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Does Age Influence the Frequency of Anxiety Symptoms and Disorders in HIV Disease?

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Introduction

Due to the effectiveness of combination antiretroviral therapy (cART) the life expectancy for persons living with HIV/AIDS (PLWHA) retained in healthcare has increased considerably over the past two decades (Leone et al., 2011). According to the Center for Disease Control (CDC), approximately 30% of PLWHA are over 50 years old, with prevalence rates of older PLWHA expected to continue to grow in the coming years (CDC, 2013). These older PLWHA face a number of unique stressors, including social (e.g., ‘double discrimination’ of ageism and HIV stigma; Emlet, 2006), physical (e.g., age-related diseases such as cardiovascular disease; Valcour, Shikuma, Watters, & Sacktor, 2004) and neurocognitive challenges (Ciccarelli et al., 2012) that are commonly observed by healthcare providers. Over time, HIV infection is also associated with chronic inflammation (Harezlak et al., 2011) and a compromising of the central nervous system (Ellis, Calero, & Stockin, 2009). Because of these, and possibly other reasons, several studies now show that older HIV+ adults carry a disproportionate burden of comorbid medical conditions as compared to their younger HIV+ and older HIV– counterparts (e.g., Longo, Camoni, Boros, & Suligoi, 2008; Rodriguez-Penney et al., 2013). These factors are associated with lower health-related quality of life (Rodriguez-Penney et al., 2013) and higher rates of disability and mortality among older PLWHA (Ammassari et al., 2001; Gorman, Foley, Ettenhofer, Hinkin, & van Gorp, 2009; Tsao, Dobalian, Moreau, & Dobalian, 2004).

There is little known about the expression of psychiatric disorders across the lifespan in HIV disease, yet it is likely that such biopsychosocial stressors influence the development and day-to-day impact of psychiatric disorders (e.g., anxiety) in older PLWHA in particular.

Irrespective of age, psychological disorders commonly occur in HIV disease (e.g., Bing et al., 2001; Pence, Miller, Whetten, Eron, & Gaynes, 2006) and can increase risk of disability (e.g., O'Cleirigh, Skeer, Mayer, & Safren, 2009). The presence of such biopsychosocial stressors may influence the development and day-to-day impact of psychiatric disorders in older PLWHA (e.g., anxiety, depression). In fact, early exploratory work has indicated that older PLWHA are more likely to report suicidal ideation (Kalichman, Heckman, Kochman, Sikkema, & Bergholte, 2000) and experience social isolation (Emlet, 2006) compared to younger PLWHA and seronegative persons. Although research has indicated that prevalence of many psychiatric disorders (e.g., anxiety) decreases slightly with age among the general population (Jeste, Blazer, & First, 2005), little is known about the expression of psychiatric disorders across the lifespan among PLWHA (Hughes, 2011). For instance, it may be that psychiatric disorders *increase* with age among PLWHA because of the aforementioned biopsychosocial stressors associated with HIV. Given the high rates of psychological disorders commonly occur in HIV disease (e.g., Bing et al., 2001; Pence et al., 2006) and subsequent increase risk of disability (e.g., O'Cleirigh et al., 2009), the examination of such disorders and their associated impact across the lifespan is important for this population. Given the aging of the HIV-infected population and clinically significant challenges faced by older PLWHA, it is important to examine the rates and effects of psychological symptoms and disorders that impact functional outcomes in this vulnerable subpopulation of the epidemic.

Anxiety disorders represent an important and yet understudied area of mental health research in PLWHA. Given that anxiety disorders have the highest lifetime prevalence of any psychiatric disorder, affecting up to 30% of the population over the lifespan, these findings highlight a highly prevalent and modifiable risk factor for physical disease (Demyttenaere et al., 2004; Kessler et al., 2005). Estimated rates of anxiety disorders among PLWHA are much higher than those among the general population, with rates above 25% in some large-scale studies (Bing et al., 2001; Pence et al., 2006) and above 40% in some subpopulations (e.g., substance users; Ingersoll, 2004). In particular, Panic Disorder and Generalized Anxiety Disorder (GAD) are higher among PLWHA than seronegatives (Bing et al., 2001; Pence et al., 2006). There are a number of reasons why anxiety disorders may be more common among PLWHA. For example, HIV is related to a variety of cognitive and social stressors, such as disease stigma, health worries, and disclosure concerns (Berger, Ferrans, & Lashley, 2001). Avoidance of such stressors may be related to negative reinforcement fear learning (whereby an individual avoids a feared/stressful situation and experiences reduced distress, promoting future avoidance of feared/stressful situations) and thereby increase the probability of anxiety symptoms and psychopathology (Brandt et al., 2015; Hayes, Wilson, Gifford, Follette, & Strosahl, 1996). Additionally, both HIV and cART produce a number of physical side-effects that elicit aversive interoceptive states, including headaches, nausea, and gastrointestinal symptoms (Johnson & Neilands, 2007). A cognitive misinterpretation of these interoceptive symptoms may be associated with elevations in anxiety symptoms, which may thereby further exacerbate physical sensations (Gonzalez, Zvolensky, Grover, & Parent, 2012; Gonzalez, Zvolensky, Parent, Grover, & Hickey, 2012; Lang, 1994). As such, one might expect the prevalence of anxiety disorders to be higher among older PLWHA when compared to younger PLWHA and HIV- groups.

The examination of anxiety among older PLWHA has a potential public health impact and is ostensibly relevant to the delivery of effective clinical care. Individuals who experience chronically high levels of anxiety are at increased risk for several diseases of ageing, including cardiovascular diseases (e.g., Benninghoven et al., 2006; Eaker, Sullivan, Kelly-Hayes, D'Agostino, & Benjamin, 2005; Kubzansky & Kawachi, 2000), autoimmune disorders (O'Donovan et al., 2015) and chronic inflammation (Carroll et al., 2011). The impact of anxiety disorders may be especially harmful for PLWHA, given the compromises made to the immune system as a result of HIV infection. As such, anxiety disorders represent the most common psychiatric disorder (Kessler et al., 2005) with elevated rates among PLWHA (Bing et al., 2001) that represent a modifiable risk factor for physical disease (Demyttenaere et al., 2004). One related issue is the extent to which anxiety disorders might play a role in the functional disability experienced by older PLWHA. We know much about the contributions of major depression in this regard (e.g., Heaton et al., 2004) and there is emerging research on bipolar disorder (e.g., Doyle et al., 2013). However, the effect of anxiety on functional impairment among older PLWHA is not well understood. In the limited research to date, anxiety disorders appear to increase risk of unemployment (Olagunju, Adeyemi, Ogbolu, & Campbell, 2012) and may affect certain health behaviors (e.g. medication adherence; Nel & Kagee, 2013) among PLWHA. Furthermore, there may be many factors that mediate and/or moderate the hypothesized relationship between anxiety and functional outcomes among older PLWHA. One potentially important factor in that regard is HIV-associated neuropsychological (NP) impairment (Antinori et al., 2007), which is estimated to occur in between 30–50% of the HIV+ population (Heaton et al., 2010). NP impairment has also been shown to uniquely affect functioning among this group (e.g., Morgan et al., 2012) and may be remediable (for a review, see Weber, Blackstone, & Woods, 2013). Among seronegatives, NP impairment has also been shown to have a bi-directional association with anxiety, such that each exacerbates the other (Gallacher et al., 2009; Palmer et al., 2007). As such, in the current study we have chosen to focus on NP impairment as a potentially influential variable in the relationship between anxiety and functional impairment.

Together, the present study aims to fill gaps in the existing clinical literature by examining: 1) the individual and combined effects of age and HIV disease on the frequency and clinical characteristics of anxiety disorders, controlling for potentially impacting clinical correlates of anxiety disorders common among PLWHA; and 2) the individual and combined effects of anxiety disorders and NP impairment on functional impairment among PLWHA. We hypothesized that there will be a significantly “stair step” effect regarding rates of anxiety symptoms, Panic Disorder, and GAD among this sample. Specifically, the HIV+ older group will possess the highest rates of such symptoms, followed by the HIV+ younger group, HIV – older group, and HIV– younger group, respectively. We additionally hypothesized that, among the HIV+ participants, concurrent anxiety disorder and NP impairment will significantly predict impaired functional impairment.

Materials and Methods

Participants

This study retrospectively identified 258 older (>50 years of age) and 188 younger (<40 years of age) participants recruited for an NIMH-funded study examining neurocognitive effects of aging and HIV disease through the HIV Neurobehavioral Research Program at the University of California, San Diego (UCSD). All 446 participants were recruited from local clinics and the community and had completed the anxiety disorders module of the Composite International Diagnostic Interview (CIDI version 2.1; World Health Organization, 1998) and Profile of Mood States Questionnaire (POMS). Approximately half (61.9%) of the sample was diagnosed with HIV, determined by either enzyme-linked immunosorbent assays and a Western Blot confirmatory test, or a MedMira Multiplo rapid test (MedMira Inc., Nova Scotia, Canada). HIV+ participants were recruited to serve as a comparison group (e.g., relatively high rates of substance and mood disorders) rather than a healthy cohort. Exclusion criteria for the study included the following: 1) histories of neurological conditions (e.g. seizure disorders, head injury with loss of consciousness >50 minutes) or, 2) severe psychiatric disorders (e.g. schizophrenia) that could impact neurocognitive performance, 3) a premorbid verbal IQ estimate below 70 as determined by the Wechsler Test of Adult Reading (WTAR; Wechsler, 2001), 4) a substance abuse or dependence disorder diagnosis within 30 days of evaluation, and 5) or a positive urine drug test screen for illicit substances or a positive Breathalyzer test for alcohol on the day of the evaluation.

Materials and Procedures

The parent study was approved by UCSD's Human Research Protections Program. Each participant provided written, informed consent before undergoing a comprehensive medical, psychiatric, neurocognitive, and functional assessment. Sociodemographic information was gathered by participant report during the study visit.

Psychiatric Assessment—All participants were administered the CIDI version 2.1 (World Health Organization, 1998(CIDI; Robins, Wing, & Helzer, 1983), a fully structured diagnostic interview that assessed psychiatric and substance use disorders using DSM-IV criteria. The specific anxiety and mood disorders assessed included generalized anxiety disorder, panic disorder (including agoraphobia), and major depressive disorder. The CIDI also was used to assess for alcohol and illicit substance dependence disorders (e.g. marijuana, cocaine, methamphetamines). When diagnostic criteria for these disorders were met, additional information was collected, including age of onset, duration, and recency. As is consistent with current epidemiological conventions, we report current (past 12-month) and lifetime rates of these disorders. The CIDI is commonly used in the HIV+ population (e.g., Freeman, Nkomo, Kafaar, & Kelly, 2008) and has evidenced good validity and specificity indexing psychiatric disorders (Robins et al., 1983).

Participants also completed the Profile of Mood States (POMS; McNair, Lorr, & Droppleman, 1992). The POMS is a self-report measure of affective states (e.g., anxiety, depression, confusion, fatigue) on which participants rate 65 mood-related adjectives on a

Likert-type scale ranging from 0 (not at all) to 4 (extremely) based on their mood in the past week, with higher scores representing greater levels of distress. Of particular interest to this study was the Tension/Anxiety subscale of the POMS, which is a 9-item subscale including participant rating of past-week feelings such as “anxious”, “nervous”, and “relaxed” (reverse-scored). The POMS has evidenced good internal reliability in other HIV+ samples (e.g., Gold et al., 2014).

Medical Assessment—The medical evaluation included an assessment of conditions that are often comorbid with HIV and aging that may also impact cognitive functioning (e.g. cardiovascular disease, Hepatitis C). Participants were administered a semi-structured medical history and treatment interview, including a review of symptoms and current antiretroviral and psychotropic drug use. Participants also underwent blood draw for relevant clinical disease biomarkers (e.g., CD4 cell counts, viral loads).

Neurocognitive Assessment—Each participant was administered a comprehensive neurocognitive evaluation, including an estimate of premorbid intellectual functioning (WTAR; Wechsler, 2001) and a neuropsychological test battery that assessed cognitive ability domains commonly affected by HIV and aging. Specifically, the domains and tests included in the battery were as follows: (1) *Learning* – Total learning trials 1–5 from the California Verbal Learning Test – Second edition (CVLT-II; Delis, Kramer, Kaplan, & Ober, 2000) and Logical Memory I from the Wechsler Memory Scale – Third Edition (WMS-III; Psychological Corporation, 1997); (2) *Memory* – CVLT-II Delayed Free Recall and WMS-III Logical Memory II; (3) *Attention* – Digit Span subtest from the Wechsler Adult Intelligence Scale – Third Edition (Psychological Corporation, 1997) and Trial 1 from the CVLT-II; (4) *Executive Functions* – Total Move Score from the Tower of London (ToL) – Drexel (Culbertson & Zillmer, 2001), Action Fluency (Woods et al., 2005), and Trail Making Test (TMT) Part B (Reitan & Wolfson, 1985); (5) *Speed of Information Processing (SIP)* – ToL-Drexel Total Execution Time and TMT part A; and (6) *Motor Skills* – dominant and nondominant hand total scores from the Grooved Pegboard Test (Klove, 1963). Raw scores on the neurocognitive tests were converted to demographically corrected *T* scores, which correct for age, education, sex, and ethnicity as appropriate (Heaton et al., 2004; Woods et al., 2005). Individual *T* scores were converted to deficit scores ranging from 0 (no impairment) to 5 (severe impairment) and averaged to create a global deficit score (GDS; Carey et al., 2004) for which a cutpoint of .5 is used to classify impairment.

Everyday functioning assessment—To represent general everyday functioning status, a composite of five domains were used to classify participants as “dependent” or “independent” (See Blackstone et al., 2012). Participants were classified as “dependent” if they met criteria for impairment in at least two of the following subdomains (range 0 – 5):

1. *Basic Activities of Daily Living (BADLs)*. Participant completed a modified version of the Lawton and Brody Activities of Daily Living Scale (Lawton & Brody, 1969) which included five items that assessed BADLs (housekeeping, home repairs, bathing, dressing, and laundry). Participants rated perceived “current” and “best” functioning levels on each of the BADLs. If decline from “best” to “current” functioning levels

were indicated in two or more of these domains, participants were classified as “dependent.”

2. *Instrumental Activities of Daily Living (IADLs)*. IADL status impairment status was also derived from the modified version of the Activities of Daily Living Scale (Lawton & Brody, 1969), which included 11 items that assessed IADLs (medication management, shopping, grocery shopping, managing finances, transportation, understanding reading and television material, planning social activities, cooking, child care, and work functioning). If decline from “best” to “current” functioning levels were indicated in two or more of these domains, participants were classified as “dependent.”
3. *Employment Status*. Participants self-reported current employment status during a semistructured interview and were categorized as “employed” (full- or part-time) or “unemployed”. Unemployed participants were classified as “dependent.”
4. *Functional performance status*. During the medical evaluation, a certified nurse assigned participants an overall functioning impairment rating via the Karnofsky Scale of Performance Status (Karnofsky & Burchenal, 1949). On the Karnofsky Scale, scores range from 100 (normal/no complaints/no evidence of disease) to 0 (dead). For the current study, a cutoff score of <90 was used to classify participants as “dependent”, a cutoff which has been used previously (e.g., Doyle et al., 2013; Schag, Heinrich, & Ganz, 1984).
5. *Cognitive Complaints*. The Confusion/Bewilderment subscale of the POMS (McNair et al., 1992) was used to index impairing cognitive symptoms. Participants rated mood-related adjectives on a Likert-type scale ranging from 0 (not at all) to 4 (extremely) based on their mood in the past week, with higher scores representing greater levels of distress. The Confusion/Bewilderment 7-item subscale included items such as “Forgetful” and “Uncertain.” Raw subscale scores were converted to sample-based z-scores, with a z-score cutoff of >1 used to classify participants as “dependent”, as has been used previously (Nyenhuis, Yamamoto, Luchetta, Terrien, & Parmentier, 1999).

Results

Group Classification and Differences in Demographic and Clinical Descriptive Factors

Participants were classified into one of four groups based on HIV serostatus (HIV+ or HIV−) and age (older [>50] or younger [<40]). In total, 163 older HIV+ persons (Older HIV+), 113 younger HIV+ persons (Younger HIV+), 95 older HIV− persons (Older HIV−), and 75 younger HIV− persons (Younger HIV−) were utilized for this study. Please see Table 1 for demographic, medical, and HIV disease characteristics of the study groups. Overall, the older study groups had more Caucasian participants than did the younger cohort ($p < .001$),

and the HIV+ samples had a significantly higher proportion of males than seronegatives ($p < .001$). Additionally, the older groups evidenced higher rates of Hepatitis C virus (HCV) infection ($p < .001$), with the highest frequency among older HIV+ individuals ($p < .001$). All study groups showed broadly similar rates of most substance use disorders, including alcohol, cannabis, methamphetamine, opioids, and “other” (p 's $> .05$); however, the younger HIV- group reported significantly lower rates of cocaine dependence than other study groups ($p < .001$). Within the HIV+ study cells, the older HIV+ group reported significantly longer duration of HIV infection ($p < .001$), lower nadir CD4 count ($p < .001$), and lower rates of detectable HIV RNA in plasma ($p < .001$) when compared to the younger HIV+ group. There was no significant age-related difference in current CD4 cell count or ARV status (p 's $> .10$).

Group Differences in Anxiety Disorder Diagnoses

Please see Table 2 for information regarding psychiatric characteristics of the sample, outlined by group. The planned approach to selection of model covariates was to identify variables from Table 1 that were both associated with HIV/age group status (e.g. ethnicity, gender, HCV infection) and anxiety disorder diagnoses (12-month and lifetime). No significant results were found (all p 's $> .10$), with the exception of HCV rates being higher in individuals with lifetime GAD; however, inclusion of HCV in the logistic regressions did not alter the findings reported below, and HCV was not a significant predictor in that model ($p > .10$). Additionally, inclusion of all other covariates (e.g., ethnicity, gender) did not significantly alter the findings reported below. As such, all analyses examining the independent and combined effects of age and HIV on anxiety outcomes were conducted without covariates and using a critical alpha level of .05. Specifically, a series of logistic regressions were conducted wherein each anxiety outcome was examined individually. The results of these analyses are listed below by anxiety outcome measure, and outlined in Figure 1.

Generalized Anxiety Disorder (GAD)—Regarding 12-month GAD diagnoses, the overall model was significant ($\chi^2 [3] = 12.96, p = .005$). As shown in Figure 1, results indicated a significant main effect of HIV serostatus ($\chi^2 [1] = 12.63, p < .001$; Odds Ratio [OR] = 11.73, 95% CI [2.39, 211.87]) but no significant main effect for age group ($\chi^2 [1] = 1.20, p = .273$; OR = 1.21, 95% CI [0.47, 3.34]), and no significant interaction ($\chi^2 [1] = 1.05, p = .306$). Similarly, regarding lifetime GAD the overall model was significant ($\chi^2 [3] = 20.42, p < .001$) with a significant main effect of HIV serostatus ($\chi^2 [1] = 17.97, p < .001$; OR = 4.42, 95% CI [2.06, 10.99]), but no significant main effect for age ($\chi^2 [1] = 3.65, p = .056$; OR = 1.57, 95% CI [0.84, 3.03]) or significant interaction ($\chi^2 [1] = 1.67, p = .197$).

As shown in Table 2, regarding GAD diagnosis the Younger HIV+ group reported a significantly earlier age of onset ($F(1,41) = 7.33, p = .010$, Hedge's $g = 0.85$) and fewer years since onset ($F(1,41) = 11.82, p = .001$, Hedge's $g = 1.08$) compared to the Older HIV+ group. There was no significant difference in disorder recency or years since most recent diagnosis between the groups (p 's $> .05$). Given the small number of HIV- individuals with GAD (Younger HIV- group $n = 1$; Older HIV- group $n = 6$), we excluded them from analyses of GAD characteristics.

Finally, clinical correlates of 12-mo GAD in the HIV+ Older and HIV+ Younger groups, including age, CD4 counts, MDD diagnosis, and substance use disorders were examined (see Table 1). As shown in Figure 3, results indicated that among the Younger HIV+ group, 12-month MDD was significantly associated with 12-month GAD ($p < .05$). Further, lifetime methamphetamine dependence was associated with GAD ($p < .05$). No other significant associations were found among the Younger HIV+ group (all $ps > .10$). Among the Older HIV+ group, Figure 3 shows that both 12-month and lifetime diagnoses of MDD were significantly associated with 12-month GAD ($ps < .05$). Further, lifetime methamphetamine dependence was associated with 12-month GAD ($p < .05$). No other factors presented in Table 1—including HIV disease characteristics—were significantly correlated with 12-month GAD diagnoses (all $ps > .10$).

Panic Disorder—Regarding 12-month Panic Disorder diagnoses the overall model fell at the level of a trend ($\chi^2 [3] = 7.63, p = .054$). As shown in Figure 1, results indicated a significant main effect of HIV serostatus ($\chi^2 [1] = 4.22, p = .040$; OR = 2.25, 95% CI [1.00, 5.78]), but no significant main effect for age group ($\chi^2 [1] = .005, p = .946$; OR = 1.55, 95% CI [0.74, 3.25]) and no significant interaction ($\chi^2 [1] = 2.62, p = .106$). Similarly, regarding lifetime Panic Disorder the overall model was significant ($\chi^2 [3] = 9.73, p = .021$), with a significant main effect of HIV serostatus ($\chi^2 [1] = 9.18, p = .002$; OR = 2.58, 95% CI [1.33, 5.41]), but no significant main effect for age group ($\chi^2 [1] = 7.63, p = .054$; OR = 1.20, 95% CI [0.67, 2.22]), and no significant interaction ($\chi^2 [1] = 1.04, p = .307$; see Figure 1).

As with GAD disorder characteristic analyses, the small number of HIV– individuals with Panic Disorder (Younger HIV– group $n = 3$; Older HIV– group $n = 8$) resulted in their exclusion from analyses of Panic Disorder characteristic. The Younger HIV+ group reported a significantly earlier age of onset ($F(1,40) = 8.57, p = .006$, Hedge's $g = 0.90$), earlier age at most recent episode ($F(1,40) = 100.39, p < .001$, Hedge's $g = 3.10$), and a significantly higher rate of 12-month diagnosis ($\chi^2 [1] = 7.87$, Fischer's exact $p = .011$; OR = 7.00, 95% CI [1.59, 30.80]) compared to the Older HIV+ group. No differences were found in rates of concurrent agoraphobia or years since most recent diagnosis of Panic Disorder diagnosis (all p 's $> .10$).

Finally, clinical correlates of 12-mo Panic Disorder in the HIV+ Older and HIV+ Younger groups, including age, CD4 count, lifetime MDD diagnosis and substance use disorders were examined (see Table 1). Among the Younger HIV+ group there were no significant associations with any clinically relevant variables (e.g., MDD, drug use) for either 12-month or lifetime Panic Disorder (all p 's $> .10$). Among the Older HIV+ group, however, 12-month Panic Disorder was significantly associated with both 12-month and lifetime MDD ($ps < .01$). These data are displayed in Figure 3.

POMS Tension/Anxiety—Regarding POMS Tension/Anxiety scores, the overall model was significant ($F(3,437) = 8.92, p < .001$), including a significant main effect of HIV serostatus ($t(439) = 5.07, p < .001$), but no significant main effect for age group ($t(439) = 0.41, p = .682$), and no significant interaction, ($t(439) = 1.68, p = .093$). Please see Figure 2.

Impact of Anxiety and Neuropsychological Impairment on Functional Impairment

Finally, the individual and combined effects of anxiety disorders and NP impairment on functional impairment were examined among the PLWH. Given that rates of anxiety disorder diagnoses did not differ significantly across HIV+ age groups in the current investigation, both groups were collapsed into one larger group indexing all 276 HIV+ individuals examined in this investigation. Because 12-month (MDD) diagnoses and AIDS status have been shown to affect functional impairment among PLWHA (e.g., Fellows, Byrd, & Morgello, 2013), they were chosen as covariates for this analysis. A logistic regression was run in which any 12-month anxiety disorder diagnosis, NP impairment, and their interaction were entered as predictor variables and functional impairment was entered as the criterion variable. Results indicated the overall model was significant, ($\chi^2(5) = 32.10, p < .001$). Although the main effect of 12-month anxiety disorder diagnoses did not reach statistical significance ($\chi^2(1) = 2.25, p = .134$), both NP impairment ($\chi^2(1) = 6.94, p = .008$) and the interaction between anxiety and NP impairment ($\chi^2(1) = 5.15, p = .023$) were significant predictors of functional impairment. As shown in Figure 4, individuals with lifetime anxiety disorder diagnosis and NP impairment had significantly higher rates of functional dependence (68.4%) as compared to individuals with one (or zero) risk factors (range 32.0% [No Anxiety or NP Impairment Group] to 43.4% [Anxiety Only Group]). Examination of each of the six domains that comprise our measure of NP impairment indicated that individuals with a deficit in one such domain, speed of information, as well as a 12-month anxiety disorder diagnosis had significantly higher rates of functional dependence (87.5%) compared to individuals with one (or zero) risk factors (range 34.6% [No Anxiety or Speed of Information Processing Impairment Group] to 40.0% [Speed of Information Processing Impairment Only Group]; $\chi^2(3) = 9.47, p = .024$).

Discussion

HIV disease is associated with higher rates of anxiety symptoms and disorders, but the potentially moderating effects of older age on the nature and extent of anxiety in HIV is not well understood. Findings from this study showed the expected effects of HIV disease on anxiety, as HIV+ adults had 4 to 11 times greater odds of having Panic Disorder and GAD as compared to a seronegative comparison sample. These HIV-associated risks for anxiety were independent of substance use disorders (e.g. alcohol, cannabis, methamphetamines), hepatitis C infection, and demographics, including age. Contrary to our expectations, age did not moderate the expression of anxiety symptoms or disorders among PLWH. The frequency of current anxiety symptoms, as well as 12-month and remote anxiety disorders (i.e., GAD and Panic Disorder) were highly comparable among older and younger PLWH in this study. Considering the large, well-characterized sample size, these data indicate that older PLWH may not be at disproportionate risk for anxiety relative to younger PLWHA. One possible explanation for this finding is that, despite the increased psychosocial and disease burden risks for anxiety, older persons may have developed adaptive coping strategies that buffer the development of anxiety (Baladon et al., 2015). For instance, older persons are more likely to “disengage” from stressful situations compared to younger counterparts, reducing negative emotional effects (Charles & Carstensen, 2008). As such, it may be that older age represents both a risk and protective factor for anxiety disorders among PLWH. Another possible

explanation is that older adults experience and process emotions differently than younger adults, with less bias towards negative emotion and less autonomic response (Flint et al., 1998; Gunning-Dixon et al., 2003; Neiss, Leigland, Carlson, & Janowsky, 2009). Future work might examine the factors specific to age in predicting anxiety disorders among this group.

Despite the non-significant effects of age on the frequency and severity of anxiety, there were some age effects on the onset of anxiety disorder diagnoses that are important to mention. First, regarding age of *first* anxiety disorder diagnosis, older PLWH evidenced significantly later age at onset for compared to Younger PLWH. One possibility is that older PLWH may have waited longer to seek assessment and treatment for their anxiety symptoms compared to their younger counterparts, which could reflect differing priorities regarding physical versus mental health care, differences in symptom severity, and/or generational attitudes regarding mental health. Another possible interpretation of these data is that retrospective memory recall biases may have impacted older PLWH reporting of their first diagnosis. In fact, prior studies suggest that older PLWH may be at disproportionate risk of declines in episodic memory functions (e.g., Woods et al., 2013).

With regard to the real-world implications of anxiety disorders across the lifespan, PLWHA with current NP impairment and *concurrent* anxiety disorder diagnoses were at especially high risk of functional impairment. Specifically, examination of the individual components comprising NP impairment indicated that only speed of information processing significantly predicted this association. Of note, the synergistic effects of NP impairment and anxiety were independent of important cofactors, including Major Depressive Disorder and AIDS status. There are several interpretive possibilities to explain the interplay of NP impairment and anxiety on everyday functioning; for instance, NP impairment can be associated with a range of negative affective symptoms, such as perceived memory loss and confusion, which are also common anxiety symptoms. Misinterpretation of these symptoms may serve to exacerbate anxiety, cyclically increasing NP impairment/anxiety symptoms, thereby impairing daily functioning. PLWH with HAND may not have the cognitive resources to cope or manage anxiety symptoms, and similarly anxiety may make it even more difficult for impaired individuals to effectively harness their remaining resources. Additionally, chronic health-related worry is common among PLWHA (e.g., Rohleder, Campbell, Petrak, & Matthews, 2013), and symptoms of cognitive decline may, for some individuals, be interpreted as a signal of HIV progression, increasing anxiety thereby interfering with daily functioning. Finally, it may be that the symptoms of anxiety are manageable alone, but become exponentially impactful to functioning outcomes when occurring concurrently with NP impairment. Future work employing longitudinal designs are needed to understand the directionality of the observed associations and other factors that may impact these relations.

There are a number of important secondary findings stemming from these analyses. First, as indicated in Table 1, comorbidity (or co-occurrence) of anxiety disorders and other examined disorders (i.e. Major Depressive Disorder and Substance Dependence Disorders) among PLWHA are remarkably high. Regarding MDD, less than 60% of the HIV+ study participants met diagnostic criteria, however, over 80% of anxiety-disorder diagnosed HIV+ study participants also meet MDD diagnostic criteria. This finding may indicate that anxiety

is a risk factor for depression among PLWHA. Additionally, among the HIV+ study participants rates of substance dependence were high (over 50% of the sample), which is consistent with previous literature (e.g., Bing et al., 2001). However, when examining these substance use disorders individually, methamphetamine dependence was significantly associated with 12-month GAD diagnosis across the lifespan in the HIV+ group. Existing evidence has suggested methamphetamine use among PLWHA is associated with high rates of anxiety (e.g., Shoptaw, Peck, Reback, & Rotheram-Fuller, 2003), and that withdrawal from methamphetamine subsequently causes anxiety (Semple et al., 2011). It may be that among PLWHA, a population among which methamphetamine use is high, persons with anxiety have difficulty quitting or reducing use because of a perceived inability to handle the resultant anxiety symptoms, mutually maintaining one another.

The current study contains the following limitations and must be interpreted accordingly. First, this study examined a community sample of convenience in Southern California, and therefore may not generalize to the greater PLWHA population. Second, we examined age-based group classifications rather than examining age as a continuous variable. Although this former approach is commonly used and perhaps more powerful for testing age-related effects, it does not enable us to generalize our findings to individuals in their 40s. Third, the parent study from which these data were taken utilized cross-sectional data. Future work would do well to examine the dynamic relationship between aging and the development and maintenance of anxiety disorders (including other disorders, such as social anxiety). Fourth, the CIDI is a self-report measure of psychopathology, and thus suffers from a number of limitations including self-report bias and diagnostic integrity. Future work utilizing diagnostic interviews for psychological disorders may provide more accurate information. Fifth, the POMS is a self-report measure capturing broad anxiety-based symptoms and must be interpreted accordingly. Future work may do well to use a more fine-grained analysis of anxiety symptoms to examine unique patterns or disparities. Sixth, data regarding participants' current and lifetime treatment for anxiety disorders was not assessed. Lifetime or concurrent treatment for anxiety disorders may impact these results, and future work should examine these relations. Seventh, employment status was a component of iADL while work functioning was a component of functional impairment. These variables are closely related and may artificially inflate the impact of employment difficulties in this sample. However, exclusion of employment from the everyday functioning variable did not significantly impact results. Finally, our sample was overrepresented by well-educated Caucasian men; as such, our results may not be generalizable to other subpopulations of the HIV epidemic.

In summary, the current study indicates that HIV disease is related to anxiety symptoms and diagnoses at a similar level in both younger and older adults. Across the lifespan, HIV-associated anxiety is associated with higher rates of depression and methamphetamine use disorders. Moreover, the clinical relevance of these findings is supported by the novel observation that anxiety and HIV-associated neurocognitive impairment have synergistic effects on everyday functioning outcomes. These data highlight the potential importance of including assessments for anxiety symptoms and disorders. Additionally, treatment strategies aimed at reducing anxiety symptoms that are tailored to PLWH may have a significant positive impact on real-world and health outcomes, including quality of life.

Conclusion

In summary, this cross-sectional investigation involving 163 older HIV+ persons, 113 younger HIV+ persons, 95 older HIV– persons, and 75 younger HIV– persons found that HIV serostatus, but not age nor the interaction of HIV serostatus and age, significantly impacted anxiety symptoms and disorders. Additionally, results indicated that across the lifespan of HIV+ individuals, comorbid HIV-associated neurocognitive and anxiety disorders significantly predicted reduced functional impairment. These results represent novel insight into the effects of aging with HIV on mental health and functional impairment. These results also have specific implications for social workers, highlighting the need for awareness of and appropriate screening for symptoms of anxiety across the lifespan among clients living with HIV disease, particularly among those with neurocognitive disorders. Anxiety may represent a serious barrier to engagement and retention in care (e.g., Gardner et al., in press), as well as adherence to social work interventions. As such, social workers may need to take preventative measures to ensure the success of referrals to appropriate clinical and social services for anxious clients. Well-validated anxiety screening measures (e.g., the POMS, as used in this study) may be of particular use. Future work is necessary in order to better understand underlying processes that may be affecting anxiety among older PLWHA (e.g., coping skills) and thereby impacting functional and clinical health outcomes.

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References

- Ammassari A, Murri R, Pezzotti P, Trotta MP, Ravasio L, De Longis P, Antinori A. Self-reported symptoms and medication side effects influence adherence to highly active antiretroviral therapy in persons with HIV infection. *J Acquir Immune Defic Syndr*. 2001; 28(5):445–449. [PubMed: 11744832]
- Antinori A, Arendt G, Becker JT, Brew BJ, Byrd DA, Cherner M, Wojna VE. Updated research nosology for HIV-associated neurocognitive disorders. *Neurology*. 2007; 69(18):1789–1799. [PubMed: 17914061]
- Baladon L, Fernandez A, Rubio-Valera M, Cuevas-Esteban J, Palao DJ, Bellon JA, Serrano-Blanco A. Prevalence of mental disorders in non-demented elderly people in primary care. *Int Psychogeriatr*. 2015; 27(5):757–768. [PubMed: 25643982]

- Benninghoven D, Kaduk A, Wiegand U, Specht T, Kunzendorf S, Jantschek G. Influence of anxiety on the course of heart disease after acute myocardial infarction - risk factor or protective function? *Psychother Psychosom.* 2006; 75(1):56–61. [PubMed: 16361875]
- Berger BE, Ferrans CE, Lashley FR. Measuring stigma in people with HIV: psychometric assessment of the HIV stigma scale. *Res Nurs Health.* 2001; 24(6):518–529. [PubMed: 11746080]
- Bing EG, Burnam MA, Longshore D, Fleishman JA, Sherbourne CD, London AS, Shapiro M. Psychiatric disorders and drug use among human immunodeficiency virus-infected adults in the United States. *Archives of General Psychiatry.* 2001; 58(8):721–728. [PubMed: 11483137]
- Blackstone K, Moore DJ, Heaton RK, Franklin DR Jr, Woods SP, Clifford DB, Grant I. Diagnosing symptomatic HIV-associated neurocognitive disorders: Self-report versus performance-based assessment of everyday functioning. *Journal of the International Neuropsychological Society.* 2012; 18(1):79–88. [PubMed: 22114912]
- Brandt CP, Zvolensky MJ, Vujanovic AA, Grover KW, Hogan J, Bakhshaie J, Gonzalez A. The mediating role of anxiety sensitivity in the relation between avoidant coping and posttraumatic stress among trauma-exposed HIV+ individuals. *Psychol Trauma.* 2015; 7(2):146–153. [PubMed: 25793690]
- Carey CL, Woods SP, Gonzalez R, Conover E, Marcotte TD, Grant I, Heaton RK. Predictive Validity of Global Deficit Scores in Detecting Neuropsychological Impairment in HIV Infection. *Journal of Clinical and Experimental Neuropsychology.* 2004; 26(3):307–319. [PubMed: 15512922]
- Carroll JE, Low CA, Prather AA, Cohen S, Fury JM, Ross DC, Marsland AL. Negative affective responses to a speech task predict changes in interleukin (IL)-6. *Brain, Behavior, and Immunity.* 2011; 25(2):232–238.
- Center for Disease Control. HIV Incidence. 2013. Retrieved from <http://www.cdc.gov/hiv/statistics/surveillance/incidence/index.html>
- Ciccarelli N, Fabbiani M, Baldonero E, Fanti I, Cauda R, Di Giambenedetto S, Silveri MC. Effect of aging and human immunodeficiency virus infection on cognitive abilities. *Journal of the American Geriatrics Society.* 2012; 60(11):2048–2055. [PubMed: 23110543]
- Charles, S.; Carstensen, L. *Psychology And Aging.* Vol. 23. Ipswich, MA: PsycINFO; 2008 Sep. Unpleasant situations elicit different emotional responses in younger and older adults; p. 495-504. [serial online] Available from: [Accessed January 25, 2016]
- Corporation, P. WAIS-III/WMS-III TEchnical Manual. Hardcover Brace: San Antonio; 1997.
- Culbertson, WC.; Zillmer, EA. Tower of London-Drexel Univeristy (TOLDX) Technical Manual. Tonawanda, NY: Multi-Health Systems; 2001.
- Delis DC, Kramer JH, Kaplan E, Ober BA. California Verbal Learning Test-second edition. Adult version. Manual. Psychological Corporation, San Antonio, TX. 2000
- Demyttenaere K, Bruffaerts R, Posada-Villa J, Gasquet I, Kovess V, Lepine JP, Chatterji S. Prevalence, severity, and unmet need for treatment of mental disorders in the World Health Organization World Mental Health Surveys. *JAMA.* 2004; 291(21):2581–2590. [PubMed: 15173149]
- Doyle KL, Morgan EE, Morris S, Smith DM, Little S, Iudicello JE, Woods SP. Real-world impact of neurocognitive deficits in acute and early HIV infection. *Journal of Neurovirology.* 2013; 19(6):565–573. [PubMed: 24277439]
- Eaker ED, Sullivan LM, Kelly-Hayes M, D'Agostino RB Sr, Benjamin EJ. Tension and anxiety and the prediction of the 10-year incidence of coronary heart disease, atrial fibrillation, and total mortality: the Framingham Offspring Study. *Psychosom Med.* 2005; 67(5):692–696. [PubMed: 16204425]
- Ellis RJ, Calero P, Stockin MD. HIV infection and the central nervous system: A primer. *Neuropsychology Review.* 2009; 19(2):144–151. [PubMed: 19415500]
- Emler CA. 'You're Awfully Old to Have This Disease': Experiences of Stigma and Ageism in Adults 50 Years and Older Living With HIV/AIDS. *The Gerontologist.* 2006; 46(6):781–790. [PubMed: 17169933]
- Fellows RP, Byrd DA, Morgello S. Major depressive disorder, cognitive symptoms, and neuropsychological performance among ethnically diverse HIV+ men and women. *Journal Of The International Neuropsychological Society.* 2013; 19(2):216–225. [PubMed: 23290446]
- Flint AJ, Koszycki D, Vaccarino FJ, Cadieux A, Boulenger JP, Bradwejn J. Effect of aging on cholecystokinin-induced panic. *Am J Psychiatry.* 1998; 155(2):283–285. [PubMed: 9464213]

- Freeman M, Nkomo N, Kafaar Z, Kelly K. Mental disorder in people living with HIV/AIDS in South Africa. *South African Journal of Psychology*. 2008; 38(3):489–500.
- Gardner L, Marks G, Shahani L, Giordano TP, Wilson TE, Drainoni ML, Metsch LR. Assessing efficacy of a retention in care intervention among HIV patients with depression, anxiety, heavy alcohol consumption, and illicit drug use. *AIDS*. (in press).
- Gallacher J, Bayer A, Fish M, Pickering J, Pedro S, Dunstan F, Ben-Shlomo Y. Does anxiety affect risk of dementia? Findings from the Caerphilly Prospective Study. *Psychosom Med*. 2009; 71(6):659–666. [PubMed: 19553290]
- Gold JA, Grill M, Peterson J, Pilcher C, Lee E, Hecht FM, Spudich S. Longitudinal characterization of depression and mood states beginning in primary HIV infection. *AIDS Behav*. 2014; 18(6):1124–1132. [PubMed: 24385231]
- Gonzalez A, Zvolensky MJ, Grover KW, Parent J. The role of anxiety sensitivity and mindful attention in anxiety and worry about bodily sensations among adults living with HIV/AIDS. *Behavior Therapy*. 2012; 43(4):768–778. [PubMed: 23046779]
- Gonzalez A, Zvolensky MJ, Parent J, Grover KW, Hickey M. HIV symptom distress and anxiety sensitivity in relation to panic, social anxiety, and depression symptoms among HIV-positive adults. *AIDS Patient Care and STDs*. 2012; 26(3):156–164. [PubMed: 22248334]
- Gorman AA, Foley JM, Ettenhofer ML, Hinkin CH, van Gorp WG. Functional consequences of HIV-associated neuropsychological impairment. *Neuropsychol Rev*. 2009; 19(2):186–203. [PubMed: 19472057]
- Gunning-Dixon FM, Gur RC, Perkins AC, Schroeder L, Turner T, Turetsky BI, Gur RE. Age-related differences in brain activation during emotional face processing. *Neurobiol Aging*. 2003; 24(2):285–295. [PubMed: 12498962]
- Harezlak J, Buchthal S, Taylor M, Schifitto G, Zhong J, Daar E, Navia B. Persistence of HIV-associated cognitive impairment, inflammation, and neuronal injury in era of highly active antiretroviral treatment. *AIDS*. 2011; 25(5):625–633. [PubMed: 21297425]
- Hayes SC, Wilson KG, Gifford EV, Follette VM, Strosahl K. Experimental avoidance and behavioral disorders: a functional dimensional approach to diagnosis and treatment. *J Consult Clin Psychol*. 1996; 64(6):1152–1168. [PubMed: 8991302]
- Heaton RK, Clifford DB, Franklin DR Jr, Woods SP, Ake C, Vaida F, Grant I. HIV-associated neurocognitive disorders persist in the era of potent antiretroviral therapy: Charter study. *Neurology*. 2010; 75(23):2087–2096. [PubMed: 21135382]
- Heaton RK, Marcotte TD, Mindt MR, Sadek J, Moore DJ, Bentley H, Grant I. The impact of HIV-associated neuropsychological impairment on everyday functioning. *Journal of the International Neuropsychological Society*. 2004; 10(3):317–331. [PubMed: 15147590]
- Hughes AK. HIV knowledge and attitudes among providers in aging: Results from a national survey. *AIDS Patient Care and STDs*. 2011; 25(9):539–545. [PubMed: 21823908]
- Ingersoll K. The impact of psychiatric symptoms, drug use, and medication regimen on non-adherence to HIV treatment. *AIDS Care*. 2004; 16(2):199–211. [PubMed: 14676026]
- Jeste DV, Blazer DG, First M. Aging-related diagnostic variations: need for diagnostic criteria appropriate for elderly psychiatric patients. *Biol Psychiatry*. 2005; 58(4):265–271. [PubMed: 16102544]
- Johnson MO, Neilands TB. Neuroticism, Side Effects, and Health Perceptions Among HIV-Infected Individuals on Antiretroviral Medications. *J Clin Psychol Med Settings*. 2007; 14(1):69–77. [PubMed: 18568088]
- Kalichman SC, Heckman T, Kochman A, Sikkema K, Bergholte J. Depression and thoughts of suicide among middle-aged and older persons living with HIV-AIDS. *Psychiatr Serv*. 2000; 51(7):903–907. [PubMed: 10875956]
- Karnofsky DA, Burchenal JH. Investigation of the Karnofsky performance status as a measure of quality of life. *Health Psychology*. 1949; 3(129)
- Klove H. Clinical Neuropsychology. *Med Clin North Am*. 1963; 46:1647–1658.
- Kubzansky LD, Kawachi I. Going to the heart of the matter: do negative emotions cause coronary heart disease? *J Psychosom Res*. 2000; 48(4–5):323–337. [PubMed: 10880655]

- Lang, PJ. The motivational organization of emotion: Affect-reflex connections. In: van Goozen, SHM.; Van de Poll, NE.; Sergeant, JA., editors. *Emotions: Essays on emotion theory*. Hillsdale, NJ: England: Lawrence Erlbaum Associates, Inc; 1994. p. 61-93.
- Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist*. 1969; 9(3):179-186. [PubMed: 5349366]
- Leone S, Gregis G, Quinzan G, Velenti D, Cologni G, Soavi L, Maggiolo F. Causes of death and risk factors among HIV-infected persons in the HAART era: analysis of a large urban cohort. *Infection*. 2011; 39(1):13-20. [PubMed: 21246246]
- Longo B, Camoni L, Boros S, Suligoi B. Increasing proportion of AIDS diagnoses among older adults in Italy. *AIDS Patient Care STDS*. 2008; 22(5):365-371. [PubMed: 18435593]
- McNair DM, Lorr M, Droppleman LF. *POMS Manual: Profile of Mood States*. Edits, San Diego, CA. 1992
- Neiss MB, Leigland LA, Carlson NE, Janowsky JS. Age differences in perception and awareness of emotion. *Neurobiol Aging*. 2009; 30(8):1305-1313. [PubMed: 18155323]
- Nel A, Kagee A. The relationship between depression, anxiety and medication adherence among patients receiving antiretroviral treatment in South Africa. *AIDS Care*. 2013; 25(8):948-955. [PubMed: 23231527]
- Nyenhuis DL, Yamamoto C, Luchetta T, Terrien A, Parmentier A. Adult and geriatric normative data and validation of the profile of mood states. *J Clin Psychol*. 1999; 55(1):79-86. [PubMed: 10100834]
- O'Cleirigh C, Skeer M, Mayer KH, Safren SA. Functional impairment and health care utilization among HIV-infected men who have sex with men: the relationship with depression and post-traumatic stress. *J Behav Med*. 2009; 32(5):466-477. [PubMed: 19526337]
- O'Donovan A, Cohen BE, Seal KH, Bertenthal D, Margaretten M, Nishimi K, Neylan TC. Elevated risk for autoimmune disorders in Iraq and Afghanistan veterans with posttraumatic stress disorder. *Biological Psychiatry*. 2015; 77(4):365-374. [PubMed: 25104173]
- Olagunju AT, Adeyemi JD, Ogbolu RE, Campbell EA. A study on epidemiological profile of anxiety disorders among people living with HIV/AIDS in a sub-Saharan Africa HIV clinic. *AIDS Behav*. 2012; 16(8):2192-2197. [PubMed: 22772942]
- Palmer K, Berger AK, Monastero R, Winblad B, Backman L, Fratiglioni L. Predictors of progression from mild cognitive impairment to Alzheimer disease. *Neurology*. 2007; 68(19):1596-1602. [PubMed: 17485646]
- Pence BW, Miller WC, Whetten K, Eron JJ, Gaynes BN. Prevalence of DSM-IV-defined mood, anxiety, and substance use disorders in an HIV clinic in the Southeastern United States. *J Acquir Immune Defic Syndr*. 2006; 42(3):298-306. [PubMed: 16639343]
- Reitan, RM.; Wolfson, D. *The Halstead-Reitan Neuropsychologic Test Battery: Therapy and clinical interpretation*. Rucson, AZ: Neuropsychological Press; 1985.
- Robins, L.; Wing, J.; Helzer, J. Geneva, Switzerland: World Health Organization; 1983. *Composite International Diagnostic Interview (CIDI)*.
- Rodriguez-Penney AT, Iudicello JE, Riggs PK, Doyle K, Ellis RJ, Letendre SL, Woods SP. Comorbidities in persons infected with HIV: Increased burden with older age and negative effects on health-related quality of life. *AIDS Patient Care and STDs*. 2013; 27(1):5-16. [PubMed: 23305257]
- Rohleder P, Campbell T, Petrak J, Matthews A. Working with people living with HIV. *The Psychologist*. 2013; 26(7):506-507.
- Schag CC, Heinrich RL, Ganz PA. Karnofsky performance status revisited: reliability, validity, and guidelines. *J Clin Oncol*. 1984; 2(3):187-193. [PubMed: 6699671]
- Shoptaw S, Peck J, Reback CJ, Rotheram-Fuller E. Psychiatric and substance dependence comorbidities, sexually transmitted diseases, and risk behaviors among methamphetamine-dependent gay and bisexual men seeking outpatient drug abuse treatment. *J Psychoactive Drugs*. 2003; 35(Suppl 1):161-168. [PubMed: 12825759]
- Tsao JC, Dobalian A, Moreau C, Dobalian K. Stability of anxiety and depression in a national sample of adults with human immunodeficiency virus. *J Nerv Ment Dis*. 2004; 192(2):111-118. [PubMed: 14770055]

- Valcour VG, Shikuma CM, Watters MR, Sacktor NC. Cognitive impairment in older HIV-1-seropositive individuals: prevalence and potential mechanisms. *AIDS*. 2004; 18(Suppl 1):S79–S86. [PubMed: 15075502]
- Weber E, Blackstone K, Woods SP. Cognitive neurorehabilitation of HIV-associated neurocognitive disorders: A qualitative review and call to action. *Neuropsychology Review*. 2013; 23(1):81–98. [PubMed: 23417497]
- Wechsler, D. Wechsler Test of Adult Reading; WTAR. Psychological Corporation; 2001.
- Woods SP, Hoebel C, Pirogovsky E, Rooney A, Cameron MV, Grant I, Gilbert PE. Visuospatial temporal order memory deficits in older adults with HIV infection. *Cognitive and Behavioral Neurology*. 2013; 26(4):171–180. [PubMed: 24378603]
- Woods SP, Scott JC, Sires DA, Grant I, Heaton RK, Tröster AI. Action (verb) fluency: Test-retest reliability, normative standards, and construct validity. *Journal of the International Neuropsychological Society*. 2005; 11(4):408–415. [PubMed: 16209421]

Figure 1.

Frequency of lifetime (> 12 months since last diagnosis) or 12-month (diagnosis 12 months) Generalized Anxiety Disorder (Panel A) and Panic Disorder (Panel B).

Figure 2. Box-and-whisker plots for POMS Tension/Anxiety scores (possible range 0–36) among the four HIV-serostatus and age groups.

Figure 3.
Rates of Major Depressive Disorder in Older and Younger HIV+ groups with a lifetime diagnosis of Generalized Anxiety Disorder (Panel A) or Panic Disorder (Panel B).

Figure 4. Everyday functioning impairment among HIV+ individuals grouped by presence of neuropsychological impairment and lifetime anxiety (Generalized Anxiety Disorder or Panic Disorder).

Table 1

Demographic, psychiatric, medical, and HIV disease characteristics.

	Younger HIV- (n = 75)	Older HIV- (n = 95)	Younger HIV+ (n = 113)	Older HIV+ (n = 163)	p	Group Differences
Age (years)	30.4(0.7)	56.8(0.6)	32.4(0.5)	56.2(0.5)	<.001	Y-, Y+ < O-, O+
Education (years)	14.1(0.3)	14.2(0.3)	13.4(0.2)	14.0(0.2)	--	--
Ethnicity (% White)	42.3	66.32	39.82	67.48	<.001	Y-, Y+ < O-, O+
Gender (% men)	64.0	71.58	86.73	82.82	<.001	Y-, O- < Y+, O+
Estimated Verbal IQ (WTAR)	103.1(1.2)	103.6(1.1)	100.7(1.1)	102.4(0.9)	--	--
Neuropsychological Impairment ^a (%)	16.0	15.8	23.9	26.4	--	--
12-Month Major Depression (%)	9.3	10.5	34.5	28.22	<.001	Y-, O- < Y+, O+
Lifetime Major Depression ^b (%)	28.0	40.0	56.6	55.2	<.001	Y-, O- < Y+, O+
POMS Depression/Dejection Scale	5.7	7.3	11.2	10.0	.002	Y- < Y+, O+
Substance Dependence ^c (%)	41.3	47.4	52.2	55.2	--	--
Alcohol ^d (%)	30.7	29.5	37.2	29.5	--	--
Cannabis ^d (%)	18.7	10.5	12.4	11.0	--	--
Cocaine ^d (%)	4.0	19.0	15.9	25.2	<.001	Y- < Y+, O-, O+
Methamphetamine ^d (%)	21.3	19.0	31.0	27.6	--	--
Opioids ^d (%)	10.7	10.5	6.2	8.6	--	--
Other ^d (%)	1.3	0.0	0.9	0.6	--	--
Hepatitis C infection (%)	4.1	17.0	2.7	31.2	<.001	Y-, Y+ < O- < O+
Estimated Duration of Infection (mo)	-	-	83.4(6.5)	198.3(7.2)	<.001	Y+ < O+
AIDS (%)	-	-	35.7	66.2	<.001	Y+ < O+
CD4 count (cells/ μ L)	-	-	602.6(26.6)	561.5(23.7)	--	--
Nadir CD4 (cells/ μ L)	-	-	281.5(17.5)	176.8(13.2)	<.001	Y+ > O+
Prescribed ARV (%)	-	-	80.5	88.3	--	--
Plasma RNA detectable (%)	-	-	34.6	18.1	<.001	Y+ > O+
Among those on ARV (%)	-	-	19.54	12.6	--	--

Note. Mean (standard error); Younger < 40 years; Older = 50 years; WTAR = Wechsler Test of Adult Reading; EDI = Estimated Duration of Infection; AIDS = Acquired Immune Deficiency Syndrome; CD4 = Cluster of Differentiation 4; ARV = antiretrovirals.

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Impairment defined as global deficit score ≥ 0.5 .
Includes both current (e.g., within the last 12 months) and lifetime diagnosis.
Any lifetime diagnosis of dependence on alcohol or illicit substance.
Lifetime diagnosis of dependence.

Table 2
Disease characteristics for individuals with Generalized Anxiety Disorder or Panic Disorder.

	Younger HIV ⁻	Older HIV ⁻	Younger HIV ⁺	Older HIV ⁺	p	Group Differences
Generalized Anxiety ^a						
Age at First Diagnosis (years)	25.0(0.0)	47.8(5.7)	21.7(2.0)	32.5(2.7)	.010	Y+ < O+
Years Since First Diagnosis (years)	5.0(0.0)	16.2(9.0)	9.7(1.9)	23.0(2.6)	.001	Y+ < O+
Age at Most Recent Episode (years)	27.0(0.0)	61.3(4.4)	29.5(1.4)	50.1(1.6)	< .001	Y+ < O+
Years Since Recent Diagnosis (years)	3.0(0.0)	2.7(1.1)	1.9(0.8)	5.4(1.4)	--	--
12-Month Diagnosis ^b (%)	0.0	16.7	46.7	39.3	--	--
Panic Disorder ^c						
Age at First Diagnosis (years)	19.0(6.4)	26.5(6.6)	19.1(2.4)	31.8(3.2)	.006	Y+ < O+
Years Since First Diagnosis (years)	15.7(6.3)	34.4(8.1)	12.7(2.2)	24.4(3.4)	.013	Y+ < O+
Age at Most Recent Episode (years)	28.33(5.0)	58.5(4.1)	27.6(1.6)	49.2(2.0)	< .001	Y+ < O+
Years Since Recent Diagnosis (years)	6.3(3.5)	2.4(1.7)	4.1(1.4)	7.1(1.7)	--	--
12-Month Diagnosis ^b (%)	66.7	62.5	82.4	40.0	.011	O+ < Y+
with Agoraphobia (%)	33.3	75.0	52.9	56.0	--	--
POMS Tension/Anxiety ^e (of 36)	6.5(0.5)	10.7(1.0)	12.9(1.7)	11.7(1.1)	--	--
POMS Depression/Dejection (of 60)	6.2(0.8)	13.4(2.2)	15.5(3.0)	13.1(1.7)	--	--
12-Month Major Depression ^{d,e} (%)	0.0	20.0	40.7	48.9	--	--
Lifetime Major Depression ^{d,e} (%)	75.0	80.0	77.8	84.4	--	--
Prescribed Psychotropics ^f (%)	0.0	80.0	61.9	57.89	--	--

Note. Group differences computed among HIV+ individuals only due to small number of HIV- individuals with an anxiety disorder diagnosis.

^a Sample sizes: Younger HIV⁻ = 1; Younger HIV⁺ = 15; Older HIV⁻ = 6; Older HIV⁺ = 28.

^b Denotes diagnosis within the last 12 months.

^c Sample sizes: Younger HIV⁻ = 3; Younger HIV⁺ = 17; Older HIV⁻ = 8; Older HIV⁺ = 25.

^d Includes both recent (e.g., within the last 12 months) and lifetime diagnosis.

^e Among participants with lifetime or recent (within 12 months) anxiety disorder diagnosis.

^f Among participants with anxiety disorder diagnosis within last 12 months.