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Contributions of Cerebral White Matter Hyperintensities, Age, and Pedal Perception to Postural Sway in People Living with HIV

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Abstract

Objective: With aging, people living with HIV (PLWH) have diminishing postural stability that increases liability for falls. Factors and neuromechanisms contributing to instability are incompletely known. Brain white matter abnormalities seen as hyperintense (WMH) signals have been considered to underlie instability in normal aging and PLWH. We questioned whether sway-WMH relations endured after accounting for potentially relevant demographic, physiological, and HIV-related variables.

Design: Mixed cross-sectional/longitudinal data acquired over 15 years in 141 PLWH and 102 age-range matched controls, 25–80 years old.

Methods: Multimodal structural MRI data were quantified for 7 total and regional WMH volumes. Static posturography acquired with a force platform measured sway path length separately with eyes closed and eyes open. Statistical analyses used multiple regression with mixed modeling to test contributions from non-MRI and non-path data on sway path-WMH relations.

Results: In simple correlations, longer sway paths were associated with larger WMH volumes in PWLH and controls. When demographic, physiological, and HIV-related variables were entered into multiple regressions, the sway-WMH relations under both vision conditions in the controls were attenuated when accounting for age and 2-point pedal discrimination. Although the sway-WMH relations in PLWH were influenced by age, 2-point pedal discrimination, and years with HIV infection, the sway-WMH relations endured for 5 of the 7 regions in the eyes-open condition.

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Role of authors: E.V.S., N.M.Z., S.A.S., and A.P. conceptualized the study, supervised training of staff for data collection, and oversaw data quality control. A.P., K.M.P., and Q.Z. analyzed the MRI data. A.P. analyzed the balance platform data. A.P. and E.V.S. conducted statistical analysis and interpreted the results. All authors have read, reviewed, contributed to, and approved the final manuscript.

Conflicts of interest: None of the authors have any conflicts of interest to disclose.

Conclusions: The constellation of age-related increasing instability while standing, degradation of brain white matter integrity, and peripheral pedal neuropathy is indicative of advancing frailty and liability for falls as people age with HIV infection.

Keywords

balance; age; HIV infection; sensory perception; white matter; hyperintensity

INTRODUCTION

A visually distinctive, neuroradiological marker of brain degradation is white matter hyperintense (WMH) signal occurring at the borders of the lateral ventricles and in deep white matter of cortical, cerebellar, and subcortical tissue. The presence and size of WMH increase with age even in apparently healthy individuals and can be larger in those with medical and neuropsychiatric disorders, for example, HIV infection and Alcohol Use Disorder (AUD)[1, 2], Alzheimer's disease[3], Parkinson's disease[4]; mild stroke[5–8], small cerebrovascular disease[9, 10], depression[11]. Initial reports were skeptical about the functional ramifications of the "unidentified bright objects," also known as UBOs[12], now called WMH, but dozens of reports have since noted variables that are common correlates of WMH number and size, implicating WMH as underlying functional declines in normal aging[13–19], age-related frailty [20], and numerous neuropsychiatric disorders. Variables found to be related to WMH ratings or volumes include sex[21], race[22], body mass index (BMI)[23, 24], blood pressure[25, 26], diabetes[27, 28], HIV[25, 29], and age as a reliable correlate[1, 24, 30]. Although factors of frailty, such as declining grip strength and postural imbalance, have been found to accrue with WMH burden, few studies have used posturography to assess and track this relation[31], and even fewer studies have reported on people living with HIV infection (PLWH) despite high prevalence of WMH even in virally-suppressed HIV[1, 24, 30, 32].

With successful antiretroviral treatment, PLWH have, on average, near normal life spans with current estimates indicating that more than half of PLWH are age 50 or older[33]. Extending lifespan into later years carries the liability of age-related decline affecting sensory and motor functions, setting the stage for physical frailty[34, 35], postural instability[36–38], a propensity for falls[39], and degradation of brain structural integrity of white matter observable as hyperintense signal on MR imaging[1, 24, 30, 32]. Longitudinal study of virally suppressed PLWH support these possibilities in revealing acceleration of WMH volume[1] and postural instability[37] beyond that observed in aging men and women free of serious morbidities. Despite recognition of these phenomena that are accelerated in aging PLWH, a WMH volume/balance relation has not been established in the context of concurrent somatosensory and other variables susceptible to declines with aging and that could serve to operationalize factors defining frailty[40].

Given the decades of reports on the relations between WMH presence and postural instability in aging and disease including HIV infection, we tested whether this relation was also influenced by factors we previously found to contribute to WMH presence and size or to postural instability in PLWH[37, 41]. Accordingly, we posed the following questions:

1) Does postural instability measured as sway path length correlate with WMH volumes similarly in HIV and control groups? 2) What demographic and physiological variables, suggested by the literature, moderate observed sway-WMH relations, and do the sway-WMH relations endure when variables identified to be significant are taken into account statistically? 3) Do the sway-WMH relations differ between controls and PLWH when demographic and physiological variables identified to be significant contributors are taken into account? Knowledge about modifiable factors that reduce stability have the potential to be remedied and aid in minimizing frailty and averting falls, which can be debilitating and even deadly.

METHOD

Participants

The data comprised 299 sessions (Supplemental Table 1) of balance platform testing for sway path length typically conducted within a few days (control mean=2.34 days, PLWH mean=1.56 days in between t(175.41)=0.477, p=0.634) of MRI FLAIR acquisition used for WMH volume quantification. Although much of the balance[42] and FLAIR[43] data was reported previously, the current analysis included an expanded data sample collected from 12 October 2006 to 21 July 2023 and an examination of the relation between balance and WMH. The resulting sample with brain and balance data comprised 102 control participants and 141 PLWH, 25 to 80 years old at study entry (Table 1). Participants were recruited from local HIV support centers, post card mailings, recruitment flyers, and word of mouth. The mainstay of the data acquisition and analysis methods were described previously[42–44] and are summarized herein.

These studies were approved by the Institutional Review Boards of SRI International and Stanford University School of Medicine and were carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). After providing written informed consent for study participation, all volunteers underwent Structured Clinical Interviews for DSM-IV-TR (SCID)[45] to determine diagnosis for alcohol dependence/abuse and DSM-5 diagnosis for AUD[46]. Of the 141 PLWH, 70 met DSM-5 criteria for AUD and included one man with HIV who met AUD criteria between his second and third visits. Integrated into the SCID was the Global Assessment of Functioning (GAF) scale, which used a 0–100 scale to measure how much a person's symptoms affected their daily life. Additional interviews included structured health questionnaires and a semi-structured timeline follow-back interview to quantify lifetime alcohol use[47]. Principal exclusion criteria at study entry were history of schizophrenia, bipolar disorder, and neurological disorders other than AUD. Substance use dependence/abuse (current or in remission) for illicit drugs was common and involved cocaine, amphetamines, opiates, and cannabis (although now legal in California). All participants also completed metal screening to ensure MRI safety. Starting each study day, participants underwent breathalyzer testing for recent alcohol consumption. Participants whose breathalyzer reading exceeded 0.0 were not tested on that day and were asked to return when they had refrained from drinking.

Balance, sensory, and physiological testing

Balance platform data acquisition and analysis.—Participants wore rubber-soled socks and stood still on a force plate with feet together and arms relaxed at their side. The test comprised three, 30 sec. trials in each of two conditions: eyes open and then eyes closed. The microcomputer-controlled force plate (model 9284; Kistler, Amherst, NY) has multiple transducers and analog-digital converters and sampled data at 1000Hz to produce sway paths for each trial of each condition. Raw data were center-of-pressure displacements (x-y pairs) and subjected to a 10Hz low-pass filter (99 terms, −50db Gibbs). Sway path length was expressed as the line integral (cm)[48]. Examples of sway paths are in Figure 1A.

$$\mathrm{P}=\sum_{i=1}^{N-1}\sqrt{(x_{i+1}-x_i)^2+(y_{i+1}-y_i)^2}$$

Sensory testing: 2-point discrimination.—Starting with the dominant side determined from handedness, the examiner touched the sole of one foot with 1 or 2 points of a 3-point aesthesiometer, to which the participant (with eyes closed) responded “one” or “two.” Testing avoided calloused skin and proceeded with descending limits (starting at 50 mm distance between points); the threshold was the shortest distance on which fewer than 3 errors were made[49]; thus, high scores were in the impaired direction. The procedure was repeated with the other foot. The score was the mean of the left and right thresholds.

Blood pressure.—Sitting blood pressure was collected twice. The mean of each of the two diastolic and systolic measures was used in multiple regression analysis described below.

Falls questionnaire.—About one-third of participants in each group (33 of 102 controls and 56 of 142 PLWH) completed a simple falls questionnaire[42] and were asked how many times they had fallen to the ground in the past year. The range recorded was 0–6 occasions.

Neuroimaging acquisition and analysis

Protocols and parameters.—Scanning was conducted at SRI International on a GE 3 Tesla Discovery MR750 system (Waukesha, WI, U.S.A.) with ASSET for parallel and accelerated imaging on an 8-channel head coil. Detection and localization of WMHs used three MRI acquisition protocols: T1-weighted (T1-w) MRI for anatomical localization 3D axial IR-Prep (inversion prepared) SPGR (SPoiled Gradient Recalled); Repetition Time (TR)=6.5ms, Echo Time (TE)=1.54ms, thickness (thick)=1.25 mm, locations (loc)=124, skip=0; T2-weighted (T2-w) MRI merged with T1 data for skull stripping: [3D isotropic Fast Spin Echo; GE name=CUBE; TR=2500ms, effective TE=99ms, echo train length (ETL)=100ms, thick=1mm, loc=150, FOV=256mm, xy_matrix=256×256, resolution=1×1×1mm]; and FLAIR (FLuid-Attenuated Inversion Recovery) imaging for estimates of WMH volumes [2D axial, TR=9000ms, TE=82.5ms, inversion time (TI)=2200ms, thick=2.5mm, loc=65]. MRI structural analysis as conducted in Adeli et al.[50] is described in Supplemental Material.

WMH quantification.—WMH analysis was accomplished with the "UBO Detector," a freely-available, cluster-based, fully automated pipeline for extracting and calculating WMH on a voxel basis[51, 52]. The UBO Detector was validated on longitudinal data and gold standard Fazekas ratings[53]. This procedure yielded voxel maps of total, periventricular (PVWMH), deep (DWMH) WMHs (Figure 1B),and WMH volumes in each of four lobar regions. Analysis required that FLAIR and T1-weighted data be transformed into MNI space prior to non-rigid transformation into standard SRI atlas space. This was necessary for accurate placement of anatomical locations to enable comparisons across individuals and across imaging modalities on a voxel-wise basis without the need for further correction for intracranial volume.

Statistical analysis

Statistical analysis was performed using R 3.5.1 (R Core Team, 2019). Because several participants had multiple data sets across time, the primary statistic was a linear mixed effects model (*lmer*) used separately to test the relations between balance platform condition (i.e., eyes open or closed) and each WMH volume measure (total, periventricular, deep, and 4 WMH regions: frontal, temporal, parietal and occipital) as a function of group (control, PLWH) + age^2. Previously, we found that the relations of path length[44] and WMH volumes[43] with age were best fit with an age^2 function, which was used in all analyses herein. Because of the heteroscedasticity of WMH volumes, their values were square-root transformed before statistical analysis.

An initial regression analysis focused on the simple relation between sway path length and WMH volume in each group, first for performance with eyes closed and then with eyes open. The model outputs for each effect produced t and p values.

The second set of analyses were conducted in two parts. A set of exploratory regression analyses tested variables reported in the literature to correlate with postural instability or presence of WMH. Variables entered into these linear mixed-model multiple regression analyses were WMH volume, age^2, sex, AUD diagnosis, socioeconomic status (SES), years of education, systolic and diastolic blood pressure, body mass index (BMI), depressive symptoms (Beck Depression Inventory-II score, BDI), 2-point pedal discrimination, amount of alcohol consumed in the past year, self-identified race, years with HIV infection, and log viral load; three variables—presence or absence of AUD diagnosis, years with HIV infection, and log viral load—were relevant to the HIV group only.

The third set of regressions included only variables found to be significant contributors to the sway path-WMH relations in the second set of focused regressions. Also tested were potential interactions between diagnosis (HIV vs. control) and WMH volumes that would address whether the groups differed in the strength of the sway path/WMH volume relations.

Recognizing the overlap of WMH regions, all analyses outlined considered WMH volumes in 3 parts: total WMH volume alone; PVWMH (periventricular) and DWMH (deep); and 4 DWMH regions, namely, frontal, temporal, parietal, and occipital. Family-wise Bonferroni correction (α=0.025, 2-tailed) for 2 WMH regions required $p \leq 0.025$ and for 4 DWMH regions required $p \leq 0.0125$.

RESULTS

The statistical test results are presented in the tables and figures as noted.

Comparison of groups on demographic variables

The PLWH and control groups were not statistically different in age, BMI, diastolic or systolic blood pressure, or number of falls reported over the past year. Compared with the control group, the PLWH group had fewer years of education, lower socioeconomic status (SES) and GAF, more depressive symptoms (BDI), poorer 2-point pedal discrimination, and had consumed more alcohol. The PLWH group had a larger Black representation than the control group (Table 1).

WMH volumes as predictors of sway path length in each group

The first set of regression analyses tested the relations between sway path length under each test condition and WMH volumes per group. For all comparisons in both groups, longer sway paths were related to larger WMH volumes. The only comparison not meeting correction for multiple comparisons was for the relation between sway path with eyes closed and temporal WMH volume (Table 2; Figure 2; Supplemental Figures 1–2).

WMH, demographic, and disease variables as predictors of sway path length by group

These exploratory multiple regression analyses included 15 variables for PLWH potentially influencing the primary relations between sway path length and WMH volume: age^2, sex, AUD diagnosis, SES, years of education, systolic and diastolic blood pressure, body mass index (BMI), depressive symptoms (Beck Depression Inventory-II score, BDI), 2-point pedal discrimination, amount of alcohol consumed in the past year, race, years with HIV infection, and log viral load. These analyses were also conducted in controls but included only the 12 non-HIV-related variables. The only variables contributing significantly to relations between sway with eyes open or closed and WMH volumes in PLWH were age and 2-point discrimination; systolic blood pressure and years with HIV infection contributed significantly to the eyes open sway-WMH relations. In the controls, only age contributed (Supplemental Table 2).

The variables identified as significant in the exploratory regression, namely, age^2, systolic blood pressure, 2-point pedal discrimination, and years with HIV infection, were then used in follow-up regressions separately for each group. In the controls, total WMH and PVWMH volumes endured as a significant predictors of sway path with eyes closed (Table 2). In the HIV group, only two WMH volumes (DWMH and frontal) weakly endured as significant predictors of sway with eyes closed. By contrast, the relations for WMH volumes and sway were more widespread and stronger for the eyes open condition and included 5 of the 7 WMH regions (total WMH, DWMH, frontal, parietal, and occipital; Table 2). In further consideration of HIV-related disease status as influencing the primary sway-MWH relations, CD4 nadir[34] at the test sessions was used in place of HIV infection length but failed to exert significant contributions to any comparison.

Tests of group differences in predictors of sway path-WMH volume relations

This third set of multiple regression analyses in PLWH and controls included variables identified above as contributing to the sway path-WMH relations. The results revealed age and 2-point discrimination as the most consistent and strongest contributor to the primary relation of sway path-WMH volume (Table 3). Tests of diagnosis (HIV vs. control) by WMH volume interactions were significant only for relations between sway path with eyes open and DWMH, temporal, parietal, and occipital volumes, indicating stronger relations between WMH and balance in the PWLH than controls after adjusting for contributory variables (Table 3; Figure 2; Supplemental Figures 1–2).

DISCUSSION

In answer to our posed questions, we found that longer sway paths in PLWH and controls were highly correlated with WMH volumes in all locations and under both vision testing conditions (eyes closed and eyes open) without regard for potentially contributing variables. Exploration of variables potentially affecting the primary relationship of sway and WMH volumes revealed age and 2-point pedal discrimination as attenuating factors in all regional WMH-sway comparisons for the control group and in all but 2 of 7 regions for the HIV group. Variables significantly affecting the sway-WMH relations in PLWH were systolic blood pressure and years with HIV infection. Follow-up to the large exploratory regression analysis focused on the five variables that significantly affected the sway-WMH relations identified age and 2-point discrimination in both groups and years with HIV infection in PLWH as the most meaningful contributors. Sway-WMH relations that endured in the control group involved total and PVWMH in the eyes closed condition, and none persisted in the eyes open condition. Sway-WMH relations that endured in PLWH were with DWMH and frontal WMH for eyes closed, and all but PVWMH and temporal WMH volume with eyes open.

Seeking diagnosis-by-WMH interactions to test whether the groups differed in sway-WMH relations after accounting for targeted variables revealed significant interactions for total DWMH and regional (temporal, parietal, and occipital) volumes only for eyes open. In these cases, the sway path-WMH volume relations were steeper in the PLWH than controls. Thus, the relation between postural stability and disruption of brain white matter integrity was largely influenced by biological aging and physiological factors in both groups, but those factors did not completely account for all sway path-WMH volume relations.

The search of neural, physiological, and demographic contributors to complex behaviors such as maintenance of postural stability seldom identifies single substrates. Accordingly, it may not be surprising that WMH volumes were not sole predictors of sway path length. Critically, if the myriad other factors were not considered as also contributing to sway path variance, conclusions indicating WMH as the only or primary correlate of postural instability would have been inaccurate. Indeed, age and 2-point pedal discrimination were more consistently related to sway path in both vision conditions than was WMH volume. In PLWH, age and 2-point discrimination were also influential to sway path with eyes open; however, in that condition WMH volume endured as a significant contributor to sway in all but two relations (PVWMH and temporal WMH).

Factors contributing to sway were different with and without visual information and may be related to differential contributions from underlying physiological functioning. Specifically, the greater disparity between PLWH and controls in sway path length when balance with eyes closed than with eyes open supports vision as a stabilizing force to override peripheral nervous system compromise of pedal sensory discrimination, which likely resulted in poor detection of plantar pressure[54] and possible peripheral or central nervous system compromise of vestibular responses[55]. Despite significant enhancement to stability from vision, older PLWH were still impaired in the eyes-open condition relative to controls, implicating age-related decline in visual motion perception as contributing to imbalance even with the advantage of visual information[56].

The constellation of variables relevant to the primary sway path-WMH volume relations observed in our HIV group were only partially overlapping with those we recently observed in AUD without HIV[57]. In the AUD study, age and 2-point pedal discrimination were also salient contributors to the sway-WMH relations, as were sex and race, but in contrast to the current findings in the HIV group, those four variables nearly fully accounted for the primary relations between sway and WMH volume. In the current HIV study, age and 2-point pedal discrimination contributed significantly to all sway-WMH relations, yet WMH volume endured as a significant predictor of sway path length in 2 of 7 comparisons with eyes closed and in 5 of 7 comparison with eyes open. Thus, it appears that disturbance resulting from the presence and size of WMH, regardless of location, is a neural mechanism influencing static imbalance in HIV, thereby differentiating it from causes of instability observed in AUD.

Aging with HIV, unimaginable in the early days of the epidemic, is commonplace given current formulations of ART[33]. Associated with longevity, however, is the potential of developing age-related physical declines, considered frailty[34], which has been operationalized as fatigue, unintentional weight loss, restricted mobility, low physical activity, and muscle weakness[40]. Sensory compromise of visual acuity and touch discrimination also accompanies aging even in healthy individuals[58]. This array of age-related sensorimotor decline of the peripheral nervous system together with central nervous system degradation of white matter structural integrity can be exacerbated or even accelerated by chronic diseases, including HIV infection[43], and contribute to postural instability[41, 42] and falls[34, 35]. Relevant to the current study, greater instability of quiet standing was heralded by larger volumes of brain WMH, poorer sensory discrimination measured on the soles of the feet, and length of HIV infection, each of which worsens in aging with HIV and increases the risk of falls.

Limitations

Several limitations of this study are noted. Although the sample sizes were comparatively large, the analysis was a mixed model of cross-sectional and longitudinal data available from our ongoing laboratory studies; thus, longitudinal questions could not be fully addressed. Further, our groups did not undergo formal vestibular testing, and so we can only speculate on potential contributions of vestibular input to observed instability. Similarly, we did not assess cardiorespiratory fitness, which can enhance stability[59]. In addition, exploration of

the many variables known from other studies to influence either static postural stability or WMH volume stretched statistical power; that acknowledged, we did account for multiple comparisons by using Bonferroni adjustment. Finally, participant recruitment extended over 17 years (2006–2023), thus spanning the evolution of HIV treatment regimens with attendant efficacy and iatrogenic effects. This span potentially included PLWH who were not treated initially and who might carry legacy effects, which may be considered AIDS-defining events and could contribute to postural instability and brain structural compromise. Despite potential cohort effects related to the evolution of HIV, nearly all PLWH—92.9% of the HIV-only group and 93.1% of the HIV+AUD group—were receiving ART during the testing sessions.

Conclusion

This study provides evidence for longer sway paths to be related to larger WMH volumes in health and PLWH. Critical moderating variables were older age and diminished somatosensory detection on the soles of the feet in PLWH and their control counterparts. Recognizing these findings in the context of another study reporting that PLWH were 3 times more likely to report balance problems and 4 times more likely to have chronic distal polyneuropathy than controls[39] places the aging population of PLWH at heightened risk of falling. This vulnerability may be ameliorated with positive intervention, such as exercise, healthy nutrition, and use of stabilizing forces including lighting for night-time walking to compensate for physiological declines in somatosensory, visual motion detection, and vestibular functioning.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

1. Pfefferbaum A, Zhao Q, Pohl KM, Sassoon SA, Zahr NM, Sullivan EV. Age-Accelerated Increase of White Matter Hyperintensity Volumes Is Exacerbated by Heavy Alcohol Use in People Living With HIV. Biol Psychiatry 2023.
2. McMurtray A, Nakamoto B, Shikuma C, Valcour V. Small-vessel vascular disease in human immunodeficiency virus infection: the Hawaii aging with HIV cohort study. Cerebrovasc Dis 2007; 24(2–3):236–241. [PubMed: 17630484]
3. Ogama N, Sakurai T, Shimizu A, Toba K. Regional white matter lesions predict falls in patients with amnestic mild cognitive impairment and Alzheimer's disease. J Am Med Dir Assoc 2014; 15(1):36–41. [PubMed: 24359699]
4. Pozorski V, Oh JM, Okonkwo O, Krislov S, Barzgari A, Theisen F, et al. Cross-sectional and longitudinal associations between total and regional white matter hyperintensity volume and cognitive and motor function in Parkinson's disease. Neuroimage Clin 2019; 23:101870. [PubMed: 31150958]

5. Hua M, Ma AJ, Liu ZQ, Ji LL, Zhang J, Xu YF, et al. Arteriolosclerosis CSVD: a common cause of dementia and stroke and its association with cognitive function and total MRI burden. Front Aging Neurosci 2023; 15:1163349. [PubMed: 37520130]

6. Liu B, Zhao G, Jin L, Shi J. Association of Static Posturography With Severity of White Matter Hyperintensities. Front Neurol 2021; 12:579281. [PubMed: 33643184]

7. Chen K, Jin Z, Fang J, Qi L, Liu C, Wang R, et al. The impact of cerebral small vessel disease burden and its imaging markers on gait, postural control, and cognition in Parkinson's disease. Neurol Sci 2023; 44(4):1223–1233. [PubMed: 36547777]

8. Dai S, Piscicelli C, Lemaire C, Christiaens A, Schotten MT, Hommel M, et al. Recovery of balance and gait after stroke is deteriorated by confluent white matter hyperintensities: Cohort study. Ann Phys Rehabil Med 2022; 65(1):101488. [PubMed: 33450367]

9. Ibitoye RT, Castro P, Cooke J, Allum J, Arshad Q, Murdin L, et al. A link between frontal white matter integrity and dizziness in cerebral small vessel disease. Neuroimage Clin 2022; 35:103098. [PubMed: 35772195]

10. Pinter D, Ritchie SJ, Doubal F, Gattringer T, Morris Z, Bastin ME, et al. Impact of small vessel disease in the brain on gait and balance. Sci Rep 2017; 7:41637. [PubMed: 28134332]

11. Cahn DA, Malloy PF, Salloway S, Rogg J, Gillard E, Kohn R, et al. Subcortical hyperintensities on MRI and activities of daily living in geriatric depression. J Neuropsychiatry Clin Neurosci 1996; 8(4):404–411. [PubMed: 9116476]

12. McArthur JC, Kumar AJ, Johnson DW, Selnes OA, Becker JT, Herman C, et al. Incidental white matter hyperintensities on magnetic resonance imaging in HIV-1 infection. Multicenter AIDS Cohort Study. J Acquir Immune Defic Syndr (1988) 1990; 3(3):252–259.

13. Sullivan EV, Rose J, Rohlfing T, Pfefferbaum A. Postural sway reduction in aging men and women: relation to brain structure, cognitive status, and stabilizing factors. Neurobiology of aging 2009; 30(5):793–807. [PubMed: 17920729]

14. Baloh RW, Ying SH, Jacobson KM. A longitudinal study of gait and balance dysfunction in normal older people. Archives of neurology 2003; 60(6):835–839. [PubMed: 12810488]

15. Starr JM, Leaper SA, Murray AD, Lemmon HA, Staff RT, Deary IJ, et al. Brain white matter lesions detected by magnetic resonance [correction of resosnance] imaging are associated with balance and gait speed. J Neurol Neurosurg Psychiatry 2003; 74(1):94–98. [PubMed: 12486275]

16. Taylor ME, Lord SR, Delbaere K, Wen W, Jiang J, Brodaty H, et al. White matter hyperintensities are associated with falls in older people with dementia. Brain Imaging Behav 2019; 13(5):1265–1272. [PubMed: 30145714]

17. Willey JZ, Moon YP, Dhamoon MS, Kulick ER, Bagci A, Alperin N, et al. Regional Subclinical Cerebrovascular Disease Is Associated with Balance in an Elderly Multi-Ethnic Population. Neuroepidemiology 2018; 51(1–2):57–63. [PubMed: 29953989]

18. Zheng JJ, Lord SR, Close JC, Sachdev PS, Wen W, Brodaty H, et al. Brain white matter hyperintensities, executive dysfunction, instability, and falls in older people: a prospective cohort study. J Gerontol A Biol Sci Med Sci 2012; 67(10):1085–1091. [PubMed: 22403055]

19. Blahak C, Baezner H, Pantoni L, Poggesi A, Chabriat H, Erkinjuntti T, et al. Deep frontal and periventricular age related white matter changes but not basal ganglia and infratentorial hyperintensities are associated with falls: cross sectional results from the LADIS study. J Neurol Neurosurg Psychiatry 2009; 80(6):608–613. [PubMed: 19204027]

20. Kallianpur KJ, Sakoda M, Gangcuangco LM, Ndhlovu LC, Umaki T, Chow D, et al. Frailty Characteristics in Chronic HIV Patients are Markers of White Matter Atrophy Independently of Age and Depressive Symptoms: A Pilot Study. Open Med J 2016; 3:138–152. [PubMed: 27721908]

21. Mina Y, Wu T, Hsieh HC, Hammoud DA, Shah S, Lau CY, et al. Association of White Matter Hyperintensities With HIV Status and Vascular Risk Factors. Neurology 2021; 96(14):e1823–e1834. [PubMed: 33637630]

22. Turney IC, Lao PJ, Renteria MA, Igwe KC, Berroa J, Rivera A, et al. Brain Aging Among Racially and Ethnically Diverse Middle-Aged and Older Adults. JAMA Neurol 2023; 80(1):73–81. [PubMed: 36374494]

23. Bauer LO. HIV/AIDS and an overweight body mass are associated with excessive intra-individual variability in response preparation. J Neurovirol 2018; 24(5):577–586. [PubMed: 29777461]
24. Samboju V, Cobigo Y, Paul R, Naasan G, Hillis M, Tsuei T, et al. Cerebrovascular Disease Correlates With Longitudinal Brain Atrophy in Virally Suppressed Older People Living With HIV. J Acquir Immune Defic Syndr 2021; 87(4):1079–1085. [PubMed: 34153014]
25. Su T, Wit FW, Caan MW, Schouten J, Prins M, Geurtsen GJ, et al. White matter hyperintensities in relation to cognition in HIV-infected men with sustained suppressed viral load on combination antiretroviral therapy. Aids 2016; 30(15):2329–2339. [PubMed: 27149087]
26. Watson C, Busovaca E, Foley JM, Allen IE, Schwarz CG, Jahanshad N, et al. White matter hyperintensities correlate to cognition and fiber tract integrity in older adults with HIV. J Neurovirol 2017; 23(3):422–429. [PubMed: 28101804]
27. Wu M, Fatukasi O, Yang S, Alger J, Barker PB, Hetherington H, et al. HIV disease and diabetes interact to affect brain white matter hyperintensities and cognition. Aids 2018; 32(13):1803–1810. [PubMed: 29794829]
28. Novak V, Haertle M, Zhao P, Hu K, Munshi M, Novak P, et al. White matter hyperintensities and dynamics of postural control. Magn Reson Imaging 2009; 27(6):752–759. [PubMed: 19250785]
29. Trentalange A, Prochet A, Imperiale D, Cusato J, Tettoni M, Nunnari G, et al. Cerebral white matter Hyperintensities in HIV-positive patients. Brain imaging and behavior 2020; 14(1):10–18. [PubMed: 30238207]
30. Petersen KJ, Lu T, Wisch J, Roman J, Metcalf N, Cooley SA, et al. Effects of clinical, comorbid, and social determinants of health on brain ageing in people with and without HIV: a retrospective case-control study. Lancet HIV 2023.
31. Su C, Yang X, Wei S, Zhao R. Periventricular white matter hyperintensities are associated with gait and balance in patients with minor stroke. Front Neurol 2022; 13:941668. [PubMed: 35937058]
32. Petersen KJ, Strain J, Cooley S, Vaida F, Ances BM. Machine Learning Quantifies Accelerated White-Matter Aging in Persons With HIV. J Infect Dis 2022; 226(1):49–58. [PubMed: 35481983]
33. CDC. HIV Surveillance Report. In: Center For Disease Control And Prevention; 2020.
34. Crane HM, Ruderman SA, Whitney BM, Nance RM, Drumright LN, Webel AR, et al. Associations between drug and alcohol use, smoking, and frailty among people with HIV across the United States in the current era of antiretroviral treatment. Drug Alcohol Depend 2022; 240:109649. [PubMed: 36215811]
35. Crockett RA, Hsu CL, Dao E, Tam R, Alkeridy W, Eng JJ, et al. Mind the gaps: functional networks disrupted by white matter hyperintensities are associated with greater falls risk. Neurobiology of aging 2022; 109:166–175. [PubMed: 34740078]
36. Arendt G, Maecker HP, Purrmann J, Homberg V. Control of posture in patients with neurologically asymptomatic HIV infection and patients with beginning HIV-1-related encephalopathy. Archives of neurology 1994; 51(12):1232–1235. [PubMed: 7986179]
37. Sullivan EV, Zahr NM, Sassoon SA, Pfefferbaum A. Aging Accelerates Postural Instability in HIV Infection: Contributing Sensory Biomarkers. Journal of neuroimmune pharmacology : the official journal of the Society on NeuroImmune Pharmacology 2022.
38. Ryan AS, Roy A, Oursler KK. Gait and Balance Biomechanics in Older Adults With and Without Human Immunodeficiency Virus. AIDS Res Hum Retroviruses 2019; 35(11–12):1089–1094. [PubMed: 31547668]
39. Sakabumi DZ, Moore RC, Tang B, Delaney PA, Keltner JR, Ellis RJ. Chronic Distal Sensory Polyneuropathy Is a Major Contributor to Balance Disturbances in Persons Living With HIV. J Acquir Immune Defic Syndr 2019; 80(5):568–573. [PubMed: 30649035]
40. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 2001; 56(3):M146–M157. [PubMed: 11253156]
41. Sullivan EV, Zahr NM, Sassoon SA, Pohl KM, Pfefferbaum A. Postural instability in HIV infection: Relation to Central and Peripheral Nervous system markers. AIDS 2023; 37:1085–1096. [PubMed: 36927610]
42. Sullivan EV, Zahr NM, Sassoon SA, Pfefferbaum A. Aging Accelerates Postural Instability in HIV Infection: Contributing Sensory Biomarkers. *J* Neuroimmune Pharmacol 2022; 17(3–4):538–552.

43. Pfefferbaum A, Zhao Q, Pohl KM, Sassoon SA, Zahr NM, Sullivan EV. Age-Accelerated Increase of White Matter Hyperintensity Volumes Is Exacerbated by Heavy Alcohol Use in People Living With HIV. Biological psychiatry 2024; 95:231–244. [PubMed: 37597798]
44. Sullivan EV, Zahr NM, Sassoon SA, Pfefferbaum A. Disturbed sensory physiology underlies poor balance and disrupts activities of daily living in alcohol use disorder. Addiction biology 2021; 26(4):e12966. [PubMed: 33098738]
45. First M. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR). Washington, DC: American Psychiatric Association; 2000.
46. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorder (DSM-V). Washington, D.C.: American Psychiatric Association; 2013.
47. Skinner HA. Development and Validation of a Lifetime Alcohol Consumption Assessment Procedure. Toronto, Canada: Addiction Research Foundation; 1982.
48. Sullivan EV, Rose J, Pfefferbaum A. Effect of vision, touch and stance on cerebellar vermian-related sway and tremor: a quantitative physiological and MRI study. Cereb Cortex 2006; 16(8):1077–1086. [PubMed: 16221930]
49. Corkin S, Milner B, Rasmussen T. Somatosensory thresholds--contrasting effects of postcentral-gyrus and posterior parietal-lobe excisions. Archives of neurology 1970; 23(1):41–58. [PubMed: 4987142]
50. Adeli E, Zahr NM, Pfefferbaum A, Sullivan EV, Pohl KM. Novel Machine Learning Identifies Brain Patterns Distinguishing Diagnostic Membership of Human Immunodeficiency Virus, Alcoholism, and Their Comorbidity of Individuals. Biological psychiatry Cognitive neuroscience and neuroimaging 2019; 4(6):589–599. [PubMed: 30982583]
51. Jiang J, Liu T, Zhu W, Koncz R, Liu H, Lee T, et al. UBO Detector - A cluster-based, fully automated pipeline for extracting white matter hyperintensities. Neuroimage 2018; 174:539–549. [PubMed: 29578029]
52. Jiang J, Paradise M, Liu T, Armstrong NJ, Zhu W, Kochan NA, et al. The association of regional white matter lesions with cognition in a community-based cohort of older individuals. Neuroimage Clin 2018; 19:14–21. [PubMed: 30034997]
53. Fazekas F, Chawluk JB, Alavi A, Hurtig HI, Zimmerman RA. MR signal abnormalities at 1.5 T in Alzheimer's dementia and normal aging. AJR Am J Roentgenol 1987; 149(2):351–356. [PubMed: 3496763]
54. De Blasiis P, Caravaggi P, Fullin A, Leardini A, Lucariello A, Perna A, et al. Postural stability and plantar pressure parameters in healthy subjects: variability, correlation analysis and differences under open and closed eye conditions. Front Bioeng Biotechnol 2023; 11:1198120. [PubMed: 37545891]
55. Dellepiane M, Medicina MC, Mora R, Salami A. Static and dynamic posturography in patients with asymptomatic HIV-1 infection and AIDS. Acta Otorhinolaryngol Ital 2005; 25(6):353–358. [PubMed: 16749603]
56. Wood JM, Killingly C, Elliott DB, Anstey KJ, Black AA. Visual Predictors of Postural Sway in Older Adults. Transl Vis Sci Technol 2022; 11(8):24.
57. Sullivan EV, Zahr NM, Zhao Q, Pohl KM, Sassoon SA, Pfefferbaum A. Contributions of cerebral white matter hyperintensities, sex, and race to postural instability in aging with and without Alcohol Use Disorder. Biological Psychiatry: CNNI 2024; in revision.
58. Humes LE, Busey TA, Craig JC, Kewley-Port D. The effects of age on sensory thresholds and temporal gap detection in hearing, vision, and touch. Atten Percept Psychophys 2009; 71(4):860–871. [PubMed: 19429964]
59. Kilgore CB, Strain JF, Nelson B, Cooley SA, Rosenow A, Glans M, et al. Cardiorespiratory Fitness Is Associated With Better White Matter Integrity in Persons Living With HIV. J Acquir Immune Defic Syndr 2022; 89(5):558–565. [PubMed: 34966145]

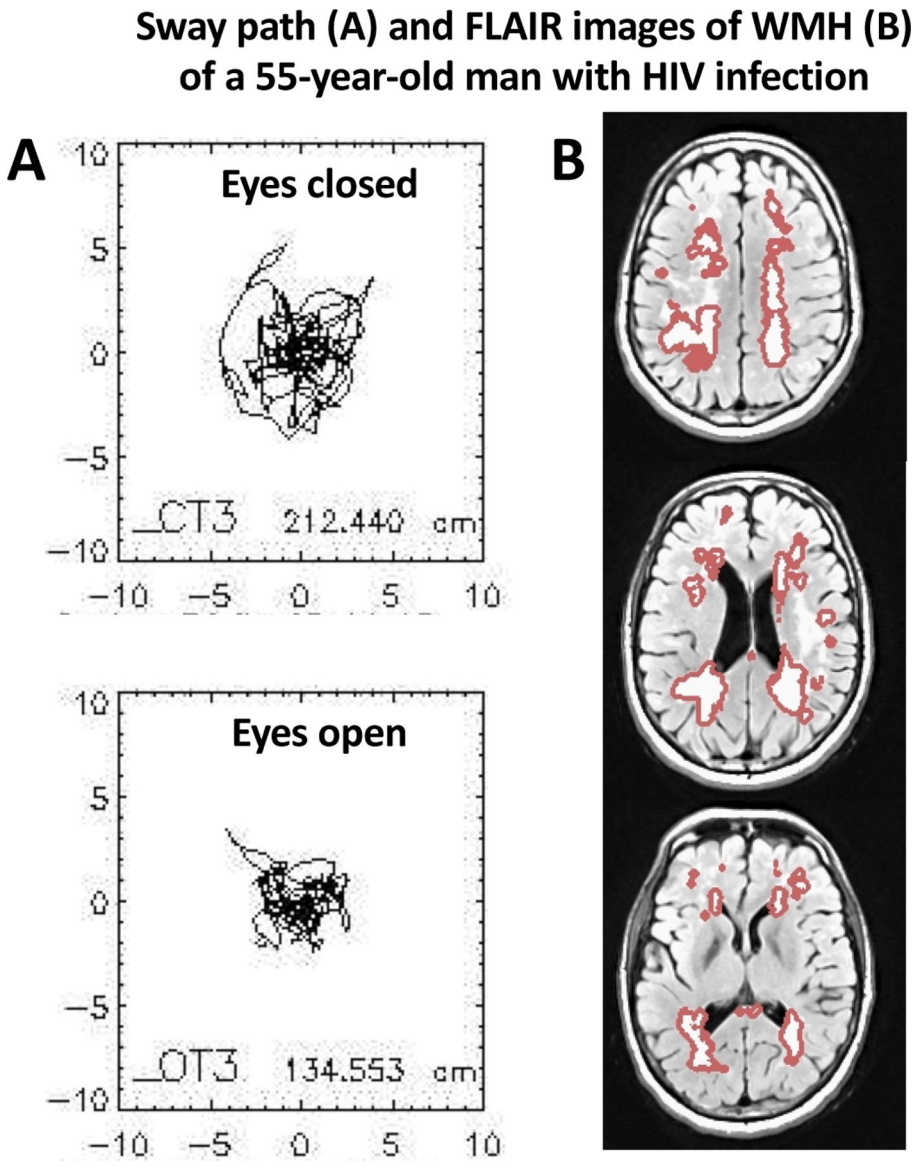

Figure 1.

A: Examples of sway paths of a 55-year-old man with HIV. The top sway path (212.4 cm long) occurred while trying to stand still with eyes closed, and the bottom sway path (134.6 cm long) occurred with eyes open. B: Axial images from FLAIR data of this participant. His WMHs are delineated in red outlining.

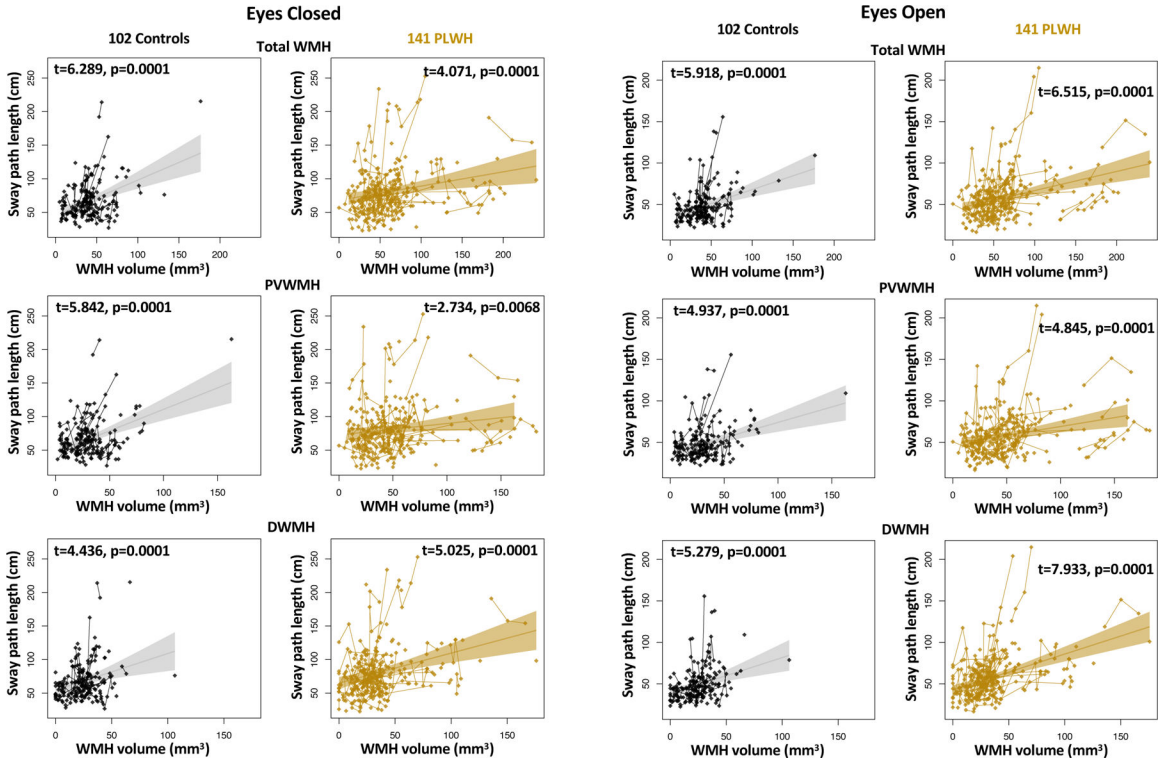

Figure 2.

Correlations between sway path length (eyes closed condition, left pair of plots; eyes open, right pair of plots) and WMH volume for total, PVWMH, and DWMH regions for 102 control participants (gray) and 141 HIV participants (gold). Participants with multiple pairs have their data points connected as shown in the spaghetti plots. Also plotted are the mean regression lines and 95% confidence intervals. All correlations were significant.

Table 1.

Study entry demographics: mean (SD) and frequency count

	Control	HIV		
Age (yrs)	53.51	53.67	t=	0.003
	(14.36)	(8.84)	p=	0.997
male/female n=	60/42	99/42	χ2=	3.394
			p=	0.065
Education (yrs)	16.21	13.40	t=	8.583
	(2.47)	(2.54)	p=	**1.878e15**
n=	99	141		
Socioeconomic status	24.86	40.90	t=	−9.457
(lower score=higher status)	(12.05)	(14.18)	p=	**<2.2e-16**
n=	100	141		
Body Mass Index (BMI)	25.97	26.16	t=	−0.328
	(4.41)	(4.23)	p=	0.743
n=	100	136		
Diastolic blood pressure (dBP)	75.99	77.45	t=	−0.909
	(11.41)	(11.01)	p=	0.365
n=	86	114		
Systolic blood pressure (sBP)	126.60	127.16	t=	−0.221
	(18.84)	(15.63)	p=	0.825
n=	86	114		
Global Assessment of Functioning (GAF)	84.32	68.78	t=	13.899
	(6.71)	(10.41)	p=	**<2.2e-16**
n=	99	136		
Beck Depression Inventory II (BDI)	2.69	9.85	t=	−8.977
	(3.75)	(8.17)	p=	**<2.2e-16**
n=	96	136		
2-point Pedal Discrimination (mm)	18.17	22.93	t=	−3.243
	(9.37)	(12.33)	p=	**0.0014**
n=	95	123		
Number of falls in past year				
0/1/2/3/4/5/6 =	14/11/6/0/1/1/0	26/11/15/1/1/1/1	χ2=	3.765
n=	33	56	p=	0.708
Lifetime alcohol consumption (kg)	40.47	525.14	t=	−7.428
	(66.66)	(765.27)	p=	**9.636e-12**
n=	101	139		
Total alcohol last visit (kg)	3.12	16.31	t=	−3.260
	(6.90)	(28.51)	p=	**0.0018**
n=	36	54		
Total alcohol in past year (kg)	1.00	6.95	t=	−5.060
	(1.61)	(13.72)	p=	**1.265e-06**

		Control	HIV		
	n=	99	139		
Length of HIV diagnosis		—	17.53		—
			(8.43)		
	n=		124		
Viral load log^{-10}(count/mL) Mean=		—	2.06		—
			(1.05)		
	n=		115		
CD4 nadir (count/mL) Mean=		—	186.55		—
			(149.20)		
	n=		108		
Virally suppressed					
HIV no/yes			26/111	χ2=	2.0344
HIV+AUD no/yes			29/80	p=	0.1538
AIDS		—			
HIV no/yes			25/35	χ2=	0.0074
HIV+AUD no/yes			27/39	p=	0.9313
Antiretroviral Treatment (ART)		—			
HIV no/yes			11/144	χ2=	0.0056
HIV+AUD no/yes			9/122	p=	0.9403
Race: Black/White/Asian/other		18/53/25/6	66/49/0/26	χ2=	57.220
				p=	**0.00001**

Viral load log^{-10} (count/mL) range = 1.3 to 5.35. Counts on average indicated viral suppression (≤200 copies).

AIDS-defining event ever in life

ART at any test session

Race was self-identified: Other includes mixed, other, and don’t know

Table 2.

Relations between sway path length and WMH volumes: simple and multiple regressions

		Simple Regression†		Multiple regression: 5 variables††									
Sway condition	**Group**	**WMH t**	**WMH p**	**WMH t**	**WMH p**	**Age t**	**Age p**	**Systolic t**	**Systolic p**	**2pt t**	**2pt p**	**Years HIV t**	**Years HIV p**
Eyes closed				**Eyes closed**									
Total WMH	**Control**	6.2886	**0.0000**	2.0185	**0.0458**	4.0395	**0.0001**	0.4837	0.6294	−0.7802	0.4368	—	—
	PLWH	4.0708	**0.0001**	0.6777	0.4989	2.8526	**0.0050**	−0.2623	0.7933	3.4762	**0.0006**	2.0343	**0.0438**
PVWMH	**Control**	5.8415	**0.0000**	2.1614	0.0325	4.2655	**0.0000**	0.7870	0.4326	−0.5318	0.5958	—	—
	PLWH	2.7339	**0.0068**	−0.5414	0.5890	3.1083	**0.0023**	−0.2820	0.7782	3.5469	**0.0005**	2.1544	0.0329
DWMH	**Control**	4.4360	**0.0000**	0.5621	0.5749	5.1542	**0.0000**	0.5790	0.5635	−0.6375	0.5250	—	—
	PLWH	5.0246	**0.0000**	2.0215	0.0446	2.6954	**0.0079**	−0.2516	0.8016	3.5376	**0.0005**	1.7308	0.0857
Frontal	**Control**	3.2100	**0.0016**	0.4221	0.6737	5.5475	**0.0000**	0.7206	0.4724	−0.5488	0.5843	—	—
	PLWH	3.9807	**0.0001**	2.3957	0.0175	2.6696	**0.0085**	−0.1432	0.8863	3.5812	**0.0004**	1.9277	0.0559
Temporal	**Control**	2.2843	0.0235	−0.4298	0.6680	5.7981	**0.0000**	0.7561	0.4509	−0.5238	0.6015	—	—
	PLWH	1.9354	0.0540	0.3852	0.7005	2.9906	**0.0033**	−0.2458	0.8060	3.5381	**0.0005**	2.1068	0.0369
Parietal	**Control**	4.0079	**0.0001**	0.3997	0.6899	5.2764	**0.0000**	0.6267	0.5319	−0.5930	0.5543	—	—
	PLWH	4.2767	**0.0000**	1.7871	0.0755	2.8536	**0.0050**	−0.3001	0.7644	3.4761	**0.0006**	1.8312	0.0692
Occipital	**Control**	3.2462	**0.0014**	−0.0477	0.9620	5.7021	**0.0000**	0.7407	0.4601	−0.5022	0.6164	—	—
	PLWH	4.0238	**0.0001**	0.4039	0.6866	2.9456	**0.0038**	−0.2964	0.7672	3.5550	**0.0005**	1.9863	0.0491
Eyes open				**Eyes open**									
Total WMH	**Control**	5.9183	**0.0000**	0.7904	0.4309	4.5276	**0.0000**	1.5972	0.1124	0.8172	0.4152	—	—
	PLWH	6.5151	**0.0000**	2.3956	**0.0178**	3.1141	**0.0022**	0.4165	0.6775	2.6744	**0.0080**	3.7053	**0.0003**
PVWMH	**Control**	4.9373	**0.0000**	0.6947	0.4885	4.7662	**0.0000**	1.7133	0.0888	0.8881	0.3760	—	—
	PLWH	4.8446	**0.0000**	1.1671	0.2451	3.3372	**0.0011**	0.3814	0.7033	2.7161	**0.0071**	3.9200	**0.0001**
DWMH	**Control**	5.2787	**0.0000**	0.3795	0.7049	5.0628	**0.0000**	1.5768	0.1170	0.8282	0.4090	—	—
	PLWH	7.9327	**0.0000**	3.7777	**0.0002**	3.0441	**0.0028**	0.4489	0.6540	2.8337	**0.0050**	3.2996	**0.0012**
Frontal	**Control**	3.3422	**0.0011**	−0.0311	0.9753	5.5633	**0.0000**	1.7390	0.0841	0.9000	0.3697	—	—
	PLWH	5.7135	**0.0000**	3.2347	**0.0014**	3.1449	**0.0020**	0.5663	0.5717	2.8883	0.0043	3.7423	**0.0003**
Temporal	**Control**	2.5551	0.0115	−0.9986	0.3198	5.8481	**0.0000**	1.7975	0.0743	0.9344	0.3517	—	—
	PLWH	3.0184	**0.0028**	0.8068	0.4207	3.5218	**0.0006**	0.4143	0.6790	2.8329	**0.0050**	3.9245	**0.0001**
Parietal	**Control**	4.8380	**0.0000**	0.2229	0.8240	5.1814	**0.0000**	1.6237	0.1066	0.8607	0.3908	—	—

Simple Regression†				Multiple regression: 5 variables††									
Sway condition	**Group**	**WMH t**	**WMH p**	**WMH t**	**WMH p**	**Age t**	**Age p**	**Systolic t**	**Systolic p**	**2pt t**	**2pt p**	**Years HIV t**	**Years HIV p**
Occipital	**PLWH**	6.7612	**0.0000**	3.2557	**0.0014**	3.3177	**0.0012**	0.3343	0.7385	2.7384	**0.0067**	3.4727	**0.0007**
	Control	4.3223	**0.0000**	0.2146	0.8304	5.4534	**0.0000**	1.6257	0.1062	0.8451	0.3995	—	—
	PLWH	7.0768	**0.0000**	2.6856	**0.0078**	3.1731	**0.0019**	0.2494	0.8033	2.9317	**0.0037**	3.3404	**0.0011**

†Simple regressions are based on 181 observations in 102 controls and on 296 observations in 140 PLWH.

††Multiple regressions are based on 153 observations in 93 control participants; 234 observations in 119 PLWH participants

Bonferroni correction (2-tailed, a=0.05) in bold font: p≤0.025 for 2 comparisons and p≤0.0125 for 4 comparisons

Color coding: p≤0.05 uncorrected with gray=controls, gold=PLWH.

Table 3.

Multiple regressions predicting sway from WMH volumes controlling only for variable found to contribute significantly to sway path

Sway condition	WMH volume		†Diagnosis		Age		Systolic blood pressure		2-point discrimination		†Diagnosis x WMH interaction	
Eyes closed	**t**	**p**	**t**	**p**	**t**	**p**	**t**	**p**	**t**	**p**	**t**	**p**
Total WMH	0.6968	0.4865	0.9055	0.3660	5.4546	**0.0000**	0.3798	0.7043	3.1358	**0.0018**	0.1415	0.8875
PVWMH	1.0169	0.3100	1.8156	0.0705	5.7602	**0.0000**	0.4692	0.6392	3.2284	**0.0013**	-0.7160	0.4745
DWMH	−0.3215	0.7480	−0.1029	0.9181	5.8932	**0.0000**	0.4610	0.6450	3.2531	**0.0012**	1.6077	0.1087
Frontal	−0.2072	0.8360	1.2124	0.2266	6.2963	**0.0000**	0.5460	0.5854	3.2780	**0.0011**	1.1054	0.2699
Temporal	−0.7947	0.4273	1.6615	0.0980	6.7381	**0.0000**	0.5332	0.5942	3.2686	**0.0012**	1.1213	0.2629
Parietal	−0.4130	0.6799	0.3340	0.7386	6.2298	**0.0000**	0.4494	0.6534	3.1815	**0.0016**	1.4351	0.1521
Occipital	−0.9370	0.3493	−0.3101	0.7566	6.3119	**0.0000**	0.5032	0.6151	3.4088	**0.0007**	1.9524	0.0516
Eyes open	**t**	**p**	**t**	**p**	**t**	**p**	**t**	**p**	**t**	**p**	**t**	**p**
Total WMH	0.0705	0.9438	−0.6812	0.4963	6.2454	**0.0000**	1.5446	0.1232	3.2355	**0.0013**	1.7736	0.0771
PVWMH	−0.0694	0.9448	−0.0023	0.9982	6.6682	**0.0000**	1.5659	0.1182	3.3097	**0.0010**	1.3141	0.1898
DWMH	−0.0159	0.9873	−1.0777	0.2820	6.3263	**0.0000**	1.5527	0.1213	3.3580	**0.0009**	2.4958	**0.0130**
Frontal	−0.4387	0.6612	0.7463	0.4562	7.0292	**0.0000**	1.7545	0.0801	3.5177	**0.0005**	1.8086	0.0715
Temporal	−1.3505	0.1778	1.2892	0.1986	7.5708	**0.0000**	1.7263	0.0851	3.5393	**0.0004**	2.0286	**0.0433**
Parietal	−0.2686	0.7884	−0.4902	0.6243	6.7979	**0.0000**	1.4959	0.1355	3.3024	**0.0010**	2.2794	**0.0233**
Occipital	−0.1107	0.9119	−1.5605	0.1195	6.4840	**0.0000**	1.3532	0.1767	3.4861	**0.0005**	3.2299	**0.0013**

†Diagnosis = Control vs. PLWH

Regressions are based on 409 observations (from 153 control visits plus 256 HIV visits) taken on 222 individuals (93 individual controls and 129 HIV participants).

Bonferroni correction for 2 PVWMH and DWMH comparisons (2-tailed, a=0.05) requires p≤0.025 and for 4 regional comparisons p≤0.0125 noted in bold font.

Interactions meeting p≤0.05 are in bold font.