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Post-traumatic stress is associated with verbal learning, memory, and psychomotor speed in HIV-infected and HIV-uninfected women

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Abstract

The prevalence of post-traumatic stress disorder (PTSD) is higher among HIV-infected (HIV+) women compared with HIV-uninfected (HIV−) women, and deficits in episodic memory are a common feature of both PTSD and HIV infection. We investigated the association between a probable PTSD diagnosis using the PTSD Checklist-Civilian (PCL-C) version and verbal learning

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and memory using the Hopkins Verbal Learning Test in 1004 HIV+ and 496 at-risk HIV− women. HIV infection was not associated with a probable PTSD diagnosis (17 % HIV+, 16 % HIV−; p=0.49) but was associated with lower verbal learning (p<0.01) and memory scores (p<0.01). Irrespective of HIV status, a probable PTSD diagnosis was associated with poorer performance in verbal learning (p<0.01) and memory (p<0.01) and psychomotor speed (p<0.001). The particular pattern of cognitive correlates of probable PTSD varied depending on exposure to sexual abuse and/or violence, with exposure to either being associated with a greater number of cognitive domains and a worse cognitive profile. A statistical interaction between HIV serostatus and PTSD was observed on the fine motor skills domain (p= 0.03). Among women with probable PTSD, HIV− women performed worse than HIV+ women on fine motor skills (p=0.01), but among women without probable PTSD, there was no significant difference in performance between the groups (p= 0.59). These findings underscore the importance of considering mental health factors as correlates to cognitive deficits in women with HIV.

Keywords

HIV; Post-traumatic stress disorder; Women; Cognition

Introduction

Trauma exposure and post-traumatic stress disorder (PTSD) are more common among HIV-infected (HIV+) individuals compared with HIV-uninfected (HIV−) individuals (Brief et al. 2004; Machtinger et al. 2012; Spies et al. 2012), particularly among women who comprise 24 % of HIV cases in the USA. The prevalence of childhood sexual abuse in HIV+ women (Machtinger et al. 2012) is approximately double that of women in the USA (Cougle et al. 2010), and the estimate of PTSD occurrence in HIV+ women (Machtinger et al. 2012) is almost three times higher than the general population of women in the USA (Breslau et al. 1998; Kessler et al. 2012; Kessler et al. 1995). According to a recent meta-analysis of 29 studies in HIV+ women, the estimated prevalence of childhood sexual abuse was 39 %, adult sexual abuse was 35 %, physical violence was 54 %, and recent PTSD was 30 % (Machtinger et al. 2012). In the Women's Interagency HIV study (WIHS), the largest prospective study of HIV+ women in the USA, 31 % of HIV+ women reported childhood sexual abuse, 66 % reported a history of domestic violence, and 21 % reported domestic violence within the previous 6 months (Cohen et al. 2000). Understanding how PTSD and trauma affect health-related outcomes in HIV+ individuals is a priority, particularly among women who experience disproportionately higher rates of these exposures.

In HIV− individuals, exposure to traumatic stressors can have profound physiological and psychological consequences including cognitive deficits and brain dysfunction (Lupien et al. 2009). In a recent meta-analysis (N=60 studies) of cognitive outcomes associated with PTSD, PTSD was associated with lower performance on tests of verbal learning and memory, attention/working memory, speed of information processing, executive functioning, and language (Scott et al. 2015). However, these findings were based primarily on small samples (PTSD median sample size=22.5; range, 7–224) of well-educated men (Scott et al. 2015). The association between PTSD and cognitive dysfunction was not

affected by comorbid psychiatric diagnoses such as depression. However, studies in the meta-analysis used a myriad of approaches to account for the high overlap between PTSD and depression; some studies excluded for depression, others included individuals with comorbid depression but did not control for depression, and others controlled for depressive symptoms. Addressing the high comorbidity between PTSD and depression is therefore critical, particularly when using self-report measures of these highly correlated constructs.

In HIV− individuals, PTSD is associated with alterations in the hippocampus and prefrontal cortex, brain regions subserving these cognitive abilities (Grossman et al. 2002; Woon et al. 2010). In a study of women with early childhood sexual abuse, women with PTSD showed a failure of left hippocampal activation during a verbal memory task compared with women without PTSD even after controlling for hippocampal atrophy (Bremner et al. 2003). PTSD and HIV infection affect similar brain regions in women. Verbal learning and memory are the cognitive domains most strongly associated with HIV infection, followed by psychomotor speed (Maki et al. 2015). In the WIHS, high levels of perceived stress and elevated anxiety were associated with decreases in verbal learning and memory only within the context of HIV (Rubin et al. 2015; Rubin et al. 2014). In WIHS participants, verbal memory deficits are associated with alterations in hippocampal function during verbal encoding and recognition as measured with functional magnetic resonance imaging (fMRI) (Maki et al. 2009). It, therefore, stands to reason that PTSD might contribute to deficits in verbal memory in HIV+ women.

Findings from cohorts of mostly HIV+ men suggest that childhood sexual or physical trauma, intense acute stress, and PTSD are each associated with an increased risk of HIV-related morbidity and mortality including increased subjective cognitive complaints (Evans et al. 1997; Leserman 2003). In a small sample of predominately HIV+ men, PTSD symptoms were associated with worse memory although no other cognitive abilities were assessed in relation to PTSD symptoms (Moradi et al. 2013). Such associations have not been examined in cohorts of HIV+ women. The current investigation examined whether PTSD further exacerbates episodic memory deficits in a large sample of HIV+ women participating in the WIHS. Our primary aim was to investigate whether a probable PTSD diagnosis using the PTSD Checklist-Civilian version (PCL-C) is associated with deficits in verbal learning and memory and processing speed observed in HIV+ women compared with HIV− women in the WIHS.

Methods

Study population

All participants were enrolled in the WIHS, a national, multi-site (Chicago, Bronx, Brooklyn, Washington DC, San Francisco, Los Angeles), longitudinal study of women with or at-risk for HIV. Enrollment occurred after approval by each site's institutional review board and the WIHS Executive Committee. All participants provided written informed consent. Study methodology, standardized data collection, training of interviewers, and retention have previously been reported (Bacon et al. 2005; Barkan et al. 1998).

An initial comprehensive neuropsychological testing battery was administered from April 2009 through April 2011 (Maki et al. 2015). Of active English-speaking WIHS participants (*n*= 1908), 1595 (84 %) women completed the cognitive test battery (Maki et al. 2015). We analyzed 1500 (1004 HIV+; 94 % of the cohort) after excluding 95 participants who met one or more of the following exclusion criteria: (1) missing data on the PCL-C (*n*=21); (2) conditions with potentially confounding effects on neurocognitive tests (e.g., hearing loss, impaired vision, acute intoxication) (*n*=11); (3) history of stroke/CVA (*n*=13); and (4) self-reported use of antipsychotic medication in the past 6 months (*n*=50). Compared with women who did not complete the cognitive test battery, the women who completed the cognitive testing were more likely to be Black non-Hispanic; to be less educated; to have a lower annual household income; to be hepatitis C virus (HCV) antibody positive; to smoke; to report recent crack, cocaine, and/or heroin and marijuana use; to be from the Bronx and Brooklyn study sites; and were less likely to be HIV+ or be from the LA and Chicago study sites (*p* values <0.05). All factors were controlled for using propensity score methods (see "Statistical analysis").

Measures

Neuropsychological outcome measures—The neurocognitive test battery assessed seven cognitive domains (Maki et al. 2015). The primary cognitive domain of interest was *verbal memory*, which was assessed with the Hopkins Verbal Learning Test (HVLT), a 12-item list-learning task (Brandt and Benedict 2001) frequently administered in studies of HAND (Heaton et al. 2010). We calculated an overall verbal memory domain T-score (M=50, SD=10) by averaging derived T-scores (see "Statistical analysis") for the following two HVLT indices: (1) number of words recalled after a 20-min delay (delayed recall) and (2) percent retention (delayed recall/maximum score on trial 2 or 3).

Secondary cognitive domains assessed included verbal learning, attention and concentration, executive functioning (behavioral inhibition, mental flexibility, working memory), psychomotor speed, verbal fluency, and fine motor skills. T-scores were computed for each of the secondary cognitive domains. The T-score for each cognitive domain was computed by averaging the derived T-scores of all individual outcomes within each domain. *Verbal learning* was assessed with the following two HVLT indices: (1) trial 1 (single trial learning) and (2) total words recalled across each of three learning trials (total learning). *Attention and concentration* were assessed with trials 1 and 2 of the Stroop test (Comalli et al. 1962), trail making test part A, and the control/attention condition from the letter-number sequence test (LNS) from the Wechsler Adult Intelligence Scale IV (WAIS IV). *Executive functioning* was assessed with trial 3, the color-word condition (interference) of the Stroop test (Comalli et al. 1962), which measures behavioral inhibition, trail making test part B, which measures mental flexibility, and the working memory condition of LNS. *Psychomotor speed* was assessed with the symbol digit modalities test (SDMT). *Verbal fluency* was assessed with a letter and category fluency task. *Fine motor skills* were assessed with the grooved pegboard test. All timed outcomes were skewed to the right and therefore log transformed.

Primary explanatory variable

PTSD Checklist-Civilian version: The PCL-C is a widely used 17-item self-report measure of the DSM-IV symptoms of PTSD (Weathers et al. 1991). The PCL-C asks about symptoms (re-experiencing, avoidance, hyperarousal) in relation to "stressful experiences." Thus, PTSD symptoms may reflect multiple events. The PCL-C is reliable and valid in civilian populations (Ruggiero et al. 2003) and the Cronbach's alpha in the present sample was 0.94. A probable PTSD diagnosis from the PCL-C correlates highly (r>.90) with clinician-administered assessments (Blanchard et al. 1996; Weathers and Ford 1996). A total symptom severity score (range=17–85) can be obtained by summing the scores from each of the 17 items. Five of the items assess re-experiencing trauma symptoms (e.g., nightmares or flashbacks concerning the trauma), seven assess avoidance symptoms (e.g., avoidance of thoughts or feelings about the trauma), and five items assess hyperarousal symptoms (e.g., difficulty concentrating, trouble falling or staying asleep). A probable PTSD diagnosis is given if DSM-IV symptom criteria are met (≥1 B item—re-experiencing, ≥3 C items—avoidance, and ≥2 D items—arousal); and total severity score exceeds a given cut-point (>44) based on previously published studies. This approach was found to be optimal in terms of diagnostic sensitivity and specificity, compared with clinician assessments, in a population (Harrington and Newman 2007) that most closely matched the WIHS study population.

Covariates

Predictors for cognition (see Maki et al. 2015) included: annual household income; hepatitis C virus antibody (HCV) status (indicative of HCV exposure); self-reported recent (within 6 months), former (>6 months), or no (never) use of marijuana, crack, cocaine, and/or heroin and smoking; self-reported recent (within 6 months) heavy alcohol use for women defined by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) (>7 drinks/week or >4 drinks in one sitting), current depressive symptoms (Center for Epidemiologic Studies Depression Scale (CES-D) score ≥16); recent antidepressant use; and study geographic site. Self-report data on a history of past abuse (sexual, physical violence, domestic coercion) were available for 92 % (n= 1380) of the women.

Statistical analysis

Differences in demographic characteristics among the four groups (HIV−/PTSD−; HIV−/PTSD+; HIV+/PTSD−; HIV+/PTSD+) were examined using two-way between subjects analysis of variance (ANOVA) for continuous variables and Chi-square tests for categorical variables. In the absence of published cognitive test norms for low-income minority women, we followed Heaton et al. (1991) and prior work within the WIHS (Maki et al. 2015; Manly et al. 2011; Rubin et al. 2015; Rubin et al. 2014; Valcour et al. 2015), using a regression approach to estimate premorbid levels of function for the total sample based on scores of the comparison group (HIV− women). We did this by regressing each cognitive outcome on age, years of education, race/ethnicity, and results of the reading recognition subtest from the *Wide Range Achievement Test—Revised* (WRAT-R) (Wilkinson 1993), as a proxy for educational quality (Manly et al. 2002). The resulting unstandardized beta weights, constants, and standard errors were used to calculate predicted scores for each test that were

then subtracted from each woman's actual score and transformed to scores (using means of 50 and standard deviations of 10) that could be more easily compared across all cognitive outcomes. This method was conducted in the largest sample of WIHS women (*N*= 1521; Maki et al. 2015) and then applied to the present sample.

We used propensity score methods to effectively control for confounding of depressive symptoms, smoking, alcohol and drug use, antidepressant use, HCV status, income, and study site (see Supplemental text/Supplemental Fig. 1). Propensity methods were selected over the more traditional approach of controlling for confounding (including variables in regression models as covariates) because they (1) eliminated the issue of multicollinearity between the primary explanatory variables (PTSD) and depressive symptoms (covariate) and (2) simplified analyses to having only HIV, PTSD, and the interaction as predictor variables in the models.

In the overall sample, we used inverse probability weighted (IPW) linear regression analyses (Robins et al. 2000) to examine the separate and interactive associations of HIV status and PTSD on the primary and secondary cognitive domains. Where significant effects were observed in cognitive domains, we also examined the separate and interactive associations of HIV and PTSD on the individual outcomes (also *T*-scores) contributing to the domain scores. Planned exploratory analyses were also conducted to examine the association of HIV and PTSD with cognition stratified by the occurrence of sexual abuse and violence. Significance was defined as $p<0.05$ (two-sided). Cohen's *d* effect sizes are also reported (small effect=0.2; medium effect=0.5; large effect=0.8) (Cohen 1992). Analyses were performed using SAS (version 9.4, SAS Institute Inc., Cary, NC).

Results

Table 1 shows demographic and clinical information for the HIV+ (*N*=1004: 830 PTSD−; 174 PTSD+) and HIV− (*N*=496: 417 PTSD−; 79 PTSD+) groups prior to using the propensity score method. Participants ranged in age from 25 to 87 years (M=46.2, SD=9.4); 64 % African American, and 20 % Hispanic. Compared with HIV− women, HIV+ women were significantly older (47 vs. 43 years, $p<0.001$), had a higher minority representation (Hispanic, 23 % vs. 18 %, $p= 0.03$), were more likely to have positive HCV serology (31 vs. 19 %, $p<0.001$) and to use antidepressant medication (17 vs. 10 %, $p<0.001$), and were less likely to engage in heavy alcohol use (15 vs. 25 %, $p<0.001$) and marijuana use (15 vs. 22 %, $p<0.001$). The proportion of women with probable PTSD was similar in HIV− (16 %) and HIV+ (18 %) groups ($p=0.49$). Regardless of HIV status, women with probable PTSD compared with women without PTSD were older (48 vs. 46, $p=0.004$); had a lower annual household income ($p<0.001$); and were more likely to have positive HCV serology (33 vs. 26 %, $p=0.01$), to use antidepressant medication (25 vs. 13 %, $p<0.001$), to smoke (56 vs. 40 %, $p<0.001$), to use marijuana (22 vs. 16 %, $p<0.001$), to use crack, cocaine, and/or heroin (12 vs. 5 %, $p<0.001$), and to have elevated depressive symptoms (CES-D cutoff ≥16; 79 vs. 20 %, $p<0.001$). After using the propensity weights, the only group differences to remain significant were heavy drinking and crack, cocaine, and/or heroin use (*p* values=0.02) (see Supplemental Table 1). Including these covariates in the final analyses did not alter the results, and they were, therefore, not included in the analyses.

Table 2 provides the cognitive test scores (mean, SE) as a function of PTSD and HIV after using the weighted database, as well as the results from the regression analyses. See Supplemental Table 2 for a comparison of the cognitive test score means before using propensity scores and after using the weighted database. In general, the IPW statistical method led to a lowering of the cognitive test scores of the HIV−/PTSD+ group compared with all other groups. In the IPW linear regression analyses, HIV+ women performed significantly worse than HIV− women on the verbal learning ($p<0.001$, $d = 0.17$) and memory ($p = 0.003$, $d = 0.17$) domains (Table 2). HIV+ women performed significantly worse than HIV− women on all individual HVLT indices (p values <0.05; d values, 0.14–0.18).

Regardless of HIV status, PTSD was significantly and inversely associated with cognitive performance (Table 2). PTSD+ women performed worse than PTSD− women on the verbal learning ($p<0.001$, $d=0.22$), memory ($p=0.001$, $d= 0.22$), and psychomotor speed ($p<0.001$, $d=0.29$) domains. Regarding individual test scores, PTSD+ women performed worse than PTSD− women on all HVLT indices (p values <0.05; d values, 0.18–0.23) and SDMT ($p<0.001$, $d=0.29$).

Unexpectedly, PTSD did not interact with HIV status to influence either verbal learning ($p=0.85$) or memory ($p= 0.88$) (Table 2/see Supplemental Fig. 2). However, PTSD interacted with HIV status to significantly influence fine motor skills ($p=0.03$); among PTSD+ women, HIV− women performed significantly worse than HIV+ women ($B=-4.45$, SE=1.73, $p=0.01$). In contrast, among PTSD− women, there was no significant difference in performance on fine motor skills between HIV+ and HIV− women ($B=0.35$, SE=0.65, $p=0.59$).

Exploratory regression analyses tested whether HIV status and PTSD status were associated with cognitive performance separately in women reporting and not reporting sexual abuse. Among women not reporting sexual abuse, HIV status showed more associations with cognitive performance compared with PTSD status (Table 3). HIV status was negatively associated with verbal learning and memory, attention, executive functioning, and psychomotor speed. By comparison, PTSD status was inversely associated only with verbal learning. Conversely, among women reporting sexual abuse, PTSD status showed more associations with cognitive performance compared with HIV status. PTSD status was negatively associated with verbal learning and memory, attention, executive functioning, psychomotor speed, and fine motor skills. However, HIV status was only negatively associated with verbal learning and memory. A similar pattern was noted for a history of violence (see Supplementary Table 3).

Discussion

Women with probable PTSD performed worse than women without PTSD irrespective of HIV status on measures of verbal learning, memory, and processing speed. The cognitive correlates of probable PTSD were broader and worse particularly among women exposed to sexual abuse and/or physical violence. Unexpectedly, there were no significant interactions for HIV and probable PTSD on the primary outcomes of interest, only on a secondary

outcome, fine motor skills. Generally, these findings indicate that probable PTSD, when examined in a sample of low-income predominately minority women with similar levels of depressive symptoms, is associated with deficits in verbal learning, memory, and processing speed, but that HIV+ women are not differentially vulnerable to these effects.

Overall, the finding that PTSD was associated with impairments in verbal learning, memory, and processing speed is consistent with the existing literature. A meta-analysis of 60 studies of PTSD in males and females demonstrated that PTSD was most strongly associated with verbal learning and memory, attention/working memory, speed of information processing, executive functioning, and language (Scott et al. 2015). The largest effect sizes, all of which were medium (Cohen's *d* values ranged from 0.43 to 0.62), were noted for verbal learning and speed of information processing, followed by attention/working memory, verbal memory, executive functioning, and language. Smaller associations were reported between PTSD and executive functioning, language, visuo-spatial abilities, and visual learning and memory (Cohen's *d* values ranged from 0.29 to 0.38). Fine motor skills were not assessed in the studies included by Scott et al. (2015). In the present WIHS study, women with probable PTSD performed worse on measures of verbal learning and memory, but these effects were small (*d* values=0.22). Although the individual studies did not uniformly control for depression or depressive symptoms, in the meta-analysis, the magnitude of the PTSD-cognition associations was not influenced by depression or anxiety disorders. Some of the differences might reflect the particular sample being studied. Studies in the meta-analyses comprised smaller samples of mostly educated men whereas the present study involved a female sample of low-income minority women. Additionally, previous studies did not rigorously control for the influence that depressive symptoms, separate from PTSD, have on cognitive function, i.e., confounding. There is a high comorbidity between depression and PTSD (as high as 69–78 %)(Brown et al. 2001; Kessler et al. 1995). In the present study, we used propensity scores to mitigate confounding by depression as well as other factors (i.e., drug use). Differences between our study and others might also reflect our use of a self-reported symptom inventory versus a diagnostic interview to assess PTSD (e.g., *Structural Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders*).

In the present study, probable PTSD showed the strongest association with psychomotor speed (*d*=0.29) which is congruent with Scott et al. (2015); albeit our effect size was much smaller and *T*-scores were in the normal range, thus these associations may be statistically rather than clinically significant. In HIV− individuals with PTSD, functional abnormalities in the prefrontal cortex (Sartory et al. 2013; Simmons and Matthews 2012) are linked to processing speed impairments (Aupperle et al. 2012). Specifically, in a sample of women with PTSD related to intimate partner violence, hypoactivation in the dorsal lateral prefrontal cortex (DLPFC) was associated with impairments in a standardized measure of processing speed (Aupperle et al. 2012). The association between PTSD and processing speed may be due to stress-related alterations in the DLPFC and/or disruption of white matter integrity, as reduced white matter integrity is also associated with decreased processing speed (Madden et al. 2012) and PTSD (Kim et al. 2006; Sanjuan et al. 2013; Schuff et al. 2011).

In contrast to other studies, we found no association between PTSD symptoms and performance on tests of working memory, executive functioning, attention, and concentration (Scott et al. 2015). Associations with these measures only became apparent when stratifying by history of sexual abuse and physical violence. Exploratory analyses indicated that it was only among women exposed to sexual abuse or violence that PTSD was negatively associated with cognition, and these associations were evident in almost all cognitive domains. HIV status had greater associations with cognitive performance among women without exposure to sexual abuse or violence. The particular pattern of cognitive effects in PTSD might depend on the exposure, with exposure to sexual abuse and violence being associated with a broader and worse cognitive profile. Although we do not know the exact timing of abuse in the present study, early life trauma coupled with trauma throughout the lifespan is a risk factor for enduring functional and structural abnormalities in the hippocampus and prefrontal cortex (Lupien et al. 2007; Lupien et al. 2009). The cognitive correlates of these brain structures include learning and memory, attention, processing speed, and executive functioning deficits. These associations may in part be due to lasting alterations including epigenetic programming in the hypothalamic-pituitary-adrenal (HPA) axis (Lupien et al. 2007; Lupien et al. 2009).

Unexpectedly, we found that probable PTSD interacted with HIV status to influence fine motor skills. This interaction was in a counterintuitive direction, such that among women with probable PTSD, HIV− women performed worse on fine motor skills than did HIV+ women. The previous meta-analysis did not examine the association of PTSD and fine motor skills (Scott et al. 2015). Although HIV+ women may have a presumed vulnerability because of their medical status, HIV+ women in the WIHS and in the community have had greater access to medical care and social services compared with at-risk HIV− women (Baran et al. 2014). It is possible that greater access to care may mitigate against particular cognitive declines and mental health conditions including PTSD.

Our study had several limitations. The cross-sectional design of this study precludes causal inferences about the direction of association between PTSD and cognitive impairment. Probable PTSD was measured using the PCL-C rather than diagnostic interview (Scott et al. 2015). Although previous studies indicate that the PCL-C is a good marker of PTSD via diagnostic interview, it has yet to be examined in the WIHS. If the PCL-C has poor sensitivity, then there are probably women with PTSD in the no-PTSD group thus diluting our association between PTSD and cognition. Diagnostic assessments are ongoing in the WIHS population, and therefore, in the future, we will be able to validate these findings with a more objective measure of PTSD. We examined these effects using a cohort and not a nationally representative sample of HIV+ or HIV− women. Recall bias and positive response bias are possible for reports of negative behaviors such as substance use. The women who completed the cognitive test battery differed from the overall WIHS cohort on a number of factors (i.e., race, education, income, drug use). Additionally, we were not able to control for PTSD treatment status which might have influenced cognitive outcomes. Finally, the failure to control for use of medications (psychotropic—other than anti-psychotics, which was an exclusion criterion) may have interfered with our assessment of cognitive performance.

Conclusions

Probable PTSD was associated with difficulties in the cognitive domains of verbal learning and memory and processing speed in a large sample of ethnically diverse, low SES women, who report high rates of sexual abuse and violence. These associations were no stronger in HIV+ women than in HIV− women. Treating PTSD symptoms in order to reduce emotional distress and potentially improve cognitive functioning in women may prove beneficial, particularly among women self-reporting sexual abuse and/or violence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Background characteristics of HIV-infected and HIV-uninfected women as a function of probable PTSD

Characteristics	HIV−		HIV+	
	PTSD− (*n*=417) *n* (%)	PTSD+ (*n*=79) *n* (%)	PTSD− (*n*=830) *n* (%)	PTSD+ (*n*=174) *n* (%)
Background characteristics				
Age (M (SD))[HIV, PTSD, HIV×PTSD]	42.9 (10.10)	46.7 (9.01)	47.3 (8.93)	48.1 (8.02)
WRAT-R (M (SD))[PTSD]	92.4 (16.79)	88.7 (17.09)	92.8 (17.65)	90.1 (18.27)
Years of education (M (SD))[PTSD]	12.6 (2.73)	11.9 (2.88)	12.5 (2.86)	11.8 (3.18)
Race/ethnicity[HIV]				
African American, non-Hispanic	267 (64)	41 (52)	544 (65)	106 (61)
White, non-Hispanic	41 (10)	9 (11)	113 (14)	23 (13)
Hispanic	91 (22)	25 (32)	141 (17)	38 (22)
Other	18 (4)	4 (5)	32 (4)	7 (4)
Hepatitis C virus antibody (HCV)[HIV, PTSD]	74 (18)	19 (24)	247 (30)	65 (37)
Recent				
Average annual household income (M (SD))[PTSD]	3.7 (2.26)	2.8 (1.92)	3.9 (2.29)	3.0 (1.90)
Alcohol use[HIV]				
Abstainer	200 (48)	43 (54)	498 (60)	109 (63)
Not heavy	120 (29)	11 (14)	201 (24)	42 (24)
Heavy	97 (23)	25 (32)	131 (16)	23 (13)
Antidepressant medication use[HIV, PTSD, HIV×PTSD]	31 (7)	17 (22)	134 (16)	46 (26)
Depressive symptoms (CES-D ≥16)[PTSD]	87 (21)	63 (80)	163 (20)	138 (79)
Smoking[PTSD]				
Never	109 (26)	5 (6)	242 (29)	29 (17)
Former	129 (31)	21 (27)	267 (32)	55 (32)
Recent	179 (43)	53 (67)	321 (39)	90 (52)
Marijuana use[HIV, PTSD]				
Never	90 (22)	8 (10)	231 (28)	31 (18)
Former	239 (57)	51 (64)	485 (58)	107 (61)
Recent	88 (21)	20 (25)	114 (14)	36 (21)
Crack, cocaine, and/or heroin use[PTSD]				
Never	190 (46)	13 (16)	346 (42)	52 (30)
Former	202 (48)	52 (66)	446 (54)	106 (61)
Recent	25 (6)	14 (18)	38 (4)	16 (9)
Abuse ever (sexual, violence, or domestic)[a, PTSD]	262 (68)	58 (88)	533 (69)	142 (89)
Sex abuse [PTSD]	155 (40)	37 (55)	315 (41)	90 (56)
Violence[PTSD]	212 (55)	52 (79)	442 (57)	125 (78)
Domestic coercion[PTSD]	164 (43)	43 (65)	356 (46)	108 (67)
HIV-related clinical characteristics				
Nadir CD4 count (cells/μl; M (SD)	–	–	217.2 (157.96)	201.3 (158.24)

Characteristics	HIV−		HIV+	
	PTSD− (*n*=417) *n* (%)	PTSD+ (*n*=79) *n* (%)	PTSD− (*n*=830) *n* (%)	PTSD+ (*n*=174) *n* (%)
CD4 count (cells/μl)	–	–		
>500			436 (53)	76 (44)
≥200 and <500			294 (35)	69 (40)
<200			100 (12)	29 (17)
Viral load (HIV RNA (cp/ml))	–	–		
Undetectable			440 (53)	86 (50)
<10,000			279 (34)	58 (33)
≥10,000			111 (13)	30 (17)
Medication use	–	–		
No cART			194 (23)	42 (24)
cART+ <95 % medication adherence			100 (12)	32 (18)
cART+ ≥95 % medication adherence			536 (64)	100 (57)
ART duration (years; M (SD))	–	–	11.1 (4.67)	11.5 (4.17)

HIV main effect of HIV status is significant at $p<0.05$, *PTSD* main effect of PTSD is significant at $p<0.05$, *HIV×PTSD* interaction between HIV status and PTSD is significant at $p<0.05$, *Recent* within 6 months of the most recent WIHS visit, *Former* any previous use but not within the past 6 months, *WRAT-R* Wide Range Achievement Test Standard Score, *CES-D* Center for Epidemiologic Studies Depression Scale, *Heavy alcohol use* >7 drinks/week or >4 drinks at a sitting, *Undetectable* <48 copies/ml, *cART* combination antiretroviral therapy, *ART* antiretroviral therapy

[a]One hundred twenty women were missing data as these data were not collected at the LA and San Fran WIHS sites. For income: 1=≤$6000; 2= $6001–12,000; 3=$12,001–18,000; 4=$18,001–24000; 5=$24,001–30,000; 6=$30,001–$36,000; 7=$36,001–$75,000; 8=>$75,000

Table 2

Associations of HIV status and PTSD with cognitive test performance

Outcomes	*n*	Estimated means (SE)				HIV infection (HIV+ vs. HIV−)		Probable PTSD (yes vs. no)		HIV×PTSD
		HIV−/PTSD−	HIV−/PTSD+	HIV+/PTSD−	HIV+/PTSD+	B (SE)	Cohen's *d*	B (SE)	Cohen's *d*	B (SE)
Primary										
Verbal memory	1496	50.3 (0.5)	46.9 (1.3)	48.4 (0.3)	46.9 (0.7)	−1.66 (0.54)**	0.17	−2.13 (0.70)**	0.22	1.95 (1.61)
Delayed recall	1496	50.1 (0.5)	47.6 (1.4)	48.3 (0.3)	46.1 (0.8)	−1.81 (0.56)**	0.18	−2.30 (0.74)**	0.23	0.39 (1.69)
% retention	1496	50.6 (0.5)	46.3 (1.4)	48.5 (0.4)	47.7 (0.8)	−1.50 (0.59)*	0.14	−1.96 (0.77)*	0.19	2.97 (1.70)
Verbal learning	1496	50.3 (0.4)	48.4 (1.3)	48.7 (0.3)	46.7 (0.7)	−1.58 (0.52)**	0.17	−2.02 (0.68)**	0.22	−0.17 (1.56)
Trial 1	1496	50.4 (0.5)	48.2 (1.3)	48.7 (0.3)	47.2 (0.7)	−1.66 (0.55)**	0.17	−1.77 (0.71)*	0.18	0.73 (1.64)
Total trials 1–3	1496	50.1 (0.5)	48.6 (1.4)	48.8 (0.3)	46.2 (0.7)	−1.51 (0.55)**	0.15	−2.28 (0.72)**	0.23	−1.07 (1.66)
Secondary										
Attention	1321	50.1 (0.4)	49.1 (1.1)	49.2 (0.3)	48.9 (0.6)	−0.79 (0.43)	0.11	−0.60 (0.58)	0.10	0.66 (1.31)
Executive function	1253	50.2 (0.4)	49.5 (1.2)	49.8 (0.3)	49.2 (0.7)	−0.38 (0.51)	0.04	−0.64 (0.67)	0.08	0.11 (1.51)
Psychomotor speed	1488	50.1 (0.5)	48.0 (1.4)	49.3 (0.3)	45.9 (0.7)	−1.06 (0.56)	0.11	−2.93 (0.73)***	0.29	−1.24 (1.68)
Verbal fluency	1487	49.7 (0.4)	48.9 (1.2)	49.7 (0.3)	49.8 (0.7)	0.17 (0.50)	0.02	−0.13 (0.66)	0.01	0.92 (1.51)
Fine motor skills	1443	48.8 (0.5)	46.1 (1.5)	49.1 (0.4)	50.5 (0.9)	1.03 (0.61)	0.09	0.11 (0.83)	0.01	4.09 (1.85)*

Results from inverse probability-weighted (IPW) linear regression analyses on the primary and secondary cognitive outcomes. Totals do not add to 1500 because not all women completed all cognitive tests due to participant refusal or other known (e.g., neuropathy) or unknown reasons

B parameter estimates, *SE* standard errors, *n* sample size

*** $p<0.001$;

** $p<0.01$;

* $p<0.05$

Table 3

Associations of HIV status and PTSD with cognitive test performance stratified by sexual abuse

Outcomes	No sexual abuse (*n*=784)		Sexual abuse (*n*=597)	
	HIV infection (HIV+ vs. HIV−) B (SE)	Probable PTSD (yes vs. no) B (SE)	HIV infection (HIV+ vs. HIV−) B (SE)	Probable PTSD (yes vs. no) B (SE)
Primary				
Verbal memory	−2.27 (1.13)*	−2.01 (1.97)	−1.43 (0.62)*	−2.05 (0.73)**
Delayed recall	−2.15 (1.19)	−1.89 (2.08)	−1.98 (0.67)**	−2.18 (0.78)**
% retention	−2.40 (1.22)*	−2.14 (2.13)	−0.88 (0.67)	−1.92 (0.79)*
Verbal learning	−1.75 (0.72)*	−2.39 (1.00)*	−1.32 (0.84)	−2.46 (0.96)*
Trial 1	−1.76 (0.75)*	−3.24 (1.06)**	−1.12 (0.89)	−2.03 (1.01)*
Total trials 1–3	−1.75 (0.77)*	−1.55 (1.07)	−1.51 (0.89)	−2.88 (1.01)**
Secondary				
Attention	−2.79 (0.88)**	1.92 (1.53)	−1.18 (0.53)*	−2.57 (0.63)***
Executive				
Function	−2.34 (1.02)*	−0.67 (1.87)	−0.79 (0.63)	−1.64 (0.74)*
Psychomotor				
Speed	−2.60 (1.16)*	−3.14 (2.02)	−0.61 (0.65)	−3.20 (0.76)***
Verbal				
Fluency	−1.20 (1.00)	−1.23 (1.78)	−0.10 (0.60)	−1.12 (0.70)
Fine motor skills	−0.92 (1.16)	3.72 (2.11)	0.64 (0.74)	−1.86 (0.86)*

Results from inverse probability weighted (IPW) linear regression analyses on the primary and secondary cognitive outcomes stratified by sexual abuse

B parameter estimates, *SE* standard errors

*** $p<0.001$;

** $p<0.01$;

* $p<0.05$