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Synergistic Effects of HIV Infection and Older Age on Daily Functioning

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ABSTRACT

Objective: To determine whether HIV infection and aging act synergistically to disrupt everyday functioning.

Design: Cross-sectional, factorial study of everyday functioning in the context of HIV serostatus and age (< 40 years vs > 50 years).

Methods: 103 HIV+ and 87 HIV- participants were administered several measures of everyday functioning, including self-report indices of health-related quality of life (HRQoL) and instrumental and basic activities of daily living (IADLs and BADLs), and objective measures of functioning including employment and Karnofsky Performance Scale (KPS) ratings.

Results: Significant interaction effects of HIV and aging were observed for IADL and BADL declines, as well as KPS ratings (*p*s<.05), independent of potentially confounding factors. Follow-up contrasts revealed significantly worse functioning in the older HIV+ group for all functional outcome measures relative to the other study groups (*p*s<.05). A significant interaction effect was also observed on the emotional functioning HRQoL subscale, and additive effects of both age and HIV were observed for the physical functioning and general health perceptions HRQoL subscales (*p*s<.05). Significant predictors of poorer functioning in the older HIV+ group included current major depressive disorder for all outcomes, and comorbid medical conditions, lower estimated premorbid functioning, neurocognitive impairment, and nadir CD4 count for selected outcomes.

Conclusion: Findings suggest that older age may exacerbate the adverse effects of HIV on daily functioning, which highlights the importance of evaluating and monitoring the functional status of older HIV-infected adults. Early detection of functional difficulties could facilitate delivery of compensatory strategies (e.g., cognitive remediation) or assistive services.

Keywords. HIV; aging; assessment; daily functioning; health status; disability

INTRODUCTION

Due in large part to advances in combined antiretroviral therapy (cART), there is a growing population of older adults who are aging with HIV. Indeed, the Centers for Disease Control (CDC) recently reported that more than a quarter of adults with HIV are 50 years of age and older [1]. As individuals grow older with HIV infection, they may be susceptible to a host of different aging-related comorbidities, including cardiovascular disease [2], changes in bone density [3], metabolic dysregulation [4], and neurocognitive impairment [5, 6]. Importantly, these conditions may be associated with poor long-term clinical outcome.

The increased mental and physical health burden of aging with HIV infection may increase older HIV-seropositive adults' vulnerability to disruption in basic (e.g., grooming) and instrumental (e.g., financial management) aspects of everyday functioning that are critical to optimal health outcomes. Important predictors of daily functioning problems in the context of both HIV and aging include certain demographics (e.g., male sex; [7]), depressed mood [8], overall burden of disease [9], and neurocognitive deficits (e.g., memory and executive impairment; [10]). A recent study revealed a synergistic effect of age and neurocognitive status on functional task performance in HIV+ individuals, such that the older impaired group evidenced worse medication and finance management than the younger groups [11]. Irrespective of neurocognitive status, older age has been significantly associated with both physical difficulty (e.g., climbing stairs) and role limitations (e.g., employment) in persons with HIV [12]. However, no studies have yet investigated potential synergistic effects of HIV and aging on daily functioning outcomes through inclusion of an HIV-seronegative comparison group using a comprehensive assessment of daily functioning domains.

The present study aimed to investigate the combined effects of HIV and aging on everyday functioning across several measures ranging in complexity and objectivity (i.e., source of information). Self-reported indices of daily functioning included measures of instrumental and basic activities of daily living (IADLs and BADLs), and scales representing both physical and

mental health-related quality of life (HRQoL). Objective functional measures included employment status and the clinician-assigned Karnofsky Scale of Performance Status. We hypothesized that older HIV+ adults would be at greatest risk for functional problems, independent of potential confounding variables (e.g., education). Finally, we examined relationships between these outcomes and clinical factors expected to impact successful daily functioning in older HIV+ adults (e.g., mood, HIV disease severity).

METHOD

Participants

This study included 179 participants recruited from the San Diego community and local HIV clinics. Participants were classified by HIV serostatus and age (i.e., younger < 40; and older ≥ 50; See Table 1). HIV serostatus was determined by enzyme-linked immunosorbent assays and confirmed by a Western blot test. All HIV+ individuals were on stable antiretroviral therapy at the time of their assessment.

Participants were excluded if they had histories of severe psychiatric disorders (e.g., schizophrenia), chronic medical or neurological conditions such as active CNS opportunistic infections, seizure disorders, head injury with loss of consciousness greater than 30 minutes, stroke with neurological sequelae, and non-HIV-associated dementias, or if they had an estimated verbal IQ score (VIQ) below 70 on the Wechsler Test of Adult Reading (WTAR [14]). Individuals were also excluded if they met *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; DSM-IV) [13] criteria for substance use disorders within six months of evaluation or if they tested positive on a urine toxicology (u-tox) screen for illicit drugs (except marijuana) on the day of testing. Demographic, cognitive, psychiatric, and medical characteristics of the sample may be found in Table 1.

[Insert Table 1 about here]

Materials and Procedure

The study procedures were approved by the human subjects institutional review board.

Each participant provided written, informed consent, and was administered a comprehensive medical, psychiatric, and neuropsychological medical evaluation.

Evaluation of daily functioning. Each participant completed a modified form of the Lawton and Brody [15] Activities of Daily Living (ADL) Scale (e.g., [8]). This scale requires participants to rate their current and best levels of functioning with regard to seven IADLs (i.e., finance management, purchasing groceries, cooking, using transportation, shopping, medication management, and social activity planning) and five BADLs (i.e., housekeeping/cleaning, laundry, home repairs, bathing, and dressing), with the summed difference scores interpreted so that higher values denote poorer functioning (see [16]). Ranges of the IADL and BADL subscales are 0-17 and 0-13, respectively. Second, each participant was assigned an overall functional impairment rating by a certified nurse based on the Karnofsky Scale of Performance Status (KPS; [17]), which has been validated in HIV [18], and ranges from 100 (i.e., able to carry on normal activity) to zero (i.e., death).

Each participant was also administered the RAND 36-item Short Form Health Survey (SF-36), which is a disease non-specific 36-item self-report questionnaire assessing physical and mental health well-being, that has been validated as an index of health-related quality of life (HRQoL) in HIV [19, 20]. The SF-36 consists of eight subscales that range from 0 to 100, with higher scores indicating better HRQoL.

Employment status was coded via a semi-structured neurobehavioral interview (see [21]). Each participant was classified as employed (full-time only) or unemployed, which included those classified as disabled (i.e., 29.3%).

Medical Evaluation. Each individual received a medical evaluation including a blood draw and an assessment of medical conditions common in HIV-infected and aging populations including diabetes mellitus (DM), cardiovascular disease (e.g., hypertension), respiratory disease (e.g., chronic obstructive pulmonary disease), and hepatitis C virus (HCV; see Table 1). A composite medical comorbidities index (i.e., the “Medical Comorbidity Burden”) was derived

by summing the total number of medical conditions endorsed [22]. An estimated five-year risk of developing coronary heart disease was calculated for each participant using published Framingham Risk Score equations [23].

Neuropsychological Evaluation. The neuropsychological evaluation included an estimated measure of pre-morbid VIQ (i.e., WTAR), alongside a comprehensive neuropsychological test battery designed to assess the cognitive domains most frequently impacted in HIV-associated neurocognitive disorders (HAND) in accordance with Frascati research criteria [24], including executive functions, attention/working memory, episodic learning and memory, verbal fluency, information processing speed, and motor skills (see [16] for details). Clinical ratings ranging from 0 (above average) to 9 (severely impaired) were assigned for each participant by trained neuropsychologists using published, standardized, and well-validated blind clinical ratings procedures [25] that have been previously demonstrated to be predictive of daily functioning outcomes in HIV+ individuals [8]. A cut-point of 5 or greater indicating global neuropsychological impairment (i.e., Global NPI; see Table 1 for rates of impairment). HIV+ individuals with HAND were further classified as having asymptomatic neurocognitive impairment (ANI), minor neurocognitive disorder (MND), or HIV-associated Dementia (HAD) using Antinori et al. [24] research criteria (see Table 1).

Each participant was also assigned a score representing their highest occupational level based on the Hollingshead (HH) Occupational Scale [26], which rates occupations along a continuum ranging from 1 (e.g., managers or other professionals) to 7 (e.g., non-specialized manual labor). Each participant's HH score was converted to a population-based z-score and averaged with population-based z-scores for years of education and WTAR verbal IQ to derive a putative estimate of premorbid functioning, also known as cognitive reserve, in which higher scores reflect greater levels of estimated reserve.

Psychiatric Evaluation. Current mood symptoms were assessed using the Profile of Mood States (POMS [27]), which is a 65-item, self-report measure of current affective distress.

Current (i.e., within the last 30 days) and lifetime major depressive disorder (MDD) and substance use disorders were determined using the Composite International Diagnostic Interview (CIDI version 2.1; [28]).

Data Analysis

Statistical analyses were conducted using a JMP software package (version 9.0.2) and the critical alpha was set at $p < 0.05$. Multiple linear regression analyses were used to evaluate the models involving continuous criterion variables (i.e., ADL declines, Karnofsky, and SF-36). A logistic regression was conducted to examine the model involving the dichotomous employment variable. To address potential confounding effects, several factors that differed across the groups were included as covariates, including ethnicity, POMS Total, Global NPI, and the Framingham. Although significant group differences were observed for other potentially important factors (i.e., HCV, antidepressants, and marijuana u-tox), these variables were not included in our regression models due to low prevalence rates. Nevertheless, when respective regression models were conducted including these factors, the pattern of findings was unchanged. For the planned *post hoc* analyses, we used one-way ANOVA (and Cohen's d effect size estimates) or chi-square tests as appropriate. Multiple linear regression models were used to investigate predictors of each functional outcome within the Older HIV+ group, and included: current MDD diagnosis, nadir CD4 count, plasma viral load, global NPI, medical comorbidity burden, and cognitive reserve.

RESULTS

Results of the anlayses examining the independent and synergistic effects of age and HIV infection on self-reported IADL and BADL declines, Karnofsky scores, and employment are displayed in Table 2. Significant synergistic effects of age and HIV infection were observed for IADL and BADL declines as well as Karnofsky scores ($ps<0.05$), though no significant interaction was observed for employment ($p>0.10$; See Table 2). Significant main effects of HIV were observed for all four functional outcomes ($ps<0.05$), although a significant main effect of

age was only observed for Karnofsky scores (p=0.010). With regard to the SF-36 HRQoL subscales, a significant age by HIV interaction was observed only for the emotional functioning subscale (β=-0.13, p=0.026). Independent effects of both age and HIV (i.e., additive effects) were observed for physical functioning (age: β=-0.29, HIV: β=0.17, ps<0.05) and general health perceptions (age: β=-0.24, HIV: β=0.16, ps<0.01) subscales. A main effect of aging was observed for the bodily pain subscale (β=-0.19, p=0.040), and a main effect of HIV was observed for the role limitations due to physical health problems subscale (β=0.19, p=0.005). No significant age, HIV, or interaction effects were observed for the emotional well-being, role limitations caused by emotional problems, and social functioning subscales (ps > 0.05).

[*Insert Table 2 about here*]

As displayed in Figures 1 and 2, the Older HIV+ group reported a significantly higher number (i.e., reported greater severity) of both IADL and BADL declines, and had significantly lower Karnofsky ratings relative to each of the remaining groups (ps<0.05). Lastly, the Older HIV+ group had greater proportions of individuals who were unemployed or disabled relative to both HIV- groups (ps<0.05) though they had similar rates of employment to their Younger HIV+ counterparts (p=0.117; see Figure 2).

[*Insert Figures 1 and 2 about here*]

Results for the analyses used to determine predictors of ADL declines, Karnofsky ratings, and unemployment within the Older HIV+ group are presented in Table 3. Current MDD was a significant predictor of all four functional outcomes (ps < 0.05). Additional significant predictors of IADL declines included global NPI, nadir CD4 count, and cognitive reserve (ps<0.05). Lower cognitive reserve was also associated with BADL disability, albeit at a trend-level (p=0.055). A greater medical comorbidity burden and lower cognitive reserve were both significant predictors of lower Karnofsky ratings (ps<0.05), and reached a trend-level of significance as predictors of unemployment (ps<0.10). For the SF-36 HRQoL subscales, significant regression models were observed for physical functioning [$F(6,53)=2.3$; adjusted R^2=0.12; p=0.048], emotional well

being [F(6,51)=5.35; adjusted R^2=0.31; *p*=0.002], role limitations caused by emotional problems [F(6,54)=4.37; adjusted R^2=0.25; *p*=0.001] and social functioning [F(6,54)=3.22; adjusted R^2=0.18; *p*=0.009]. Presence of current MDD was the only significant predictor of these HRQoL subscales (*p*s<0.01). Additional associations, albeit at a trend level, were observed between the medical comorbidity burden and the physical functioning subscale (β=-0.22), and between global NPI and social functioning (β=-0.21; *p*s<0.10).

[*Insert Table 3 about here*]

DISCUSSION

Everyday functioning impairment is an important sequelae of HIV infection to which older infected adults may be particularly vulnerable. This study demonstrated synergistic adverse effects of HIV and aging on daily functioning outcomes, including self-reported decline in both instrumental and basic activities of daily living and poorer scores on a clinician-assigned rating of overall functional status. The interaction of HIV infection and aging observed for these functional outcomes persisted despite controlling for important cofactors upon which the groups differed (e.g., demographic or medical factors). For each of the functional outcomes, the older HIV+ group demonstrated poorer everyday functioning relative to the other study groups. With the foundation of a rigorous and comprehensive study design, these findings extend prior literature due to inclusion of both older and younger HIV-seronegative individuals for comparison to the HIV+ groups and by examining a wide range of everyday functioning measures. Accordingly, these findings suggest that older age may exacerbate HIV-associated disability in daily life.

Such findings raise important questions about the specific clinical characteristics that may increase older HIV-infected adults' vulnerability to poorer functional outcomes. Importantly, several of these predictors are highly amenable to proper screening and treatment, which may facilitate efforts to improve the health status of this high-risk group. For example, MDD was arguably the most reliable predictor of adverse functional outcomes in our older HIV+ cohort,

which is consistent with abundant evidence from the HIV literature (e.g., [8]). Notably, this relationship may be bidirectional such that depressed mood may negatively impact performance of daily activities, but also poor performance of everyday functions may itself precipitate depressed mood [29]. These findings highlight the need to regularly screen older HIV+ adults for symptoms of depression given that episodes of major depression can disrupt performance of important daily activities and are potentially remediable (see [30]). It is important to note, however, that in the present sample, 44% of the older HIV+ adults with lifetime MDD diagnoses were currently taking antidepressants, and a *posthoc* analysis revealed that antidepressant use was not associated with better daily functioning in the older HIV+ individuals with MDD (current or lifetime). As such, future studies should explore the most effective interventions for MDD and ameliorating the impact of MDD on functioning, which may include a combination of pharmacologic and psychotherapeutic intervention.

The presence of HAND was a significant predictor of greater levels of IADL declines, which is consistent with prior studies demonstrating disproportionate effects of HAND among older HIV+ individuals, particularly as it relates to medication and finance management [11]. Older HIV+ individuals who report difficulty with complex daily activities might benefit from neurocognitive screening and training in compensatory strategies (e.g., pill boxes, automatic bill pay). Interestingly, estimated premorbid functioning, also known as cognitive reserve, was uniquely associated with aspects of everyday functioning among older HIV+ adults. This construct represents the effects of enrichment of cognitive resources through educational and vocational experiences coupled with elements of innate intellectual ability that have been proposed to moderate the relationship between central nervous system insults, such as infection and neurobehavioral outcomes (e.g., [31]). For example, HIV+ individuals with low cognitive reserve are at greater risk for concurrent [32] and incident HAND [33]. In the present study, lower cognitive reserve was associated with greater IADL declines and lower Karnofsky ratings. This evidence suggests that in older HIV-infected adults, lower cognitive reserve may

interfere with the adaptive ability to engage alternate brain networks and/or initiate the use of compensatory strategies when they encounter problems in their daily life, resulting in disability.

Medical comorbidity burden, which summarizes the extent of each individual's concurrent medical comorbidities including diabetes mellitus, cardiovascular disease, respiratory disease, and HCV, was associated with lower Karnofsky ratings. It is possible that the gross nature of the Karnofsky score is sensitive to the problems imposed by managing comorbid conditions, especially given that HIV+ individuals may be particularly vulnerable to these conditions as they age, including cardiovascular and metabolic conditions (e.g., hypertension, diabetes [3, 34]). Furthermore, information regarding the patient's medical history that is available to the clinician assigning the rating may also contribute to the contribution of medical comorbidity burden to prediction of the Karnofsky score.

While the index of current HIV disease status (i.e., detectable plasma viral load) was not related to any of the functional outcomes in the older HIV+ group, lower nadir CD4 count (i.e., a marker of worse historical HIV disease) was significantly associated with greater IADL declines. This is consistent with evidence suggesting that low nadir CD4 predicts development of HAND, which is a robust predictor of daily functioning outcomes in older HIV+ adults (e.g., [11]). The lack of associations between current detectable plasma load and everyday functioning outcomes could be due in part to the improved HIV management in the cART era, which may decrease the relevance of HIV disease-specific markers for predicting a downstream outcome such as daily functioning performance. Indeed, the entire HIV+ sample in this study was on stable antiretroviral medications at the time of evaluation, and only about 10% of our older HIV+ group had detectable plasma viral loads. Furthermore, HIV+ individuals who have reached older age may carry a survival bias that should temper conclusions regarding the association between HIV disease characteristics and disability. With regard to markers of current disease status, in the present cohort of older HIV+ adults, many of whom may be long-term survivors, the added burden of comorbid conditions such as cardiovascular disease or diabetes appears to be much

more likely to negatively impact performance of daily activities (e.g., [35]). Moreover, the significant negative association between low nadir CD4 count and increased daily functioning difficulty may actually be a cohort effect that is most relevant to long-term survivors who have experienced greater disease severity in the past and recovered. In the current cART era, individuals who are treated earlier with more effective and less neurotoxic regimens may not experience periods of such drastic disease severity (as evidenced by low nadir CD4), thereby reducing the likelihood that this historic disease marker would represent a significant risk for disability in future older HIV+ cohorts.

With regard to HRQoL, the disproportionately worse emotional functioning observed among older HIV+ adults is consistent with the high prevalence of depression among older HIV+ adults. Indeed, among the older HIV+ group only, current MDD emerged as the sole important risk factor for reductions in several types of HRQoL, including worse emotional well-being and role limitations due to emotional functioning, as well as lower physical and social functioning. This evidence further supports the need for careful depression screening and effective treatment among older HIV+ individuals whose HRQoL can be negatively impacted by depression across many dimensions. Although synergistic effects were not observed for the other HRQoL subscales, additive effects of HIV and aging were observed for the physical functioning and general health perceptions subscales. As such, it is likely that older patients with HIV may experience incremental rather than synergistic limitations in their physical activities and changes in their beliefs about their health overall than would be associated with HIV or aging alone. These results are consistent with prior evidence of lower quality of life relating to limitations in physical activities demonstrated among HIV+ individuals [12], and they extend these prior findings by demonstrating the additive component of aging in reducing this aspect of HRQoL.

The present study has limitations worth noting that may also inform future work. First, the cross-sectional nature of the study does not allow for interpretations regarding potential synergistic effects of HIV and aging on decline in daily functioning status over time. This is an

important future direction given that it would inform daily functioning prognosis for older HIV+ individuals. In addition, it would be helpful to replicate our study with a sample that included greater numbers of individuals at more advanced age (e.g., over 65 years of age). It is likely that the observed interaction effect would be strengthened in such a sample, but it would also be interesting to examine whether the cognitive reserve relationship holds at older ages such that higher levels of reserve protect again daily functioning failures. As discussed above, survivor bias is also an important consideration, especially in light of the fact that current HIV disease status was not a significant predictor of any everyday functioning measures, and risk for disability may change as the characteristics of the cohorts of older adults living with HIV evolve over time (e.g., the nature of the predictors may change as people age with better managed HIV disease). Moreover, although the current study utilized both self-reported and objective indices of daily functioning, performance-based measures of functional capacity were not included. Such ecologically valid measures would be another important criterion for examining the combined effects of HIV and aging. Finally, although all individuals in the HIV+ sample were prescribed a stable cART regimen, the present study did not specifically examine measures of medication adherence among the selected daily functioning outcomes. On one hand, some evidence suggests that older HIV+ adults without cognitive impairment are more adherent to their cART regimens for a variety of reasons [36]. On the other hand, medication nonadherence could be particularly problematic in older HIV+ adults, not only for proper maintenance of HIV disease but also of comorbid conditions related to aging (e.g., hypertension). Given the evidence that HIV and aging in combination negatively impact other important daily activities, future studies investigating these combined effects on medication adherence are warranted.

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Table 1. Demographic, psychiatric, medical, and HIV disease characteristics of the four study groups.

Variable	HIV-		HIV+		*p**
	Young n = 43	Old n = 44	Young n = 31	Old n = 61	
Demographic Characteristics					
Age	29.2 (5.9)	55.3 (4.1)	31.4 (5.3)	55.1 (4.5)	--
Ethnicity (% Caucasian)	46.5	68.2	38.7	70.5	0.005
Gender (% male)	67.4	63.6	83.9	80.3	0.100
HDS Total	15.1 (1.4)	14.3 (2.3)	13.6 (2.5)	13.2 (3.0)	0.001
Global Rating	3.5 (1.2)	3.4 (1.2)	3.7 (1.4)	4.2 (1.6)	0.010
Global NPI (% impaired)	20.9 (n=9)	18.2 (n=8)	22.6 (n=7)	39.3 (n=24)	0.060
HAND Classifications					
ANI (%)	--	--	71 (n=5)	50% (n=12)	--
MND (%)	--	--	29 (n=2)	50% (n=12)	--
HAD (%)	--	--	0 (n=0)	0 (n=0)	--
Cognitive Reserve Components					
Education	13.7 (2.2)	14.3 (2.4)	13.4 (2.4)	14.0 (2.7)	0.414
HH Occupational Score	3.8 (1.4)	3.1 (1.1)	3.5 (1.6)	3.1 (1.0)	0.021
Estimated VIQ	101.8 (8.9)	104.2 (10.1)	100.0 (10.2)	101.8 (11.5)	0.320
Psychiatric Characteristics					
POMS Total[1]	36.0 [22.0, 60.0]	37.5 [19.3, 56.0]	37.0 [22.0, 79.0]	51.5 [30.0, 76.2]	0.032
Current MDD (%)	2.3	2.3	12.9	24.6	<0.001
Lifetime MDD (%)	23.3	38.6	48.4	49.2	0.038
Antidepressant Medication (% on)	4.7	13.6	19.4	31.0	0.004
Any Lifetime SUD (%)	62.8	65.9	48.4	73.8	0.120
MJ Utox (% positive)	9.3	2.3	22.6	17.5	0.018
Medical Characteristics					
Framingham 5-year Risk	0.5 (0.4)	1.7 (1.2)	0.5 (0.3)	2.0 (1.3)	< 0.001
Medical Comorbidity Burden	0.1 (0.2)	0.6 (0.7)	0.2 (0.4)	1.1 (1.0)	< 0.001
Cardiovascular Disease (%)	0	9.1	0	9.8	0.011
Respiratory Disease (%)	0	4.6	0	4.9	0.023
Diabetes Mellitus (%)	0	6.8	0	14.8	0.002
Hepatitis C Virus (%)	2.3	15.9	3.2	36.7	< 0.001
HIV Disease Characteristics					
Duration of Infection (years)[1]	--	--	4.6 [2.4, 10.8]	17.9 [12.7, 21.6]	< 0.001
CD4 Nadir (cells/μl)[1]	--	--	247.0 [163.1, 345.0]	148.0 [52.0, 250.0]	0.012
Plasma VL (% undetectable)	--	--	87.1	90.2	0.659
CSF VL (% undetectable)	--	--	84.0	93.5	0.212
AIDS (%)	--	--	29.0	65.6	< 0.001

Note. Data represent means (SD) unless otherwise noted. *p-value reflects omnibus group difference. [1]median (interquartile range); HDS = HIV Dementia Scale; NPI = neuropsychological impairment; HAND = HIV-associated neurocognitive disorders; ANI = asymptomatic neurocognitive impairment; MND = minor neurocognitive disorder; HAD = HIV-associated dementia; HH = Hollingshead; VIQ = Verbal IQ (based on the Wechsler Test of Adult Reading); POMS Total = Profile of Mood States, total mood disturbance score; MDD = Major Depressive Disorder; SUD = substance use disorder; MJ = Marijuana; Utox = urine toxicology screen; CD4 = cluster of differentiation 4; AIDS = Acquired Immune Deficiency Syndrome; VL = viral load; CSF = cerebrospinal fluid; cART = combined antiretroviral therapy.

Table 2. Multiple regression analyses showing synergistic effects of HIV infection and aging on IADL/BADL decline severity, Karnofsky score, and employment status.

Multiple Linear Regression	***Adjusted R^2***	***F***	***β***	***p*-value**
IADL Severity	**0.18**	**6.44**		**<0.001***
Age			0.07	0.463
HIV Status [HIV-]			-0.20	0.007*
HIV Status * Age			-0.16	0.025*
Ethnicity [Caucasian]			0.09	0.248
POMS Total			0.26	<0.001*
Global NPI [Impaired]			0.09	0.188
Framingham 5-year Risk			0.02	0.810
BADL Severity	**0.17**	**6.29**		**<0.001***
Age			0.16	0.100
HIV Status [HIV-]			-0.23	0.002*
HIV Status * Age			-0.14	0.043*
Ethnicity [Caucasian]			0.03	0.741
POMS Total			0.25	<0.001*
Global NPI [Impaired]			0.09	0.194
Framingham 5-year Risk			-0.08	0.382
Karnofsky Score	**0.42**	**18.8**		**<0.001***
Age			-0.21	0.010*
HIV Status [HIV-]			0.36	<0.001*
HIV Status * Age			0.16	0.001*
Ethnicity [Caucasian]			0.00	0.991
POMS Total			-0.31	<0.001*
NPI [Impaired]			-0.11	0.075
Framingham 5-year Risk			-0.06	0.457
Logistic Regression			***X^2***	***p*-value**
Employment Status [Employed] (*df*=7)			**26.65**	**<0.001***
Age			0.34	0.559
HIV Status [HIV-]			9.41	0.002*
HIV Status * Age			2.48	0.115
Ethnicity [Caucasian]			0.00	0.948
POMS Total			2.39	0.123
Global NPI [Impaired]			3.47	0.062
Framingham 5-year Risk			1.38	0.240

Note: IADL = Instrumental activities of daily living; BADL = Basic activities of daily living; POMS = Profiles of Mood States; NPI = neuropsychological impairment.

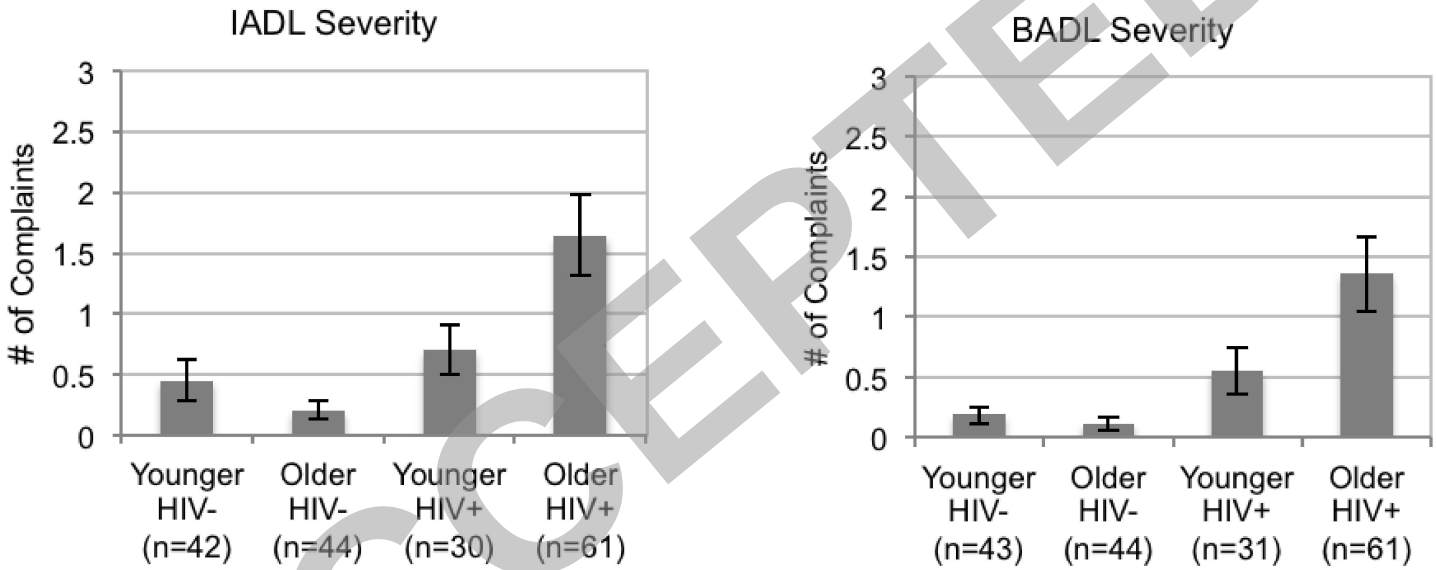
Table 3. Predictors of functional outcomes within older HIV+ individuals (n=61).

Multiple Linear Regression	***Adjusted R^2***	***F***	***β***	***p*-value**
IADL Severity	**0.24**	**4.10**		**0.002***
Global NPI [Impaired]			0.24	0.043*
Current MDD [No]			-0.38	0.002*
CD4 Nadir			0.28	0.023*
Plasma VL [Detectable]			0.05	0.655
Medical Comorbidity Burden			0.17	0.174
Cognitive Reserve			-0.27	0.028*
BADL Severity	**0.12**	**2.38**		**0.041***
Global NPI [Impaired]			0.14	0.261
Current MDD [No]			-0.35	0.007*
CD4 Nadir			0.14	0.262
Plasma VL [Detectable]			0.11	0.357
Medical Comorbidity Burden			0.10	0.441
Cognitive Reserve			-0.26	0.055
Karnofsky Score	**0.28**	**4.90**		**<0.001***
Global NPI [Impaired]			-0.18	0.124
Current MDD [No]			0.37	0.002*
CD4 Nadir			-0.13	0.250
Plasma VL [Detectable]			0.08	0.467
Medical Comorbidity Burden			-0.32	0.008*
Cognitive Reserve			0.29	0.016*

Logistic Regression	***B***	***SE***	***X^2***	***p*-value**
Employment Status [Employed] (*df*=6)			**17.74**	**0.007***
Global NPI [Impaired]	0.63	0.42	2.52	0.112
Current MDD [No]	-1.17	0.59	5.81	0.016*
CD4 Nadir	0.00	0.00	0.27	0.606
Plasma VL [Detectable]	0.07	0.68	0.01	0.913
Medical Comorbidity Burden	0.81	0.46	3.42	0.064
Cognitive Reserve	-1.40	0.79	3.53	0.060

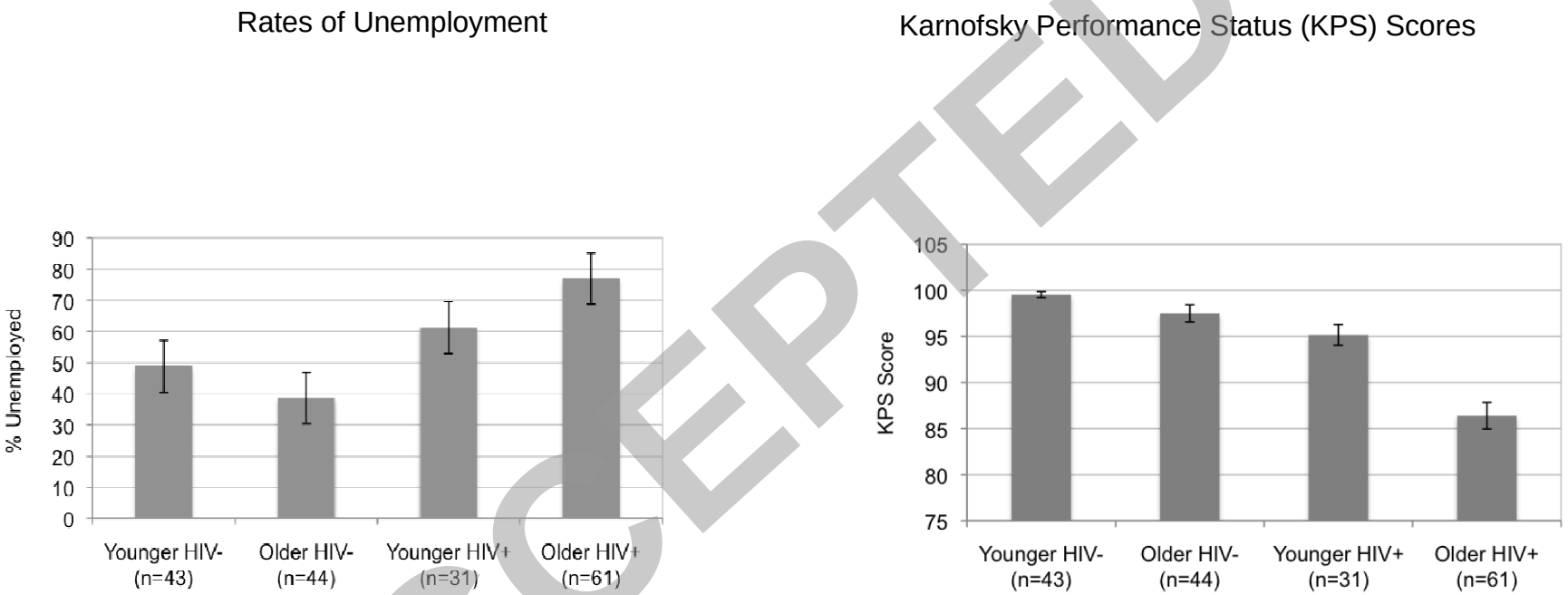
Note: *significant, $p < 0.05$; IADL = Instrumental activities of daily living; BADL = Basic activities of daily living; NPI = global neuropsychological impairment; MDD = Major Depressive Disorder; CD4 = Cluster of differentiation 4.

Figure 1. Significantly greater severity of IADL and BADL decline severity among old HIV+ individuals relative to all other groups (*p*s < 0.001).



Note. IADL = instrumental activities of daily living; BADL = basic activities of daily living; Cohen's d effect sizes of the difference between old HIV+ and all other groups on IADL decline severity were as follows: young HIV+ = 0.42; old HIV- = 0.71; young HIV- = 0.56.Cohen's d effect sizes of the difference between old HIV+ and all other groups on BADL decline severity were as follows: young HIV+ = 0.40; old HIV- = 0.67; young HIV- = 0.63.

Figure 2. Higher rates of unemployment and lower Karnofsky Performance Status (KPS) scores among the older HIV+ individuals



Note. Omnibus group differences significant (*p*s < .001); Cohen's d effect sizes of the difference between old HIV+ and all other groups on KPS scores were as follows: young HIV+ = -0.89; old HIV- = -0.99; young HIV- = -1.50.