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Impaired Cognition Predicts Falls Among Women with and Without HIV Infection

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Abstract

Objective: To determine if domain-specific neurocognitive (NC) impairments predict falls in HIV+ compared to HIV- women.

Design: Cross-sectional data analysis from 825 HIV+ and 392 HIV- women in the Women's Interagency HIV Study (WIHS) with NC testing within two years prior to falls surveys.

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Methods: NC impairment (T score <40) was assessed in seven domains: executive function, psychomotor speed, attention, learning, memory, fluency, and fine motor function. For domains associated with any fall within 6 months in simple logistic regression (p<.05), hierarchical regression models evaluated associations between NC impairment and odds of falling, adjusting for: (1) study site and HIV, (2) demographics, (3) comorbid conditions, (4) substance use/CNS active medications, and HIV-specific factors.

Results: Median age was higher in HIV+ than HIV- women (51yrs vs. 48yrs); prevalence of falls was similar (19% HIV+, 16% HIV-). Overall, executive function (OR [odds ratio]=1.82, 95%CI [confidence interval] 1.21–2.74; *P*=0.004), psychomotor speed (OR=1.59, 95%CI 1.05–2.42, *P*=0.03), and fine motor (OR 1.70, 95%CI 1.11–2.61, *P*=0.02) impairments were associated with greater odds of falls in fully adjusted models. In fully adjusted models, associations of executive function, psychomotor speed, and fine motor were non-significant among HIV+ women; conversely, among HIV- women, associations with impaired executive and fine motor functions were strengthened, and remained significant.

Conclusions: Cognitive impairment was associated with falls among middle-aged HIV- but not HIV+ women. Additional studies should elucidate mechanisms by which domain-specific NC impairment impacts fall risk among older HIV+ and HIV- women, and how different factors modify relationships between cognition and falls.

Keywords

Fall; HIV; aging; women; cognition

INTRODUCTION

As a result of the survival benefit of potent antiretroviral therapy (ART), the life-expectancy of persons with HIV (PWH) in Western nations now approaches that of HIV-uninfected (HIV-) persons.[1–4] It is estimated that half of PWH in the United States (U.S.) are now age 50 or older,[5] and this growing demographic will comprise a substantial group of older persons in clinical care.[6] PWH experience a high burden of non-AIDS comorbidities typically associated with advanced age and chronic inflammation,[7,8] including cardiovascular disease,[9–11] osteoporosis,[12] and neurocognitive impairment (NCI), as well as geriatric syndromes such as falls, frailty, and functional and mobility impairment.[13–15]

Almost half of U.S. PWH demonstrate mild-to-moderate NCI despite use of suppressive ART.[16,17,18] Neurocognition, gait, and vascular disease are strongly linked in aging,[19–21] and there is unequivocal evidence that mobility and neurocognitive functions are interrelated. Mild NCI is associated with falls in geriatric populations,[22,23] particularly among older women.[24] Moreover, older women are at a greater fall risk compared to older men, although the reasons for these differences remain elusive.[25–27]

Emerging data suggest an unexpectedly high prevalence of falls in middle-aged PWH on ART, and greater fall risk among women compared with men.[28] Although the prevalence and incidence of self-reported falls was similar between HIV-infected (HIV+) and HIV- women with a mean age of 48 years in the Women's Interagency HIV Study (WIHS) cohort,

we identified several factors associated with increased risk of falls, including use of multiple central nervous system (CNS) active medications, cannabis use, and subjective cognitive complaints.[29,30] To date, no studies have investigated the association between NCI and falls in PWH. Therefore, the objective of this study is to examine the relationships between objectively measured NCI and falls among HIV+ and HIV- WIHS women. We hypothesized that domain-specific NCI would predict falls among HIV+ women.

METHODS

Study Population

The WIHS is a multicenter prospective cohort study of the natural and treated history of HIV infection in women with or at-risk for HIV infection that enrolled initially in 1994–95 at six sites nationally (Bronx/Manhattan NY, Brooklyn NY, Chicago IL, Washington DC, San Francisco CA, and Los Angeles, CA), and additionally in 2001–02 and 2011–12. WIHS methods and baseline cohort characteristics have been described previously.[31,32] Overall WIHS recruitment focused on African-American and Latina women to reflect the domestic HIV epidemic in the US; for the HIV- group, recruitment was also targeted to include women who engaged in high-risk behaviors to ensure comparability with HIV+ women such as injection drug use, having a sexually transmitted disease, having unprotected sex with three or more men or protected sex with more than five men, or having exchanged sex for drugs, money, or shelter. At semiannual visits, participants complete physical examinations, provide biological specimens, and undergo extensive assessment of clinical, behavioral, and demographic characteristics via face to-face interviews. A comprehensive neuropsychological test battery is administered every 2 years. Informed consent was obtained using procedures approved by committees on human research at each of the collaborating institutions.

Neuropsychological Test Battery

A neuropsychological test battery was first administered between 2009 and 2011, and repeated every 2 years thereafter; the current analyses utilize neurocognitive tests performed from 10/01/2013 to 9/30/2015. The battery includes 8 tests: Hopkins Verbal Learning Test-Revised (HVLT-R), Letter-Number Sequencing (LNS), Trail Making (TMT), Stroop Test, Symbol Digit Modalities Test (SDMT), Controlled Oral Word Association Test (COWAT), Category Fluency Test (Animals), and Grooved Pegboard (GPEG). Seven domains were assessed using these tests: (1) executive function (outcomes=time to completion on TMT Part B and Stroop Trial 3); (2) psychomotor speed (outcomes=total correct on SDMT, time to completion on Stroop Trial 2); (3) attention (outcomes=total correct on LNS control and experimental conditions); (4) learning (outcome=total learning across HVLT-R trials); (5) memory (outcome=HVLT-R delayed recall); (6) fluency (outcomes=total correct on COWAT and category fluency); and (7) fine motor function (outcomes=total time to completion for each hand on GPEG). Timed outcomes were log transformed to normalize distributions and reverse scored so higher values equated to better performance.

Consistent with our previous publications[33] and other large scale cohort studies (e.g., Multicenter AIDS Cohort Study (MACS)[34], demographically adjusted T-scores were

created[35–38] for each outcome. For each domain, a composite T-score was derived based on the number of outcomes in the domain and the individual T-score for each outcome. If a single T-score was available, it was assigned as the domain T-score. If ≥2 T-scores were available, the average T-score was assigned to the domain if all T-scores were >40 or <40. If the lowest T-score was <40 and the highest T-score >40, the domain was scored as (lowest T-score+5). The exception to this was the fine motor domain, scored as the lowest T-score for the grooved pegboard tests. If a single rating was available, it was assigned outcomes as impaired (ratings 5=definite mild impairment through 9=severe impairment); the average of these scores were assigned the domain rating. If the assessments included both impaired and low average or above assessments, the domain rating is the most impaired rating +1 (e.g., a 7=moderate impairment becomes 6=mild-to-moderate impairment). The primary exposure variables of interest was domain-specific NCI, defined as a T-score <40.

Falls Ascertainment

Beginning in 2014 (visit 40) and in subsequent semi-annual study visits, WIHS participants were asked to report any history of fall within the prior 6 months. Participants reporting any fall were then asked whether they had either “1” or “2 or more” falls in the prior 6 months, sought medical attention for any of these falls, or if any of these falls resulted in fracture. Fall was defined for participants as: “an unexpected event, including a slip or trip, in which you lost your balance and landed on the floor, ground or lower level, or hit an object like a table or chair” and participants were further instructed that “Falls that result from a major medical event (for example, a stroke or seizure) or an overwhelming external hazard (for example, hit by a truck or pushed) should not be included.”[39] The primary outcome was report of at least one fall during the prior six months compared with no fall.

Covariates

Candidate covariates based on our previous publications included WIHS site and year of enrollment (2001–2, 2011–14, vs. 1994–5), sociodemographic factors, behavioral factors, clinical factors, and central nervous system (CNS) active medications, and HIV-related factors.[29,30,33] Covariates were time invariant being measured at the last visit prior to the first self-reported assessment of falls (referred to as the index visit) to avoid potential for reverse causality. **Demographic factors** included: age per 10 years, race/ethnicity (White non-Hispanic, Black, other), years of education (≥high school graduate), annual household income (≤$12,000). **Behavioral factors** included tobacco (current, former, never), alcohol (moderate/heavy (≥3 drinks/wk), light (<3 drinks/wk), none), marijuana (current [last 6 months], former, never), and crack, cocaine, and/or heroin use (current, former, never). **Clinical factors** were assessed at the index visit, prior to administration of the falls questionnaire, and included the following medical conditions, symptoms, or pre-clinical indices associated with falls in published literature: peripheral neuropathy (self-report of numbness, tingling, or burning sensations in arms, legs, hands or feet lasting for more than two weeks); obesity (body mass index (BMI) >30 kg/m^2); depressive symptoms (defined as Center for Epidemiology Studies Depression (CES-D) 16 cutoff);[40] diabetes mellitus as previously operationalized in WIHS;[41] renal dysfunction (estimated glomerular filtration rate (eGFR) <60 ml/min using the Modification of Diet in Renal Disease calculation);[42] hypertension (self-report of hypertension in addition to diastolic blood pressure 90 mmHg or

greater, systolic blood pressure 140 mmHg or greater, or current receipt of antihypertensive medication);[43] and Hepatitis C Virus (HCV) infection (defined as positive HCV antibody with HCV RNA detectable tested shortly after study entry). **CNS active medication classes** included anticonvulsants, antidepressants, antipsychotics, benzodiazepines/sedatives, and muscle relaxants.[44,45] CNS active medications were cumulatively analyzed as the number of classes being "currently" used at index visit (categorized 0, 1, 2, or ≥3). **HIV-related specific factors** included: nadir CD4+ count (lowest CD4 measured in cells per mm^3 prior to index) and current (i.e. at index visit) CD4+ count, current Log_{10} HIV RNA level, current suppressed (<20 copies/mL) HIV RNA, history of prior AIDS-defining illness (ADI), current ART use, and current and prior use of the following ART drugs often reported to be associated with a CNS side effects or neuropathy: Didanosine, Stavudine, Zidovudine, or Efavirenz.

Statistical Analyses

A series of univariate logistic regression analyses (overall sample and by HIV serostatus) were initially conducted to evaluate domain-specific NCI with odds of falls. Next, a series of hierarchical models (stratified by HIV-serostatus) were conducted to examine factors associated with falls after sequentially adjusting for demographics, clinical factors, behavioral factors and CNS active agents, and HIV-specific factors (HIV+ women only). In order to explore the combined effects of having impairment in multiple NC domains on the odds of sustaining a fall within 6 months, we summed the number of impaired domains specifically found to be associated with falls in univariate analyses and created models analyzing the effects of having 0 or 1 impaired domain vs 2–3 impaired domains on the odds of sustaining any fall, by using the same series of hierarchical models outlined above.

RESULTS

Participant characteristics

A total of 825 HIV+ and 392 HIV- women completed the neuropsychological test battery and falls questionnaire and are included in the current analyses (Table 1). HIV+ women were older and more likely to be HCV-infected, have renal dysfunction, and report symptoms of peripheral neuropathy. HIV+ women were less likely than HIV- women to be obese, or to report current smoking, recent marijuana, heroin, cocaine, or crack use, or moderate/heavy alcohol consumption. Among HIV+ women, median CD4+ count was 611 cells/μl, 44% reported a prior ADI, 91% reported taking ART at the study visit, and 67% had suppressed HIV RNA level. HIV+ women demonstrated greater percent impairment on only attention/working memory and fine motor function compared to HIV- women. The overall proportion of women reporting any fall in the prior 6 months was similar between HIV+ and HIV- women (19%, N=154/825 for HIV+ and 16%, N=66/392 for HIV- women, P=0.44).

Associations between NCI and Odds of Any Fall

In the simple models (adjusting only for study site) and fully adjusted models in the overall sample, executive function, processing speed, and fine motor impairment were associated with a greater odds of having sustained a fall in the prior six months (P's<0.01, Tables 2&3). In simple models, the association between executive function, fine motor function, and falls

was significant among HIV+ and HIV- women whereas the association between processing speed and falls was only related among HIV- women. In fully adjusted models restricted to HIV+ women, there were no longer any associations between domain-specific neurocognitive impairment and falls (*P*'s>0.08, Table 4). However, among HIV- women, in fully adjusted models, executive function and fine motor impairment remained significant predictors of falls (*P*'s<0.05, Table 5).

In fully adjusted models analyzing the number of impaired domains (out of executive function, processing speed, and fine motor function) on odds of falling, in the overall sample, women with impairment in 2 or 3 domains had over double the odds of having a fall compared with women who were impaired in 0 or 1 of these three domains (Table 3). Among HIV+ women, women demonstrating impairment in 2 out of 3 domains had 2.2 times greater odds of having a fall in the prior six months (Table 4 Model 5: OR=2.22, 95%CI, 1.25–3.96; *P*=0.0069) compared with women who were impaired in 0 or 1 of these three domains. Among HIV- women, those impaired in 2 or 3 domains had 3.8 times greater odds of having a fall in the prior (Table 5 Model 4: OR=3.80; 95%CI 1.45–9.94; *P*-value=0.0065).

DISCUSSION

To our knowledge, ours is the first study investigating the impact of domain-specific cognitive impairment on risk of falls in PWH, or specifically in women. Contrary to expectations, we found that domain-level cognitive impairment was associated with risk of falls among HIV- women only. Among HIV+ women, the associations of executive function, psychomotor speed, and fine motor function were attenuated and no longer significant after adjustment for demographic and co-morbid conditions, whereas among HIV- women, impairments in executive and fine motor function were associated with falls in unadjusted models, and these associations were strengthened in fully adjusted models.

Although the overall occurrence of falls did not differ between HIV+ and HIV- women, the prevalence of reported falls is strikingly high when considering the age of the WIHS cohort, and is similar to that observed in older uninfected adults (age 65 and older).[30,46,47] We previously found that in unadjusted analyses in WIHS, subjective cognitive complaints were associated with greater odds of sustaining a fall over 24 months, but that in fully adjusted models this association remained significant only for HIV- women; whereas among HIV+ women, the effect was attenuated and no longer significant after adjustment for co-morbid conditions.[46] In the current study, using *objective* measures of cognition, we were able to identify specific cognitive domains in which impairment is associated with greater risk of falls among the combined sample of HIV+ and HIV- women. However, consistent with our prior findings of subjective cognitive complaints in WIHS, these objective measures of cognition were significantly associated with falls only among HIV- women in fully adjusted models. While we are unable to demonstrate statistically significant relationships between cognitive impairment and risk of falls in HIV+ women, it is likely that these relationships exist and are similar to those observed in the HIV- women, but that given the age of the women under study, may not become apparent during middle age and rather may emerge with age-associated cognitive decline. Furthermore, we previously demonstrated that factors

affecting cognition such as use of multiple CNS active medications and substance use are important and potentially modifiable risks contributing to the unexpectedly high rate of falls among HIV+ women as well as among comparable HIV- women.

In healthy older adults with subclinical cognitive deficits, gait and NCI have been found to be inter-related, and executive dysfunction in particular has been implicated in fall risk. Executive function plays a key role in maintaining attention and inhibiting distracting stimuli, which is important for performance of physical tasks for older persons, particularly walking. In a study by Herman of well-functioning older persons, those with lower baseline executive function experienced faster time to first fall and recurrent falls over the next 2 years, and having impaired executive function tripled the odds of sustaining a fall; however, other cognitive domains and general measures of cognitive function were not related to falls.[48] While we did not find a relationship between executive function and falls among women with HIV, WIHS participants are substantially younger, yet more likely to have multiple medical comorbidities, polypharmacy, depressive symptoms, and substance use history compared to the healthy, active older population under study by Herman (median age 76, range 70–90 years). It is possible that executive functions will assume a greater importance in falls risk as PWH survive into older age, whereas factors such as polypharmacy, multimorbidity, and substance use may play a greater role in the development of falls among middle-age PWH.

Dual task gait, which tests the ability to walk while simultaneously performing another task, is considered an everyday task requiring executive control. Dual task gait predicts future falls and multiple falls in the older persons, suggesting that impaired executive function may specifically contribute to fall risk via its role in multitasking.[48] Relationships between impaired executive function and dual-tasking with risk of falling have been reported among older HIV+ populations,[49–53] and some[54–56] but not all[57,58] studies suggest that a dual-task paradigm is a more sensitive marker of fall risk than single task (either gait or cognitive) conditions alone; however, this area remains unstudied in PWH. Although surprisingly, we did not find an association between executive function and risk of falls, it is possible that use of more sensitive measures of executive function such as dual task gait may be required to reveal existing associations between executive function and fall risk among PWH. Because executive function impairment among HIV+ women persists despite virologic suppression,[38] it may represent a potential target area for interventions to prevent and reduce falls among women as they age, even among those with well treated HIV infection. Application of dual task paradigms may hold promise in identifying fall risk among PWH as they age and develop impairments in cognition, balance and gait.

We found that impaired psychomotor speed was associated with greater falls risk. Ours is the first study to evaluate the contribution of psychomotor speed on falls risk in persons with or at-risk for HIV. Studies on a similar domain, processing speed, have yielded mixed results. And then describe the literature and how you feel your sum score of impairment adds to that literature. In the Longitudinal Aging Study Amsterdam (LASA), Sanders and colleagues showed that the combination of slowing in processing speed and gait speed predicted not only falls, but also persistent cognitive decline and mortality; the authors also found an interaction such that slowed processing speed only predicted falls in the presence of slowed

gait.[59] That research led to creation of a "slowing sum score" using gait speed and processing speed scored from 1 (slowest) to 4 (fastest) and added to obtain the composite, which was found to predict falls, persistent cognitive decline, and mortality.[59] In an accompanying editorial, symptoms of slowing in thought and movement were proposed as early clinical markers of decline and future adverse health events in older adults, and were postulated to share a common pathway in hastening disability and death.[60] Similarly, in an 8-year prospective study of community-dwelling older adults, declines in Mini-Mental Status Exam (MMSE), verbal ability, processing speed, and immediate recall were all significantly associated with falling; decline in processing speed and immediate recall were also associated with greater risk of injurious falls.[61] In contrast, among cognitively intact community-dwelling older persons enrolled in the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) trial, Vance et al found that older age, female sex, Caucasian race, poor lower limb mobility, and better baseline memory (attributed to recall bias) were associated with self-reported falls over 2 years, whereas processing speed and reasoning were not.[62] Van Schoor et al. found that in LASA, poor immediate memory was associated with recurrent falls, whereas non-verbal and abstract reasoning and processing speed were not associated with an increased fall risk.[63] While we did not specifically evaluate the contribution of gait speed, we found that a sum score of NC impairment predicted falls, in our case across cognitive domains of executive function, fine motor skills, and psychomotor speed. Our study extends the scientific literature by showing how the combination of impairment in distinct NC domains conveys additional falls risk among HIV + and HIV- women. Future studies should evaluate the contribution of slowed gait on risk of falls in persons with or at-risk for HIV, both alone and in conjunction with psychomotor slowing and other cognitive domains.

Our study has a number of strengths. The WIHS is a predominantly racially and ethnically minority cohort that includes women with HIV with similar demographic and behavioral characteristics to women without HIV, allowing comparison by HIV serostatus. Participants are well characterized with regard to cognition as well as comorbid medical conditions that may affect risk of sustaining a fall. Our study also has several limitations. Fall ascertainment was based on participants' self-report of events in the prior 6 months, which may result in underreporting of falls, particularly in older participants or those with cognitive impairment. We also do not have data on seasonality of falls, circumstances of fall, such as activity at the time of fall, environmental conditions associated with fall, or location of fall (i.e. indoor vs. outdoor); over reporting and misclassification of falls are also possible. Our study also includes only women, and findings may not be generalizable to men.

Because women experience greater vulnerability than men as the age for the development of disability, cognitive impairment, and geriatric syndromes such as falls and fracture, future studies should examine sex differences in the impact of global or domain-specific measures of cognition on risk of falls in PWH. Additional studies to elucidate mechanisms by which neurocognition, gait, and falls are related in PWH are also needed. As women with HIV continue to age, cognitive screening, particularly in domains of executive function, psychomotor speed, and fine motor skills, is an important clinical tool to identify those at greatest risk of falls in order to develop targeted falls prevention strategies.

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References

1. Wada N, Jacobson LP, Cohen M, French A, Phair J, Munoz A. Cause-specific mortality among HIV-infected individuals, by CD4(+) cell count at HAART initiation, compared with HIV-uninfected individuals. AIDS (London, England) 2014;28:257–65.
2. Lewden C, Chene G, Morlat P, et al. HIV-infected adults with a CD4 cell count greater than 500 cells/mm3 on long-term combination antiretroviral therapy reach same mortality rates as the general population. Journal of acquired immune deficiency syndromes (1999) 2007;46:72–7. [PubMed: 17621240]
3. Lewden C, Bouteloup V, De Wit S, et al. All-cause mortality in treated HIV-infected adults with CD4 >/=500/mm3 compared with the general population: evidence from a large European observational cohort collaboration. International journal of epidemiology 2012;41:433–45. [PubMed: 22493325]
4. Rodger AJ, Lodwick R, Schechter M, et al. Mortality in well controlled HIV in the continuous antiretroviral therapy arms of the SMART and ESPRIT trials compared with the general population. AIDS (London, England) 2013;27:973–9.
5. Luther VP, Wilkin AM. HIV infection in older adults. Clinics in geriatric medicine 2007;23:567–83, vii. [PubMed: 17631234]
6. Guaraldi G, Palella FJ Jr. Clinical implications of aging with HIV infection: perspectives and the future medical care agenda. AIDS (London, England) 2017;31 Suppl 2:S129–s35.
7. Hasse B, Ledergerber B, Furrer H, et al. Morbidity and aging in HIV-infected persons: the Swiss HIV cohort study. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 2011;53:1130–9. [PubMed: 21998280]
8. Guaraldi G, Orlando G, Zona S, et al. Premature age-related comorbidities among HIV-infected persons compared with the general population. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 2011;53:1120–6. [PubMed: 21998278]
9. Sackoff JE, Hanna DB, Pfeiffer MR, Torian LV. Causes of death among persons with AIDS in the era of highly active antiretroviral therapy: New York City. Annals of internal medicine 2006;145:397–406. [PubMed: 16983127]
10. Berry SA, Fleishman JA, Moore RD, Gebo KA. Trends in reasons for hospitalization in a multisite United States cohort of persons living with HIV, 2001–2008. Journal of acquired immune deficiency syndromes (1999) 2012;59:368–75. [PubMed: 22240460]
11. Freiberg MS, Chang CC, Kuller LH, et al. HIV infection and the risk of acute myocardial infarction. JAMA internal medicine 2013;173:614–22. [PubMed: 23459863]

12. Brown TT, Qaqish RB. Antiretroviral therapy and the prevalence of osteopenia and osteoporosis: a meta-analytic review. AIDS (London, England) 2006;20:2165–74.
13. Greene M, Covinsky KE, Valcour V, et al. Geriatric Syndromes in Older HIV-Infected Adults. Journal of acquired immune deficiency syndromes (1999) 2015;69:161–7. [PubMed: 26009828]
14. Greene M, Justice AC, Lampiris HW, Valcour V. Management of human immunodeficiency virus infection in advanced age. Jama 2013;309:1397–405. [PubMed: 23549585]
15. Greene M, Justice AC, Covinsky KE. Assessment of geriatric syndromes and physical function in people living with HIV. Virulence 2017;8:586–98. [PubMed: 27715455]
16. Heaton RK, Clifford DB, Franklin DR Jr., et al. HIV-associated neurocognitive disorders persist in the era of potent antiretroviral therapy: CHARTER Study. Neurology 2010;75:2087–96. [PubMed: 21135382]
17. Simioni S, Cavassini M, Annoni JM, et al. Cognitive dysfunction in HIV patients despite long-standing suppression of viremia. AIDS (London, England) 2010;24:1243–50.
18. Clifford DB, Ances BM. HIV-associated neurocognitive disorder. The Lancet Infectious diseases 2013;13:976–86. [PubMed: 24156898]
19. Rosano C, Brach J, Longstreth WT Jr., Newman AB. Quantitative measures of gait characteristics indicate prevalence of underlying subclinical structural brain abnormalities in high-functioning older adults. Neuroepidemiology 2006;26:52–60. [PubMed: 16254454]
20. Verghese J, Derby C, Katz MJ, Lipton RB. High risk neurological gait syndrome and vascular dementia. Journal of neural transmission (Vienna, Austria : 1996) 2007;114:1249–52.
21. Verghese J, Lipton RB, Hall CB, Kuslansky G, Katz MJ, Buschke H. Abnormality of gait as a predictor of non-Alzheimer's dementia. N Engl J Med 2002;347:1761–8. [PubMed: 12456852]
22. Tyrovolas S, Koyanagi A, Lara E, Santini ZI, Haro JM. Mild cognitive impairment is associated with falls among older adults: Findings from the Irish Longitudinal Study on Ageing (TILDA). Experimental gerontology 2016;75:42–7. [PubMed: 26707711]
23. Delbaere K, Kochan NA, Close JC, et al. Mild cognitive impairment as a predictor of falls in community-dwelling older people. The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry 2012;20:845–53. [PubMed: 23011051]
24. Liu-Ambrose T, Ashe MC, Graf P, Beattie BL, Khan KM. Mild Cognitive Impairment Increases Falls Risk in Older Community-Dwelling Women. Physical therapy 2008;88:1482–91. [PubMed: 18820094]
25. Campbell AJ, Spears GF, Borrie MJ. Examination by logistic regression modelling of the variables which increase the relative risk of elderly women falling compared to elderly men. Journal of clinical epidemiology 1990;43:1415–20. [PubMed: 2254780]
26. Tinetti ME, Doucette J, Claus E, Marottoli R. Risk factors for serious injury during falls by older persons in the community. Journal of the American Geriatrics Society 1995;43:1214–21. [PubMed: 7594154]
27. Sattin RW, Lambert Huber DA, DeVito CA, et al. The incidence of fall injury events among the elderly in a defined population. American journal of epidemiology 1990;131:1028–37. [PubMed: 2343855]
28. Erlandson KM, Allshouse AA, Jankowski CM, et al. Risk factors for falls in HIV-infected persons. Journal of acquired immune deficiency syndromes (1999) 2012;61:484–9. [PubMed: 23143526]
29. Sharma A, Shi Q, Hoover DR, et al. Increased Fracture Incidence in Middle-Aged HIV-Infected and HIV-Uninfected Women: Updated Results From the Women's Interagency HIV Study. Journal of acquired immune deficiency syndromes (1999) 2015;70:54–61. [PubMed: 26322667]
30. Sharma A, Hoover DR, Shi Q, et al. Falls among middle-aged women in the Women's Interagency HIV Study. Antiviral therapy 2016.
31. Bacon MC, von Wyl V, Alden C, et al. The Women's Interagency HIV Study: an observational cohort brings clinical sciences to the bench. Clinical and diagnostic laboratory immunology 2005;12:1013–9. [PubMed: 16148165]
32. Barkan SE, Melnick SL, Preston-Martin S, et al. The Women's Interagency HIV Study. WIHS Collaborative Study Group. Epidemiology (Cambridge, Mass 1998;9:117–25.
33. Rubin LH, Maki PM, Springer G, et al. Cognitive trajectories over 4 years among HIV-infected women with optimal viral suppression. Neurology 2017;89:1594–603. [PubMed: 28904086]

34. Sacktor N, Skolasky RL, Seaberg E, et al. Prevalence of HIV-associated neurocognitive disorders in the Multicenter AIDS Cohort Study. Neurology 2016;86:334–40. [PubMed: 26718568]
35. Maki PM, Rubin LH, Valcour V, et al. Cognitive function in women with HIV: findings from the Women's Interagency HIV Study. Neurology 2015;84:231–40. [PubMed: 25540304]
36. Rubin LH, Cook JA, Weber KM, et al. The association of perceived stress and verbal memory is greater in HIV-infected versus HIV-uninfected women. Journal of neurovirology 2015;21:422–32. [PubMed: 25791344]
37. Rubin LH, Pyra M, Cook JA, et al. Post-traumatic stress is associated with verbal learning, memory, and psychomotor speed in HIV-infected and HIV-uninfected women. Journal of neurovirology 2016;22:159–69. [PubMed: 26404435]
38. Rubin LH, Maki PM, Springer G, et al. Cognitive trajectories over 4 years among HIV-infected women with optimal viral suppression. Neurology 2017;89:1594–603. [PubMed: 28904086]
39. Lamb SEJ-SE, Hauer K, et al. Prevention of Falls Network E, Outcomes Consensus G. Development of a common outcome data set for fall injury prevention trials: the Prevention of Falls Network Europe consensus. J Am Geriatr Soc 2005;53:1618–22. [PubMed: 16137297]
40. LS R The CES-D scale: a self-report depression scale for research in the general population. . Appl Psychol Measur 1977;1:385–401.
41. Tien PCSM, Cox C, et al. Association of HIV infection with Incident Diabetes Mellitus: Impact of using Hemoglobin A1C as a Criterion for Diabetes. Journal of acquired immune deficiency syndromes (1999) 2012;61:334–40. [PubMed: 22878421]
42. Levey AS. BJ, Lewis JB, Greene T, Rogers N, Roth D A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med 1999;130:461–70. [PubMed: 10075613]
43. Khalsa AKR, Mack WJ, et al. Correlates of prevalent hypertension in a large cohort of HIV-infected women: Women's Interagency HIV Study. AIDS 2007;21:2539–41. [PubMed: 18025894]
44. Radtke KK, Bacchetti P, Anastos K, et al. Use of Nonantiretroviral Medications That May Impact Neurocognition: Patterns and Predictors in a Large, Long-Term HIV Cohort Study. Journal of acquired immune deficiency syndromes (1999) 2018;78:202–8. [PubMed: 29762344]
45. Rubin LH, Radtke KK, Eum S, et al. Cognitive Burden of Common Non-antiretroviral Medications in HIV-Infected Women. Journal of acquired immune deficiency syndromes (1999) 2018;79:83–91. [PubMed: 29781879]
46. Sharma A, Hoover DR, Shi Q, et al. Longitudinal study of falls among HIV-infected and uninfected women: the role of cognition. Antiviral therapy 2017.
47. Tinetti ME. Preventing Falls in Elderly Persons. New England Journal of Medicine 2003;348:42–9. [PubMed: 12510042]
48. Herman T, Mirelman A, Giladi N, Schweiger A, Hausdorff JM. Executive control deficits as a prodrome to falls in healthy older adults: a prospective study linking thinking, walking, and falling. The journals of gerontology Series A, Biological sciences and medical sciences 2010;65:1086–92.
49. Holtzer R, Friedman R, Lipton RB, Katz M, Xue X, Verghese J. The relationship between specific cognitive functions and falls in aging. Neuropsychology 2007;21:540–8. [PubMed: 17784802]
50. Atkinson HH, Rosano C, Simonsick EM, et al. Cognitive function, gait speed decline, and comorbidities: the health, aging and body composition study. The journals of gerontology Series A, Biological sciences and medical sciences 2007;62:844–50.
51. Springer S, Giladi N, Peretz C, Yogev G, Simon ES, Hausdorff JM. Dual-tasking effects on gait variability: the role of aging, falls, and executive function. Mov Disord 2006;21:950–7. [PubMed: 16541455]
52. http://www.unaids.org/sites/default/files/media_asset/UNAIDS_Gap_report_en.pdf.)
53. Ayers EITA, Holtzer R, Verghese J. Walking while talking and falls in aging. Gerontology 2014;60:108–13. [PubMed: 24192342]
54. Bloem BR, Valkenburg VV, Slabbekoorn M, Willemsen MD. The Multiple Tasks Test: development and normal strategies. Gait Posture 2001;14:191–202. [PubMed: 11600322]
55. de Hoon EW, Allum JH, Carpenter MG, et al. Quantitative assessment of the stops walking while talking test in the elderly. Arch Phys Med Rehabil 2003;84:838–42. [PubMed: 12808535]

56. Verghese J, Buschke H, Viola L, et al. Validity of divided attention tasks in predicting falls in older individuals: a preliminary study. Journal of the American Geriatrics Society 2002;50:1572–6. [PubMed: 12383157]
57. Beauchet O, Allali G, Annweiler C, et al. Does change in gait while counting backward predict the occurrence of a first fall in older adults? Gerontology 2008;54:217–23. [PubMed: 18408360]
58. Bootsma-van der Wiel A, Gussekloo J, de Craen AJ, van Exel E, Bloem BR, Westendorp RG. Walking and talking as predictors of falls in the general population: the Leiden 85-Plus Study. Journal of the American Geriatrics Society 2003;51:1466–71. [PubMed: 14511170]
59. Sanders JB, Bremmer MA, Comijs HC, van de Ven PM, Deeg DJH, Beekman ATF. Gait Speed and Processing Speed as Clinical Markers for Geriatric Health Outcomes. The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry 2017;25:374–85. [PubMed: 28063852]
60. Stahl ST, Albert SM. Slowing Symptoms as Early Markers of Decline in Older Adults. The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry 2017;25:386–7. [PubMed: 28187955]
61. Anstey KJ, von Sanden C, Luszcz MA. An 8-year prospective study of the relationship between cognitive performance and falling in very old adults. Journal of the American Geriatrics Society 2006;54:1169–76. [PubMed: 16913981]
62. Vance DE, Ross LA, Crowe MG, Wadley VG, Edwards JD, Ball KK. The relationship of memory, reasoning, and speed of processing on falling among older adults. Physical & occupational therapy in geriatrics 2008;27:212–28. [PubMed: 20216922]
63. van Schoor NM, Smit JH, Pluijm SM, Jonker C, Lips P. Different cognitive functions in relation to falls among older persons. Immediate memory as an independent risk factor for falls. Journal of clinical epidemiology 2002;55:855–62. [PubMed: 12393072]

Table 1.

Characteristics of Women's Interagency HIV Study Participants

Characteristic, N (%)	HIV-infected (N=825)	HIV-uninfected (N=392)	P value*
Age, years, median (IQR)	51 (45, 57)	48 (41, 55)	<0.0001
Education level high school or greater	562 (68.2)	261 (66.8)	0.61
Annual Income ≥$12,000/yr	424 (51.8)	214 (55.4)	0.24
Enrollment year			0.0002
94–95	413 (50.1)	152 (38.8)	
01–02	270 (32.7)	174 (44.4)	
11–14	142 (17.2)	66 (16.8)	
WIHS Site			0.025
Bronx /Manhattan	142 (17.2)	94 (24.0)	
Brooklyn	202 (24.5)	83 (21.2)	
Washington DC	147 (17.8)	68 (17.3)	
San Francisco	164 (19.9)	85 (21.7)	
Chicago	170 (20.6)	62 (15.8)	
Race			0.078
White	137 (16.6)	48 (12.2)	
Black	584 (70.8)	283 (72.2)	
Hispanic/Other	104 (12.6)	61 (15.6)	
Injection Drug Use			0.42
Never	631 (76.5)	308 (78.6)	
Past/Current	194 (23.5)	84 (21.4)	
Smoking status			0.0055
Never	224 (27.2)	82 (20.9)	
Past	298 (36.1)	130 (33.2)	
Current	303 (36.7)	180 (45.9)	
Cocaine, crack, or heroin use			0.025
Never	338 (41.0)	140 (35.7)	
Past	432 (52.4)	210 (53.6)	
Current	55 (6.7)	42 (10.7)	
Marijuana use			0.0021
Never	205 (24.8)	78 (19.9)	
Past	465 (56.4)	207 (52.8)	
Current	155 (18.8)	107 (27.3)	
Current alcohol use			<0.0001
None	482 (58.5)	178 (45.4)	
Light (< 3 drinks/wk)	256 (31.1)	141 (36.0)	
Moderate (3–13 drinks/wk)	32 (3.9)	22 (5.6)	

Characteristic, N (%)	HIV-infected (N=825)	HIV-uninfected (N=392)	P value*
Heavy (≥14 drinks/wk)	54 (6.6)	51 (13.0)	
Postmenopausal status **	466 (56.5)	174 (44.4)	<0.0001
Comorbidities			
Hepatitis C Virus infection	150 (18.2)	51 (13.0)	0.023
Diabetes Mellitus	195 (23.6)	91 (23.2)	0.87
Hypertension	387 (46.9)	184 (46.9)	0.99
Renal dysfunction (eGFR <60)	104 (12.6)	25 (6.4)	0.001
Depressive symptoms (CESD ≥16)	240 (29.1)	95 (24.2)	0.076
Peripheral neuropathy	160 (19.4)	54 (13.8)	0.016
Obesity (≥30kg/m^2)	363 (44.3)	206 (53.1)	0.0044
CNS active medication currently used			
Anticonvulsants	130 (15.8)	40 (10.2)	0.009
Antidepressants	225 (27.3)	63 (16.1)	<0.0001
Antipsychotics	79 (9.6)	40 (10.2)	0.73
Benzodiazepines and other sedatives	113 (13.7)	49 (12.5)	0.57
Muscle relaxants	39 (4.7)	26 (6.6)	0.17
Number of current CNS active medication types			0.0001
0	478 (57.9)	273 (69.6)	
1	191 (23.2)	51 (13.0)	
2	92 (11.2)	44 (11.2)	
≥3	64 (7.8)	24 (6.1)	
Fall status at any time during study			0.44
No fall	671 (81.3)	326 (83.2)	
Had fall	154 (18.7)	66 (16.8)	
HIV disease related characteristics			
AIDS defining illness ever	365 (44.2)	N/A	N/A
Current CD4+ cell count (cells/μl), median (IQR)	611 (395, 805)	N/A	N/A
Nadir CD4+ cell count (cells/μl), median (IQR)	224 (117, 367)	N/A	N/A
Suppressed HIV RNA viral load (<20c/mL)	540 (66.5)	N/A	N/A
Current ART use	753 (91.4)	N/A	N/A
T scores, median (IQR)			
Executive function	50 (43, 56)	51 (44, 56)	0.28
Psychomotor speed	50 (43, 55)	51 (44, 57)	0.011
Attention/Working Memory	49 (42, 55)	49 (44, 56)	0.031
Learning	48 (41, 56)	50 (42, 57)	0.068
Memory	49 (42, 57)	51 (42, 57)	0.33
Fine Motor	51 (44, 56)	52 (46, 57)	0.085
Fluency	49 (44, 55)	50 (44, 55)	0.19
Impairment			

Characteristic, N (%)	**HIV-infected (N=825)**	**HIV-uninfected (N=392)**	**P value***
Executive function	145 (17.6)	57 (14.5)	0.18
Psychomotor speed	140 (17.0)	53 (13.5)	0.12
Attention/Working Memory	157 (20.4)	47 (12.8)	0.0017
Learning	187 (22.9)	79 (20.2)	0.30
Memory	164 (20.1)	73 (18.9)	0.61
Fine Motor	134 (16.5)	40 (10.3)	0.0047
Fluency	114 (13.9)	42 (10.8)	0.13
Number of domains impaired (among executive function, motor, processing speed)			0.11
0 or 1	714 (87.8)	352 (91.0)	
2 or 3	99 (12.2)	35 (9.0)	

*Comparison between groups using Chi-Square test for categorical variables and Wilcoxon test for continuous variable

**Postmenopausal status is defined by self-reported amenorrhea at 2 consecutive visits for women aged >=45 years old and no resumption of menses

Table 2.

Domain-specific relationships between neurocognitive impairment and odds of any fall in WIHS [*]

	Combined Sample		HIV+ Women		HIV- Women	
Domain	**OR (95%CI)**	**P value**	**OR (95%CI)**	**P value**	**OR (95%CI)**	**P value**
Executive Function	1.75 (1.22, 2.50)	0.002	1.99 (1.03, 3.85)	0.041	1.65 (1.08, 2.52)	0.02
Processing Speed	1.76 (1.22, 2.52)	0.002	1.54 (0.76, 3.13)	0.23	1.83 (1.20, 2.79)	0.005
Attention/Working Memory	0.81 (0.53, 1.23)	0.33	1.23 (0.56, 2.69)	0.61	0.69 (0.42, 1.13)	0.14
Learning	1.06 (0.75, 1.50)	0.74	1.20 (0.63, 2.27)	0.58	1.00 (0.66, 1.52)	1.00
Memory	1.08 (0.75, 1.56)	0.67	1.25 (0.65, 2.42)	0.50	1.01 (0.65, 1.57)	0.96
Fine Motor	1.92 (1.32, 2.79)	0.0006	2.49 (1.19, 5.21)	0.016	1.73 (1.12, 2.68)	0.01
Learning	0.90 (0.57, 1.41)	0.64	1.41 (0.64, 3.11)	0.39	0.74 (0.43, 1.28)	0.28

[*] Adjusted for study site

Table 3.

Relationship between Neurocognitive Impairment and Odds of Any Fall in WIHS

	Executive Function		Psychomotor Speed		Fine Motor Skills		Number of Impaired Domains (≥2 vs. 0–1)	
	Multivariable OR (95% CI)	**P value**	**Multivariable OR (95% CI)**	**P value**	**Multivariable OR (95% CI)**	**P value**	**Multivariable OR (95% CI)**	**P value**
Model 1: Impairment in domain								
Adjusted for study site and HIV serostatus	1.83 (1.26, 2.64)	0.0013	1.75 (1.21, 2.54)	0.0032	1.90 (1.29, 2.80)	0.0012	2.43 (1.60, 3.68)	<0.0001
Model 2: Adjusted for Model 1								
+ **Demographics** *	1.72 (1.17, 2.51)	0.0055	1.61 (1.09, 2.36)	0.016	1.79 (1.20, 2.67)	0.0041	2.27 (1.47, 3.48)	0.0002
Model 3: Adjusted for Model 2								
+ **Comorbidities** †	1.68 (1.13, 2.49)	0.0098	1.54 (1.03, 2.31)	0.035	1.73 (1.14, 2.61)	0.0095	2.22 (1.41, 3.49)	0.0005
Model 4: Adjusted for Model 3								
+ **Substance Use & CNS Active Medications** ‡	1.82 (1.21, 2.74)	0.0039	1.59 (1.05, 2.42)	0.028	1.70 (1.11, 2.61)	0.016	2.30 (1.44, 3.68)	0.0005

*Demographics: age per 10 years, race/ethnicity, annual household income; high school education or more; and year of WIHS enrollment.

†Comorbidities: peripheral neuropathy; obesity (BMI>30 kg/m^2); CESD≥16; diabetes mellitus; renal dysfunction (eGFR <60 ml/min); hypertension; and HCV infection

‡Substance Use: tobacco use; cocaine, crack, and/or heroin use; marijuana use; and alcohol use (heavy, moderate, light, or none); CNS Active medications included anticonvulsants, antidepressants, antipsychotics, benzodiazepines/sedatives, and muscle relaxants and were analyzed as the number of classes being used at index visit (0, 1, 2, or ≥3).

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Table 4.

Relationship between Cognitive Impairment and Odds of Any Fall among Women with HIV in WIHS

	Executive Function		Psychomotor Speed		Fine Motor Skills		Number of Impaired Domains (≥2 vs. 0–1)	
	Multivariable OR (95% CI)	**P value**	**Multivariable OR (95% CI)**	**P value**	**Multivariable OR (95% CI)**	**P value**	**Multivariable OR (95% CI)**	**P value**
Model 1: Impairment in domain	1.73 (1.11, 2.68)	0.015	1.87 (1.21, 2.90)	0.0051	1.72 (1.09, 2.69)	0.019	2.41 (1.48, 3.93)	0.0004
Model 2: Adjusted for Model 1 + **Demographics** *	1.55 (0.98, 2.45)	0.063	1.69 (1.07, 2.67)	0.026	1.64 (1.03, 2.61)	0.038	2.26 (1.36, 3.76)	0.0016
Model 3: Adjusted for Model 2 + **Comorbidities** †	1.43 (0.89, 2.32)	0.14	1.57 (0.96, 2.56)	0.071	1.58 (0.97, 2.58)	0.065	2.20 (1.28, 3.79)	0.0043
Model 4: Adjusted for Model 3 + **Substance Use & CNS Active Medications** ‡	1.52 (0.92, 2.53)	0.10	1.59 (0.95, 2.67)	0.078	1.55 (0.92, 2.60)	0.099	2.25 (1.26, 4.00)	0.0061
Model 5: Adjusted for Model 4 + **Prior AIDS** §	1.50 (0.91, 2.49)	0.11	1.57 (0.93, 2.63)	0.088	1.55 (0.92, 2.61)	0.097	2.22 (1.25, 3.96)	0.0069

*Demographics: age per 10 years, race/ethnicity, annual household income; high school education or more; and year of WIHS enrollment.

†Comorbidities: peripheral neuropathy; obesity (BMI>30 kg/m^2); CESD≥16; quality of life summary score; diabetes mellitus; renal dysfunction (eGFR <60 ml/min); hypertension; and HCV infection

‡Substance Use: tobacco use; cocaine, crack, and/or heroin use; marijuana use; and alcohol use (heavy, moderate, light, or none); CNS Active medications included anticonvulsants, antidepressants, antipsychotics, benzodiazepines/sedatives, and muscle relaxants and were analyzed as the number of classes being used at index visit (0, 1, 2, or ≥3).

§History of any prior AIDS-defining illness

Table 5.

Relationship between Cognitive Impairment and Odds of Any Fall among Women without HIV in WIHS

	Executive Function		Psychomotor Speed		Fine Motor Skills		Number of Impaired Domains (≥2 vs. 0–1)	
	Multivariable OR (95% CI)	**P value**	**Multivariable OR (95% CI)**	**P value**	**Multivariable OR (95% CI)**	**P value**	**Multivariable OR (95% CI)**	**P value**
Model 1: Impairment in Domain	2.14 (1.08, 4.22)	0.029	1.48 (0.72, 3.06)	0.29	2.65 (1.24, 5.70)	0.012	2.45 (1.08, 5.55)	0.032
Model 2: Adjusted for Model 1 + **Demographics** *	2.37 (1.16, 4.84)	0.017	1.52 (0.72, 3.22)	0.28	2.85 (1.27, 6.42)	0.011	2.71 (1.14, 6.43)	0.024
Model 3: Adjusted for Model 2 + **Comorbidities** †	2.87 (1.37, 6.04)	0.0054	1.76 (0.81, 3.81)	0.15	2.85 (1.22, 6.64)	0.016	3.21 (1.31, 7.88)	0.011
Model 4: Adjusted for Model 3 + **Substance Use & CNS Active Medications** ‡	3.75 (1.70, 8.25)	0.0010	1.89 (0.84, 4.28)	0.13	2.72 (1.10, 6.71)	0.030	3.80 (1.45, 9.94)	0.0065

*Demographics: age per 10 years, race/ethnicity, annual household income; high school education or more; and year of WIHS enrollment.

†Comorbidities: peripheral neuropathy; obesity (BMI>30 kg/m^2); CESD≥16; quality of life summary score; diabetes mellitus; renal dysfunction (eGFR <60 ml/min); hypertension; and HCV infection

‡Substance Use: tobacco use; cocaine, crack, and/or heroin use; marijuana use; and alcohol use (heavy, moderate, light, or none); CNS Active medications included anticonvulsants, antidepressants, antipsychotics, benzodiazepines/sedatives, and muscle relaxants and were analyzed as the number of classes being used at index visit (0, 1, 2, or ≥3).