(1, 85) = 6.59, p = 0.012$]. In contrast to these significant effects, revealed when depression is treated as a categorical variable, the continuous BDI-II score was not significantly associated with any cognitive test scores in any disease group, irrespective of presence of a past lifetime history of unipolar mood disorder.

Diagnostic group factor yielded significant main effects for ROCF immediate recall and the FAS test. On ROCF immediate recall, ALC+HIV patients performed significantly worse than HIV ($p = 0.05$), with ALC falling between the 2 HIV groups [$F(2, 179) = 3.09, p = 0.048$]. Furthermore, ALC+HIV [$t(125) = 3.89, p < 0.001$] and ALC [$t(129) = 2.49, p < 0.001$], but not HIV, were impaired relative to the healthy comparison group. On the FAS test, ALC ($p = 0.007$) and ALC+HIV ($p = 0.023$) produced significantly more words than HIV [$F(2, 177) = 5.54, p = 0.005$], but not significantly more than healthy comparison participants.

To test our hypothesis that SDS+ALC+HIV patients would show poorer cognitive function than either SDS+HIV or SDS+ALC participants, we used ANCOVAs, controlling for age and education as detailed above, to compare performance of the subgroups with significant depressive symptoms only. Group differences were found only on the FAS test [$F(2, 60) = 3.65, p = 0.032$], where SDS+HIV produced significantly fewer words than SDS+ALC ($p = 0.030$), with SDS+ALC+HIV falling in between. Thus SDS+ALC+HIV participants did not perform significantly worse on any cognitive tests than their MDS counterparts.

3.3 Hepatitis C and medication status effects on cognitive functioning in HIV, alcoholism, and their comorbidity

We conducted exploratory analyses to test whether Hepatitis C seropositivity or use of HAART medication contributed to cognitive functioning in each disease group. Each variable was assessed by comparing Fine Finger Movement and ROCF immediate recall performance in patients with and without the condition. The incidence of Hepatitis C ranged from 28% to 39% across the three disease groups, and was comparable in those with and without significant depressive symptoms. While Fine Finger Movement performance was comparable for patients with and without Hepatitis C infection in each disease group (all p 's $> .05$), ROCF immediate recall performance was consistently poorer in those with Hepatitis C infection than those without, regardless of primary diagnosis (ALC: $p = 0.03$; HIV: $p = 0.001$; ALC+HIV: $p = .05$).

The majority of all HIV infected patients were on HAART medication, ranging from 63% to 77% and medication use was comparable in those with and without significant depressive symptoms. There was no difference in Fine Finger Movement or ROCF immediate recall performance between those on or not on HAART medication in either HIV group (all p values $> .20$).

3.4 Depressive symptoms, disease severity, and life functioning in HIV infection, alcoholism, and their comorbidity

The relations among disease severity, life stressors, clinician-rated assessment of life functioning, self-reported quality of life, and depression levels were examined across disease group to test the hypothesis that SDS+HIV or SDS+ALC would manifest greater disease severity and poorer life functioning than their MDS counterparts, and that SDS+ALC+HIV would have greatest disease severity and poorest life functioning of all groups.

SDS+HIV and SDS+ALC+HIV participants had similar CD4 cell counts, viral loads, approximate age of HIV onset to their MDS counterparts (CD4 cell count means ranged from 423 – 529 cells/mm³; log viral load means ranged from 2.9 to 3.1 copies/ml; age of HIV onset means ranged from 32.2 to 35.9 years). The groups were also similar in AIDS status (18 – 39%). Likewise, SDS+ALC and SDS+ALC+HIV had similar alcohol consumption history to their MDS counterparts; mean age of reported onset of alcoholism ranged from age 22 to 26, mean lifetime quantity of alcohol consumed ranged from 806 to 1169 kg, and mean length of sobriety ranged from 8 to 24 weeks. Furthermore, BDI-II total score was not significantly correlated with any HIV-related or alcohol-related variable above except for length of sobriety in ALC ($r = -.27$, $p = 0.025$).

Participants with significant depressive symptoms were more likely (49%) to meet DSM-IV lifetime criteria for unipolar mood disorder than those without significant depressive symptom (30%) [$\chi^2(1) = 6.92$, $p = 0.009$]. Post hoc analysis revealed that this effect was attributable to ALC and ALC+HIV groups (see Table 3). Patients with current significant depressive symptoms were more likely to be on antidepressant medication than those with minimal depressive symptoms, irrespective of disease group [$\chi^2(1) = 14.25$, $p < 0.001$]. A past history of drug dependence/abuse was not associated with current significant depressive symptoms but was associated with a diagnosis of alcoholism, with or without comorbid HIV: SDS+ALC (74%), SDS+ALC+HIV (79%), SDS+HIV (32%) [$\chi^2(2) = 12.55$, $p = 0.002$]; MDS+ALC (56%), MDS+HIV+ALC (87%), MDS+HIV (38%) [$\chi^2(1) = 19.12$, $p < 0.001$].

Participants with significant depressive symptoms reported more psychosocial stressors than those without [$F(1, 173) = 3.79$, $p = 0.05$]. Participants with ALC reported more psychosocial stressors than those with HIV, while ALC+HIV fell in between [$F(2, 173) = 4.35$, $p = 0.01$]; however, the disease group by depressive symptom level interaction was not significant. Clinician-rated Global Assessment of Functioning (GAF) scores were significantly lower in participants with depressive symptoms than those without [$F(1, 179) = 39.19$, $p < 0.001$]. Participants with ALC and ALC+HIV had poorer functioning than HIV [$F(2, 179) = 21.21$, $p < 0.001$]. The disease-by-depressive symptom level interaction, however, was not significant. By contrast, self-rated quality of life revealed a significant interaction between level of depressive symptoms and disease group [$F(2, 162) = 3.44$, $p = 0.034$]. Those with significant depressive symptoms reported significantly worse quality of life than those with minimal depressive symptoms [$F(2, 162) = 78.68$, $p < 0.001$], and those with significant depressive symptoms and HIV infection (SDS+HIV and SDS+ALC+HIV) reported substantially poorer quality of life than SDS+ALC [$F(2, 162) = 14.30$, $p < 0.001$].

4. Discussion

This study examined the association effect of current depressive symptomatology in patients with alcoholism alone, HIV infection alone, or both diseases combined on neurocognitive and life functioning. Current significant depressive symptoms were reported in 28% of patients with alcoholism, 39% of patients with HIV infection, and 38% of patients with both disorders. Of these, 53% of ALC, 32% of HIV, and 63% of ALC+HIV also met DSM-IV criteria for a unipolar mood disorder at some point in their lifetime. These findings are consistent with previous reports of prominent depressive symptoms and disorders in individuals with alcoholism or HIV infection (Bing et al., 2001, Dube et al., 2005, Fergusson et al., 2009, Morrison et al., 2002, Sullivan et al., 2005), and extend these findings by documenting prominent current depressive symptoms with cognitive and motor impairment in alcoholism-HIV comorbidity. Individuals comorbid for alcoholism and HIV infection, however, did not have a higher incidence of current significant depressive symptoms or lifetime unipolar mood disorders than individuals with alcoholism or HIV infection alone. Furthermore and non-supportive of our hypothesis, this “triple hit” was not significantly associated with more severe cognitive deficits than the “double hit” of either alcoholism or HIV infection and significant depressive symptoms. Nevertheless, a compounded effect of the “triple hit” was seen in quality of life.

Of the cognitive functions assessed, two were affected by depressive symptom levels: manual motor speed and visuospatial memory. HIV patients with significant depressive symptoms, irrespective of presence or absence of alcoholism, demonstrated the greatest impairment in motor speed relative to healthy comparison participants, consistent with known effects of HIV (Heaton et al., 1995) and depressive symptoms (Beats et al., 1996, Channon and Green, 1999, Purcell et al., 1997) on motor speed. By contrast, alcoholics with significant depressive symptoms demonstrated greatest impairment in visuospatial memory relative to healthy comparison participants consistent with known effects of depression (Austin et al., 2001) and alcoholism (Liu et al., 2010) on visuospatial memory. No additional exacerbation of visuospatial memory or motor speed was found with alcoholism, HIV infection, and depressive symptom trimorbidity..

Group differences in cognitive deficits were not related to use of HAART medication. Even though the incidence of Hepatitis C seropositivity was statistically equivalent among the six groups, performance of patients with Hepatitis C was poorer on ROCF immediate recall than those who were Hepatitis C seronegative, consistent with the known effects of Hepatitis C seropositivity on memory (Huckans et al., 2009). The impact of additional diseases, such as Hepatitis C, on the “trimorbidity” of depressive symptoms, HIV infection, and alcoholism clearly warrants investigation with larger samples.

While categorically defined levels of depression using the cut-off score of 14 on the BDI-II identified group differences in performance of selective cognitive tests across the disease groups, continuous BDI-II scores were not associated with cognitive performance in any of the disease groups, regardless of lifetime diagnosis of unipolar mood disorder. The lack of direct correlation between current depression symptom severity and cognitive performance in patients with a lifetime mood disorder diagnosis suggests that it is the state of current mood rather than mood disorder history that affects selective cognitive functions. The present results persisted even after somatic symptoms were removed from the BDI-II total score to minimize potential bias from HIV-related physical symptoms (see Kalichman et al., 2000).

Contrary to our hypothesis, depressive symptoms were not related to disease severity, measured as CD4 and viral load levels in HIV disease severity, or quantitative measures of

alcohol exposure in alcohol dependence. However, depressive symptoms were related to psychosocial variables. As predicted, individuals with significant depressive symptoms reported more life stressors (e.g., interpersonal discord, financial/economic problems, or legal issues), had poorer clinician-rated life functioning, and lower self-rated quality of life than patients with minimal depressive symptoms. While, as predicted, individuals with “trimorbidity” had the poorest overall quality of life, those with alcoholism and depressive symptoms, irrespective of HIV diagnosis, had the poorest clinician-rated life functioning. Our findings extend those of Tozzi and colleagues (Tozzi et al., 2003), who found that cognitive and functional abilities influence quality of life in those with HIV infection, and extend our previous findings of poorer health-related quality of life in alcoholism and HIV-comorbidity than in either single diagnosis (Rosenbloom et al., 2007).

This study does not address several factors that may have contributed to the results reported. These include sex differences and group differences in age, education, and ethnicity. Other studies report that women have greater vulnerabilities to the untoward effects of alcohol (Ceylan-Isik et al., 2010) and alcoholic women show selective cognitive deficits different from men (e.g., working memory) (Liu et al., 2010). HIV-infected women have also shown differing motor and procedural learning patterns of performance from HIV-infected men (Martin et al., 2011). Given the relatively small proportions of women in the HIV groups, sex differences were not addressed. Significant group differences in age, education, and ethnicity could have contributed to effects observed but were minimized by using age or education where appropriate as covariates. Further, our test battery did not encompass the full scope of cognitive domains; clearly, continued study is needed to clarify the specific cognitive domains that are particularly vulnerable to depressive symptoms in alcoholism and HIV infection.

This study focused on the effect of current depressive symptomatology rather than a current or lifetime DSM-IV diagnosis of a unipolar mood disorder. Further, it did not include a comparison group with mood disorder only or address the etiology of depressive symptoms. Among those with alcoholism, higher BDI-II scores were associated with shorter sobriety, suggesting scope for improvement with longer sobriety, but whether symptoms are primarily biologically determined or are environmentally driven (e.g., stressful life events) remains unclear.

Depression symptoms and alcoholism remain underdiagnosed and undertreated in those with HIV infection (Conigliaro et al., 2006, Fritz et al., 2010, Mello et al., 2010), leaving cognitive and life impairments associated with this trimorbid condition unaddressed. In our current sample, the incidence of significant current depressive symptoms, easily assessed with a simple questionnaire such as the BDI-II, in patients with alcohol and HIV comorbidity was high and was associated with impaired motor and visuospatial memory skills. That Hepatitis C infection, also common in patients with either HIV infection (Center for Disease Control And Prevention, 2011) or alcoholism (Lieber, 2001), can produce additional cognitive deficits should alert the clinician to the importance of a thorough medical work-up. As individuals with alcoholism and HIV infection grow older without assessment or treatment for their depressive symptoms, they are at heightened risk of experiencing a declining quality of life and are therefore likely to manifest significant cognitive and functional impairment. This study suggests the relevance of a comprehensive treatment approach that includes assessment and management of depressive symptoms in conjunction with alcoholism and HIV treatment to reduce cognitive compromise and life impairment, prevent further disability associated with the combined diseases, and improve productivity and quality of life.

Acknowledgments

This research was supported by grants from the National Institute on Alcohol Abuse and Alcoholism AA017347, AA005965, and AA017168.

References

- Austin MP, Mitchell P, Goodwin GM. Cognitive deficits in depression: Possible implications for functional neuropathology. *British Journal of Psychiatry*. 2001; 178:200–206. [PubMed: 11230029]
- Baldewicz TT, Leserman J, Silva SG, Petitto JM, Golden RN, Perkins DO, Barroso J, Evans DL. Changes in neuropsychological functioning with progression of HIV-1 infection: Results of an 8-year longitudinal investigation. *AIDS and Behavior*. 2004; 8:345–355. [PubMed: 15475681]
- Beats BC, Sahakian BJ, Levy R. Cognitive performance in tests sensitive to frontal lobe dysfunction in the elderly depressed. *Psychological Medicine*. 1996; 26:591–603. [PubMed: 8733217]
- Beck, AT.; Steer, RA.; Brown, GK. *Manual for the Beck Depression Inventory-II*. Psychological Corporation; San Antonio, TX: 1996.
- Benton, AL.; Hamsher, KD. *Multilingual Aphasia Examination (Manual, Revised 1978)*. University of Iowa; Iowa City: 1976.
- Bing EG, Burnam MA, Longshore D, Fleishman JA, Sherbourne CD, London AS, Turner BJ, Eggan F, Beckman R, Vitiello B, Morton SC, Orlando M, Bozzette SA, Ortiz-Barron L, Shapiro M. Psychiatric disorders and drug use among human immunodeficiency virus-infected adults in the United States. *Archives of General Psychiatry*. 2001; 58:721–728. [PubMed: 11483137]
- Bornstein RA, Pace P, Rosenberger P, Nasrallah HA, Para MF, Whitacre CC, Fass RJ. Depression and neuropsychological performance in asymptomatic HIV infection. *American Journal of Psychiatry*. 1993; 150:922–927. [PubMed: 8494070]
- Bouhnik AD, Preau M, Vincent E, Carrieri MP, Gallais H, Lepeu G, Gastaut JA, Moatti JP, Spire B, Group MS. Depression and clinical progression in HIV-infected drug users treated with highly active antiretroviral therapy. *Antiviral Therapy*. 2005; 10:53–61. [PubMed: 15751763]
- Bozzette SA, Hays RD, Berry SH, Kanouse DE, Wu AW. Derivation and properties of a brief health status assessment instrument for use in HIV disease. *Journal of Acquired Immune Deficiency Syndrome Human Retrovirology*. 1995; 8:253–65.
- Buckley TC, Parker JD, Heggie JA. A psychometric evaluation of the BDI-II in treatment-seeking substance abusers. *Journal of Substance Abuse Treatment*. 2001; 20:197–204. [PubMed: 11516588]
- Center for Disease Control And Prevention. National Center for HIV/AIDS V.H., STD, and TB Prevention. *HIV and Viral Hepatitis*. Washington, DC: 2011.
- Ceylan-Isik AF, McBride SM, Ren J. Sex difference in alcoholism: who is at a greater risk for development of alcoholic complication? *Life Sciences*. 2010; 87:133–8. [PubMed: 20598716]
- Channon S, Green PSS. Executive function in depression: The role of performance strategies in aiding depressed and non-depressed participants. *Journal of Neurology, Neurosurgery, and Psychiatry*. 1999; 66:162–171.
- Coleman SM, Blashill AJ, Gandhi RT, Safren SA, Freudenreich O. Impact of integrated and measurement-based depression care: clinical experience in an HIV clinic. *Psychosomatics*. 2012; 53:51–57. [PubMed: 22221721]
- Conigliaro J, Justice AC, Gordon AJ, Bryant K. Role of alcohol in determining human immunodeficiency virus (HIV)-relevant outcomes: A conceptual model to guide the implementation of evidence-based interventions into practice. *Medical Care*. 2006; 44:S1–6. [PubMed: 16849963]
- Conner KR, Hesselbrock VM, Meldrum SC, Schuckit MA, Bucholz KK, Gamble SA, Wines JD, Kramer J. Transitions to, and correlates of, suicidal ideation, plans, and unplanned and planned suicide attempts among 3,729 men and women with alcohol dependence. *Journal of Studies on Alcohol and Drugs*. 2007; 68:654–662. [PubMed: 17690798]

- Cook JA, Grey D, Burke J, Cohen MH, Gurtman AC, Richardson JL, Wilson TE, Young MA, Hessol NA. Depression symptoms and AIDS-related mortality among a multisite cohort of HIV-positive women. *American Journal of Public Health*. 2004; 94:1133–1140. [PubMed: 15226133]
- Corkin, S.; Growdon, JH.; Sullivan, EV.; Nissen, MJ.; Huff, FJ. Assessing treatment effects from a neuropsychological perspective. In: Poon, L., editor. *Handbook of Clinical Memory Assessment in Older Adults*. Washington DC: American Psychological Association; 1986. p. 156-167.
- Cornelius JR, Salloum IM, Mezzich J, Cornelius MD, Fabrega H, Ehler JG, Ulrich RF, Thase ME, Mann JJ. Disproportionate suicidality in patients with comorbid major depression and alcoholism. *American Journal of Psychiatry*. 1995; 152:358–364. [PubMed: 7864260]
- DeLorenze GN, Satre DD, Quesenberry CP, Tsai A-L, Weisner CM. Mortality after diagnosis of psychiatric disorders and co-occurring substance use disorders among HIV-infected patients. *AIDS Patient Care and STDs*. 2010; 24:705–712. [PubMed: 20969465]
- Dube B, Benton T, Cruess DG, Evans DL. Neuropsychiatric manifestations of HIV infection and AIDS. *Journal of Psychiatry and Neuroscience*. 2005; 30:237–246. [PubMed: 16049567]
- Dutton GR, Grothe KB, Jones GN, Whitehead D, Kendra K, Brantley PJ. Use of the Beck Inventory-II with African-American primary care patients. *General Hospital Psychiatry*. 2004; 26:437–442. [PubMed: 15567209]
- Endicott J, Spitzer RL, Fleiss JL, Cohen J. The global assessment scale. A procedure for measuring overall severity of psychiatric disturbance. *Archives of General Psychiatry*. 1976; 33:766–771. [PubMed: 938196]
- Fama R, Eisen JC, Rosenbloom MJ, Sassoon SA, Kemper CA, Deresinski S, Pfefferbaum A, Sullivan EV. Upper and lower limb motor impairments in alcoholism, HIV infection, and their comorbidity. *Alcoholism: Clinical and Experimental Research*. 2007; 31:1038–44.
- Fama R, Rosenbloom MJ, Nichols BN, Pfefferbaum A, Sullivan EV. Working and episodic memory in HIV infection, alcoholism, and their comorbidity: Baseline and 1-year follow-up examinations. *Alcoholism Clinical and Experimental Research*. 2009; 33:1815–1824.
- Fama R, Rosenbloom MJ, Sassoon SA, Thompson MA, Pfefferbaum A, Sullivan EV. Remote semantic memory for public figures in HIV infection, alcoholism, and their comorbidity. *Alcoholism: Clinical and Experimental Research*. 2011; 35:265–276.
- Fein G, Bachman L, Fisher S, Davenport L. Cognitive impairments in abstinent alcoholics. *Western Journal of Medicine*. 1990; 152:531–537. [PubMed: 2190421]
- Fergusson DM, Boden JM, Horwood LJ. Tests of causal links between alcohol abuse or dependence and major depression. *Archives of General Psychiatry*. 2009; 66:260–266. [PubMed: 19255375]
- First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. *Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) Version 2.0*. Biometrics Research Department, New York State Psychiatric Institute; New York, NY: 1998.
- Fritz K, Morojele N, Kalichman S. Alcohol: The forgotten drug in HIV/AIDS. *The Lancet*. 2010; 376:398–400.
- Galvan FH, Bing EG, Fleishman JA, London AS, Caetano R, Burnam MA, Longshore D, Morton SC, Orlando M, Shapiro M. The prevalence of alcohol consumption and heavy drinking among people with HIV in the United States: Results from the HIV Cost and Services Utilization Study. *Journal of Studies on Alcohol*. 2002; 63:179–186. [PubMed: 12033694]
- Gonzalez JS, Batchelder AW, Psaros C, Safren SA. Depression and HIV/AIDS treatment nonadherence: A review and meta-analysis. *Journal of Acquired Immune Deficiency Syndrome*. 2011; 58:181–187.
- Havlik RJ, Brennan M, Karpiak SE. Comorbidities and depression in older adults with HIV. *Sexual Health*. 2011; 8:551–559. [PubMed: 22127042]
- Heaton RK, Franklin DR, Ellis RJ, McCutchan JA, Letendre SL, Leblanc S, Corkran SH, Duarte NA, Clifford DB, Woods SP, Collier AC, Marra CM, Morgello S, Mindt MR, Taylor MJ, Marcotte TD, Atkinson JH, Wolfson T, Gelman BB, McArthur JC, Simpson DM, Abramson I, Gamst A, Fennema-Notestine C, Jernigan TL, Wong J, Grant I. HIV-associated neurocognitive disorders before and during the era of combination antiretroviral therapy: differences in rates, nature, and predictors. *Journal of Neurovirology*. 2011; 17:3–16. [PubMed: 21174240]

- Heaton RK, Grant I, Butters N, White DA, Kirson D, Atkinson JH, McCutchan JA, Taylor MJ, Kelly MD, Ellis RJ, Wolfson T, Velin R, Marcotte TD, Hesselink JR, Jernigan TL, Chandler J, Wallace M, Abramson I. The HNRC 500--neuropsychology of HIV infection at different disease stages. HIV Neurobehavioral Research Center. Journal of the International Neuropsychological Society. 1995; 1:231–251. [PubMed: 9375218]
- Heaton RK, Marcotte TD, Mindt MR, Sadek J, Moore DJ, Bentley H, McCutchan JA, Reicks C, Grant I, Group H. The impact of HIV-associated neuropsychological impairment on everyday functioning. Journal of the International Neuropsychological Society. 2004; 10:317–331. [PubMed: 15147590]
- Hendershot CS, Stoner SA, Pantalone DW, Simoni JM. Alcohol use and antiretroviral adherence: review and meta-analysis. Journal of Acquired Immune Deficiency Syndromes. 2009; 52:180–202. [PubMed: 19668086]
- Huckans M, Seelye A, Parcel T, Mull L, Woodhouse J, Bjornson D, Fuller BE, Loftis JM, Morasco BJ, Sasaki AW, Storzbach D, Hauser P. The cognitive effects of hepatitis C in the presence and absence of a history of substance use disorder. Journal of the International Neuropsychological Society. 2009; 15:69–82. [PubMed: 19128530]
- Kalichman S, Rompa D, Cage M. Distinguishing between overlapping somatic symptoms of depression and HIV disease in people living with HIV-AIDS. The Journal of Nervous and Mental Disease. 2000; 188:662–670. [PubMed: 11048815]
- Kalichman SC, Simbayi LC, Kaufman M, Cain D, Jooste S. Alcohol use and sexual risks in HIV/AIDS in Sub-Saharan Africa: Systematic review of empirical findings. Prevention Science. 2007; 8:141–151. [PubMed: 17265194]
- Kelley KW, Dantzer R. Alcoholism and inflammation: Neuroimmunology of behavioral and mood disorders. Brain, Behavior, and Immunity. 2011; 25:S13–S20.
- Kessler RC, Demler O, Frank RG, Olfson M, Pincus HA, Walters EE, Wang P, Wells KB, Zaslavsky AM. Prevalence and treatment of mental disorders, 1990 to 2003. New England Journal of Medicine. 2005; 352:2515–2523. [PubMed: 15958807]
- Klove H. Clinical Neuropsychology. Medical Clinics of North America. 1963; 47:1647–1658. [PubMed: 14078168]
- Lieber CS. Alcohol and Hepatitis C. Alcohol Research & Health. 2001; 25:245–254. [PubMed: 11910701]
- Liu I-C, Chiu C-H, Yang T-T. The effects of gender and a co-occurring depressive disorder on neurocognitive functioning in patients with alcohol dependence. Alcohol and Alcoholism. 2010; 45:231–236. [PubMed: 20353953]
- Maj M, D'Elia L, Satz P, Jansses R, Zaudig M, Uchiyama C, Starace F, Galderisi S, Chervinsky A. Evaluation of two new neuropsychological tests designed to minimize cultural bias in the assessment of HIV-1 seropositive persons: A WHO study. Archives of Clinical Neuropsychology. 1993; 8:123–135. [PubMed: 14589670]
- Maki PM, Martin-Thormeyer E. HIV, Cognition and Women. Neuropsychology Review. 2009; 19:204–214. [PubMed: 19430907]
- Martin E, Gonzalez R, Vassileva J, Maki P. HIV+ men and women show different performance patterns on procedural learning tasks. Journal of Clinical and Experimental Neuropsychology. 2011; 33:112–120. [PubMed: 20694870]
- Martin EM, Nixon H, Pitrak DL, Weddington W, Rains NA, Nunnally G, Grbesic S, Gonzalez R, Jacobus J, Bechara A. Characteristics of prospective memory deficits in HIV-seropositive substance-dependent individuals: Preliminary observations. Journal of Clinical and Experimental Neuropsychology. 2007; 29:496–504. [PubMed: 17564915]
- Mello VA, Segurado AA, Malbergier A. Depression in women living with HIV: Clinical and psychosocial correlates. Archives of Women's Mental Health. 2010; 13:193–9. [PubMed: 19760048]
- Meyers, J.; Meyers, K. Rey Complex Figure Test and Recognition Trial: Professional manual. Psychological Assessment Resources; Odessa, FL: 1995.

- Morrison MF, Petitto JM, Ten Have T, Gettes DR, Chiappini MS, Weber AL, Brinker-Spence P, Bauer RM, Douglas SD, Evans DL. Depressive and anxiety disorders in women with HIV infection. *American Journal of Psychiatry*. 2002; 159:789–796. [PubMed: 11986133]
- Nelson, HE. The National Adult Reading Test (NART). Nelson Publishing Company; Windsor, Canada: 1982.
- Oscar-Berman M, Marinkovic K. Alcohol: effects on neurobehavioral functions and the brain. *Neuropsychology Review*. 2007; 17:239–57. [PubMed: 17874302]
- Osterrieth P, Rey A. Le test de copie d'une figure complexe. *Archives de Psychologie*. 1944; 30:205–221.
- Parsons O, Nixon S. Cognitive-functioning in sober social drinkers: A review of the research since 1986. *Journal of Studies on Alcohol*. 1998; 59:180–190. [PubMed: 9500305]
- Parsons OA. Neurocognitive deficits in alcoholics and social drinkers: A continuum? *Alcoholism: Clinical and Experimental Research*. 1998; 22:954–961.
- Petry NM. Alcohol use in HIV patients: What we don't know may hurt us. *International Journal of STD and AIDS*. 1999; 10:561–570. [PubMed: 10492422]
- Pfefferbaum A, Lim KO, Zipursky RB, Mathalon DH, Rosenbloom MJ, Lane B, Ha CN, Sullivan EV. Brain gray and white matter volume loss accelerates with aging in chronic alcoholics: A quantitative MRI study. *Alcoholism: Clinical and Experimental Research*. 1992; 16:1078–1089.
- Purcell R, Maruff P, Kyrios M, Pantelis C. Neuropsychological function in young patients with unipolar major depression. *Psychological Medicine*. 1997; 27:1277–1285. [PubMed: 9403899]
- Rabkin JG. HIV and depression: 2008 review and update. *Current HIV/AIDS Reports*. 2008; 5:163–171. [PubMed: 18838056]
- Reger MA, Welsh R, Razani J, Martin DJ, Boone KB. A meta-analysis of the neuropsychological sequelae of HIV infection. *Journal of the International Neuropsychological Society*. 2002; 8:410–424. [PubMed: 11939699]
- Reitan, RM.; Davison, LA. *Clinical Neuropsychology: Current Status and Applications*. Hemisphere; New York: 1974.
- Rey A. L'examen psychologique dans les cas d'encephalopathie traumatique. *Archives de Psychologie*. 1942; 28:286–340.
- Rosenbloom MJ, Sullivan EV, Sassoon SA, O'Reilly A, Fama R, Kemper CA, Deresinski SC, Pfefferbaum A. Alcoholism, HIV infection and their comorbidity: Factors affecting self-rated health-related quality of life. *Journal of Studies on Alcohol and Drugs*. 2007; 68:115–125. [PubMed: 17149525]
- Rothlind JC, Greenfield TM, Bruce AV, Meyerhoff DJ, Flenniken DL, Lindgren JA, Weiner MW. Heavy alcohol consumption in individuals with HIV infection: effects on neuropsychological performance. *Journal of the International Neuropsychological Society*. 2005; 11:70–83. [PubMed: 15686610]
- Sacktor NC, Bacellar H, Hoover DR, Nance-Sproson TE, Selnes OA, Miller EN, Dal Pan GJ, Kleeberger C, Brown A, Saah A, McArthur JC. Psychomotor slowing in HIV infection: A predictor of dementia, AIDS and death. *Journal of Neurovirology*. 1996; 2:404–410. [PubMed: 8972422]
- Sassoon SA, Fama R, Rosenbloom MJ, O'Reilly A, Pfefferbaum A, Sullivan EV. Component cognitive and motor processes of the Digit Symbol Test: Differential deficits in alcoholism, HIV infection and their comorbidity. *Alcoholism: Clinical and Experimental Research*. 2007; 31:1315–1324.
- Skinner, HA. *Development and Validation of a Lifetime Alcohol Consumption Assessment Procedure*. Addiction Research Foundation; Toronto, Canada: 1982.
- Skinner HA, Sheu WJ. Reliability of alcohol use indices: The lifetime drinking history and the MAST. *Journal of Studies on Alcohol*. 1982; 43:1157–1170. [PubMed: 7182675]
- Smith S, Fein G. Persistent but less severe ataxia in long-term versus short-term abstinent alcoholic men and women: a cross-sectional analysis. *Alcoholism Clinical and Experimental Research*. 2011; 35:2184–92.
- Sullivan EV, Fama R, Rosenbloom MJ, Pfefferbaum A. A profile of neuropsychological deficits in alcoholic women. *Neuropsychology*. 2002; 16:74–83. [PubMed: 11853359]

- Sullivan EV, Harris RA, Pfefferbaum A. Alcohol's effects on brain and behavior. *Alcohol Research & Health*. 2010; 33:127–143.
- Sullivan EV, Rosenbloom MJ, Pfefferbaum A. Pattern of motor and cognitive deficits in detoxified alcoholic men. *Alcoholism: Clinical and Experimental Research*. 2000; 24:611–621.
- Sullivan LE, Fiellin DA, O'Connor PG. The prevalence and impact of alcohol problems in major depression: A systematic review. *American Journal of Medicine*. 2005; 118:330–341. [PubMed: 15808128]
- Sullivan LE, Goulet JL, Justice AC, Fiellin DA. Alcohol consumption and depressive symptoms over time: A longitudinal study of patients with and without HIV infection. *Drug and Alcohol Dependence*. 2011; 117:158–163. [PubMed: 21345624]
- Sullivan LE, Saitz R, Cheng DM, Libman H, Nunes D, Samet JH. The impact of alcohol use on depressive symptoms in human immunodeficiency virus-infected patients. *Addiction*. 2008; 103:1461–1467. [PubMed: 18637000]
- Taylor L. Localization of cerebral lesions by psychological testing. *Clinical Neurosurgery*. 1969; 16:269–287. [PubMed: 5811709]
- Tozzi V, Balestra P, Galgani S, Murri R, Bellagamba R, Narciso P, Antinori A, Giulianelli M, Tosi G, Costa M, Sampaolesi A, Fantoni M, Noto P, Ippolito G, Wu AW. Neurocognitive performance and quality of life in patients with HIV infection. *AIDS Research and Human Retroviruses*. 2003; 19:643–652. [PubMed: 13678465]
- Woods SP, Moore DJ, Weber E, Grant I. Cognitive neuropsychology of HIV-associated neurocognitive disorders. *Neuropsychological Review*. 2009; 19:152–168.

Figure.

Means and standard errors (SE) scores for eight neuropsychological tests for the healthy comparison group and three disease groups: Alcoholics (ALC), HIV, and ALC+HIV. Each disease group is divided by depression symptom level: significant depressive symptoms (SDS) vs. minimal depressive symptoms (MDS). Fine Finger Movement and Rey-Osterrieth immediate recall both show a significant main effect for depressive symptom level. See text for other significant results.

^aMain effect for depressive symptom level, $p < 0.05$; ^{b,c}main effect for disease group, ^b $p < 0.05$, ^c $p < 0.01$

Table 1

Participant demographic information by disease group

<i>Demographic Variables</i>	<i>N</i>	<i>Control (NC)</i>	<i>HIV (HIV)</i>	<i>Alcoholic (ALC)</i>	<i>Comorbid (ALC+ HIV)</i>	<i>post hoc pairwise comparisons</i>
Age (yrs)						
mean (SD)	64	40.8 (11.6)	43.9 (9.6)	45.6 (10.2)	45.1 (7.5)	NC < ALC *
range		20 to 70	20 to 59	22 to 67	22 to 58	
Education (yrs)						
mean (SD)		14.9 (2.1)	13.7 (2.7)	13.4 (2.2)	13.0 (2.2)	NC > HIV = ALC = ALC+HIV ***
range		11 to 19	8 to 19	8 to 21	8 to 18	
Men:Women						n.s.
		38:26	40:16	43:24	49:14	
Caucasian:Non-Caucasian						ALC > NC, ALC+HIV *
		21:42 ^a	23:33	35:32	16:47	
NART IQ						NC > HIV = ALC = ALC+HIV **
mean (SD)		111 (8.0)	106 (9.6)	107 (8.5)	105 (7.9)	
range		92 to 126	89 to 121	91 to 124	91 to 122	
Lifetime Alcohol (kg)						NC = HIV < ALC = ALC+HIV ***
mean (SD)		33 (61)	57 (55)	1093 (865)	863 (654)	
range		0.03 to 301	0 to 247	33 to 4376	22 to 2861	
BDI-II Score						NC < HIV = ALC = ALC+HIV ***
mean (SD)		2.9 (3.1)	11.2 (8.9)	10.0 (8.1)	11.8 (8.3)	
range		0 to 12	0 to 36	0 to 37	0 to 31	

^aUnknown for one participant;* $p < 0.05$;** $p < 0.01$;*** $p < 0.001$

Table 2
Participant demographic information for disease group by Beck Depression Inventory-II (BDI-II) symptom level

<i>Demographic Variables</i>	<i>BDI-II Level^a</i>	<i>HIV (HIV)</i>	<i>Alcoholic (ALC)</i>	<i>Comorbid (ALC+HIV)</i>	<i>post hoc pairwise comparisons</i>
<i>N</i>		22	19	24	
BDI-II Total Score	SDS				
	MDS	34	48	39	
	SDS	20.5 (5.9)	20.4 (6.3)	20.5 (5.6)	SDS > MDS***
	range	14 to 36	15 to 37	14 to 31	
Age (yrs)	mean (SD)	5.1 (3.8)	5.8 (3.8)	6.4 (4.4)	
	range	0 to 13	0 to 13	0 to 13	
	SDS	44.6 (10.3)	43.6 (9.2)	43.2 (6.5)	n.s.
	range	22 to 57	22 to 61	32 to 55	
Education (yrs)	mean	43.5 (9.2)	46.4 (10.6)	46.4 (7.9)	
	range	20 to 59	22 to 67	22 to 58	
	SDS	13.8 (2.0)	13.5 (1.9)	12.3 (2.0)	n.s.
	Range	8 to 19	12 to 18	8 to 17	
NART IQ	mean (SD)	13.7 (3.1)	13.3 (2.3)	13.5 (2.2)	
	Range	11 to 18	8 to 21	9 to 18	
	SDS	103.8 (10.6)	109.0 (8.0)	102.3 (8.6)	n.s.
	Range	90 to 121	92 to 120	94 to 122	
NART IQ	mean (SD)	107.9 (8.6)	106.0 (8.6)	107.1 (6.9)	
	Range	89 to 121	91 to 124	91 to 119	

^aSDS = significant depressive symptoms, BDI-II score 14; MDS = none/minimal symptoms; BDI-II < 14

 $p < 0.001$

Table 3

Hepatitis C status, alcohol consumption, psychiatric and psychosocial variables for disease groups by BDI-II symptom level

Dependent Variables	BDI-II Level ^a	HIV (HIV)	Alcoholic (ALC)	Comorbid (ALC+HIV)	post hoc pairwise comparisons
Hepatitis C					
	yes:no	7:15	5:13	14:9	n.s.
	yes:no	6:28	12:36	15:24	
Lifetime alcohol (kg)	mean (SD)	56 (51)	902 (634)	806 (515)	HIV < ALC, ALC+HIV ***
	range	0 to 161	33 to 2133	72 to 1843	
	mean (SD)	57 (58)	1169 (936)	898 (731)	
	range	24 to 247	80 to 4376	22 to 2861	
DSM-IV mood disorder history	yes:no	7:15	10:9	15:9	SDS > MDS **
	yes:no	7:27	14:34	15:24	
Current antidepressant	yes:no	8:14	9:8	11:12	SDS > MDS ***
	yes:no	6:28	7:38	9:30	
Substance dependence/abuse history	yes:no	7:15	14:05	19:5	ALC, ALC+HIV > HIV ***
	yes:no	13:21	27:21	34:5	
Psychosocial stressors	mean (SD)	.77 (.81)	1.6 (1.1)	1.13 (.98)	SDS > MDS @, ALC > HIV, ALC+HIV *
	range	0 to 2	0 to 3	0 to 3	
	mean (SD)	.69 (.74)	.93 (.98)	.88 (.92)	
	range	0 to 2	0 to 3	0 to 4	
GAF score	mean (SD)	66.2 (10.5)	55.1 (12.4)	58.9 (11.1)	SDS > MDS ***; HIV > ALC, ALC+HIV ***
	range	54 to 84	35 to 79	43 to 70	
	mean (SD)	76.0 (9.1)	65.5 (11.4)	68.2 (11.3)	
	range	60 to 90	35 to 85	45 to 89	
Quality of life	mean (SD)	51.8 (16.2)	69.2 (12.8)	47.9 (12.8)	interaction *
	range	25 to 82	52 to 88	28 to 77	
	mean (SD)	77.1 (14.8)	81.1 (11.5)	72.6 (15.9)	
	range	29 to 99	47 to 95	36 to 97	

^aSDS = significant depressive symptoms, BDI-II score 14; MDS = none/minimal symptoms; BDI-II < 14

@ p = 0.05;

* p < 0.05;

\$watermark-text

\$watermark-text

\$watermark-text

**
 $p < 0.01$;

 $p < 0.001$