

UC San Diego

UC San Diego Previously Published Works

Title

Auditory and cognitive function in older adults living with and without HIV

Permalink

<https://escholarship.org/uc/item/4h117294>

Journal

AIDS, 37(13)

ISSN

0269-9370

Authors

Torre, Peter

Sundermann, Erin E

Brandino, Amanda

et al.

Publication Date

2023-11-01

DOI

10.1097/qad.0000000000003618

Peer reviewed



Published in final edited form as:

AIDS. 2023 November 01; 37(13): 1971–1978. doi:10.1097/QAD.0000000000003618.

Auditory and Cognitive Function in Older Adults Living With and Without HIV

Peter TORRE III, PhD, MS¹, Erin E. SUNDERMANN², Amanda BRANDINO³, Anne HEATON², Julia DEVORE¹, Albert M. ANDERSON^{3,*}, Raeanne C. MOORE^{2,*}

¹San Diego State University, School of Speech, Language, and Hearing Sciences, San Diego, CA, USA

²University of California San Diego, Department of Psychiatry, La Jolla, CA, USA

³Emory University, Atlanta, Georgia, USA

Abstract

Objectives: To evaluate: 1) the peripheral hearing sensitivity and central auditory processing in persons living with HIV (PWH) and persons living without HIV (PWoH); and 2) the association between cognitive function and central auditory processing in PWH and PWoH.

Design: Cross-sectional, observational study.

Methods: Participants included 67 PWH (70.2% male; mean age=66.6 years [SD=4.7 years]) and 35 PWoH (51.4% male; mean age=72.9 years [SD=7.0 years]). Participants completed a hearing assessment and a central auditory processing assessment that included dichotic digits testing (DDT). Pure-tone air-conduction thresholds were obtained at octave frequencies from 0.25 through 8 kHz. A pure-tone average (PTA) was calculated from 0.5, 1, 2, and 4 kHz thresholds for each ear. Participants also completed a neuropsychological battery assessing cognition in seven domains.

Results: PWH had slightly lower (i.e., better) PTAs compared to PWoH, but this was not statistically significant. Conversely, PWH and PWoH had similar DDT results for both ears. Poorer verbal fluency, learning, and working memory performance was significantly related to lower DDT scores, and those defined as having verbal fluency, learning, and working memory impairment had significantly poorer DDT scores (8–18% lower) in both ears.

Conclusions: Hearing and DDT results were similar in PWH and PWoH. The relationship between verbal fluency, learning, and working memory impairment and poorer DDT results did not differ by HIV serostatus. Clinicians, particularly audiologists, should be mindful of cognitive functioning abilities when evaluating central auditory processing.

Keywords

HIV; hearing; central auditory processing; cognitive function

Correspondence: Peter Torre III, PhD, MS, School of Speech, Language, and Hearing Sciences, San Diego State University, San Diego, CA 92182-1518, Phone: (619) 594-4787, ptorre@sdsu.edu.

*Joint Senior Authors

Introduction

Hearing consists of peripheral components (outer and middle ear, cochlea) and the central auditory system (cochlear nuclei to the auditory cortex). Speech discrimination and auditory temporal discrimination rely on peripheral hearing abilities (i.e., pure-tone thresholds) and central auditory processing and cognitive functioning. Specifically, working memory, executive function, attention, and verbal fluency allow for differentiating auditory stimuli. Thus, central auditory processing deficits can be a result of peripheral hearing loss and/or cognitive impairment. Assessing central auditory processing deficits can be difficult because of these complex interactions. It is unclear whether human immunodeficiency virus (HIV) impacts the audiologic system peripherally, centrally, or both.

Persons with HIV (PWH) are at higher risk for sensorineural (i.e., peripheral) hearing loss compared to persons without HIV (PWoH) [1,2], and this association remained significant after adjusting for age, sex, and noise exposure [1]. Others have not reported poorer hearing thresholds in PWH compared to PWoH [3,4]. In PWH, those with greater HIV disease duration or late-stage disease had poorer thresholds suggestive of some effect of HIV disease mechanisms on hearing [3]. The literature on central auditory processing deficits in PWH is limited, but PWH have poorer central auditory processing compared with PWoH [4,5].

Further, HIV is a risk factor for cognitive impairment. Cognitive deficits, typically mild, are a common feature of HIV, occurring in 40–45% of PWH [6,7]. The frequency of HIV-associated dementia (HAD), the severe form of cognitive deficit, has decreased with the advent of combination antiretroviral therapy (ART), while the prevalence of milder deficits have remained stable [8–10]. Although the specific cognitive domains impacted in PWH are highly variable, episodic learning and memory, executive function and working memory are most commonly impacted [9]. The effects of aging on the central nervous system are particularly significant in PWH. In PWH, there is accelerated aging based on brain integrity despite virologic suppression [11]. Additionally, neurocognitive performance in PWH aged 50–65 years is worse than age-matched PWoH, but similar to PWoH >65 years [12], and older age among PWH is associated with higher odds of memory impairment compared to historical norms from PWoH [13]. Given that older age is associated with higher risk for hearing loss [14], more research is needed to understand the potential accelerated aging effect on hearing in PWH.

The gold standard used to clinically determine peripheral hearing loss is to use pure-tone thresholds [15]. Pure-tone threshold testing is not representative of real-world communication since pure-tone stimuli consist of single frequency energy and do not put the auditory system under strain. Dichotic digits testing (DDT) incorporates multiple frequency stimuli (i.e., numbers) and requires binaural processing, offering an assessment of central auditory processing. Any interruption in the transmission of the auditory signal along the central auditory system may result in perceptual deficits that are not always associated with hearing loss. These perceptual deficits include difficulty hearing in challenging listening environments, difficulty localizing sound sources, distorted auditory signals, and poor auditory discrimination. Even adults with normal peripheral hearing report hearing difficulties due to central auditory processing problems [16,17]. DDT is more sensitive and

specific to central auditory processing performance compared with other measures of central auditory processing [18] and has a low linguistic demand on the person under test.

Because comprehension of complex (i.e., multiple frequency) stimuli involves central auditory processing *and* cognitive function *along with* input from the periphery, an assessment battery that includes measures of these variables provides a more thorough evaluation of communication abilities. As a result, the purpose of this study was to evaluate: 1) peripheral hearing sensitivity and central auditory processing in older (age ≥ 60 years) PWH and PWOH; and 2) the association between cognitive function measures and central auditory processing in older PWH versus PWOH. It was hypothesized that PWH will have poorer peripheral hearing sensitivity and central auditory processing compared to PWOH, and that those with poorer cognitive functioning will have poorer central auditory processing, especially among PWH.

Methods

Study Participants

Participants were from the longitudinal, observational DETECT study (*A Virtual Reality Device to Assess How HIV Affects Neurocognitive Decline and Postural Instability in Older Adults*), a multi-site collaboration between UC San Diego, San Diego State University (SDSU) and Emory University. Participants in San Diego were recruited from the broader San Diego community as well as from ongoing studies at the HIV Neurobehavioral Research Program (HNRP). Participants in Atlanta were recruited from metropolitan-area clinics including those affiliated with the Emory Center for AIDS Research (CFAR). Eligibility for the DETECT Study included PWH and PWOH, aged ≥ 60 years at enrollment, fluent in English, and ability to provide informed consent. Further, PWH were required to be on ART and virally suppressed (plasma HIV RNA <200 copies/ml for at least six months). PWOH included individuals who had a clinical diagnosis of mild cognitive impairment (MCI), given its similarities with milder forms of HIV-associated neurocognitive disorder. Exclusion criteria included diagnosis of HAD, persons with probable dementia, based on scores ≥ 10 on the HIV Dementia Scale, persons in hospice, plans to move out of the area within the following three years, serious mental illness (e.g., schizophrenia, bipolar disorder) or neurological confounds unrelated to HIV (e.g., head injury with loss of consciousness for more than 30 minutes, seizure disorder, stroke, dementia), and significant visual or hearing impairments that would impact ability to complete study assessments. Baseline data were used for this study. All study procedures were approved by the institutional review boards of the three sites.

Study Procedures

HIV Disease Characteristics.—HIV serostatus was confirmed in all participants with HIV/HCV antibody point-of-care rapid test (Miriad, MedMira, Nova Scotia, Canada) and confirmatory Western blot analyses and/or by HIV RNA testing. In a majority of cases, previous AIDS diagnosis, estimated duration of HIV disease, antiretroviral therapy regimen, and nadir CD4 count were obtained via the medical record. Self-report was only used if the

electronic medical record was not available. Plasma HIV suppression (<200 copies/mL) was confirmed on study entry and current CD4 count was also measured.

Audiology Evaluation.—A certified audiologist (author AB) or fully trained research assistant (author JD), blinded to HIV status completed all hearing procedures. The hearing examination consisted of bilateral otoscopy, tympanometry, speech recognition thresholds (SRTs), pure-tone air-conduction audiometry, and DDT. Otoscopy and tympanometry were completed to evaluate potential impairment in the conductive mechanism of the auditory system that would impact further testing results. For pure-tone testing, SRTs, and DDT, participants were seated in a sound-treated room with insert earphones comfortably placed in their ear canals. Pure-tone audiometry was completed using procedures recommended by the American Speech-Language-Hearing Association [19]. Air conduction thresholds were obtained at octave frequencies from 0.25–8 kHz as well as inter-octave frequencies of 3 and 6 kHz. The SRT is the lowest level, in decibels (dB), at which a person can repeat a two-syllable word correctly. For DDT, two numbers are presented (1 through 10, except 7) in each ear simultaneously (4 numbers total) and the task is to repeat all the numbers heard. The test was completed at 50 dB above the SRT to ensure a comfortable listening level and maximum performance. The test consisted of 20 dichotic stimulus presentations, or 80 total digits (40 per ear).

Neuropsychological Evaluation.—Participants completed the HNRP's neuropsychological test battery which assesses seven cognitive domains: learning, recall, verbal fluency, working memory, speed of information processing, executive function, and complex motor function. The specific cognitive tests are presented in Table 1 and have been described in detail elsewhere [20]. Raw test scores were transformed into scaled scores (SSs), with a mean of 10 and standard deviation of 3. SSs from all tests within each domain were averaged together to create domain-specific SSs, and all SSs were averaged together to create a global SS. The study began prior to the COVID-19 pandemic and, due to evolving restrictions on in-person data collection during the height of the pandemic, site-specific modifications to neuropsychological testing were made. UCSF had more preventative restrictions on in-person visits during the pandemic than Emory, and thus remote visits were implemented. For a portion of the testing (Table 1), assessments were administered remotely via video conferencing. This method of teleneuropsychological evaluation has been validated against in-person neuropsychological evaluations among both PWH and PWOH [21]. Participants were asked to complete the remote visit in a quiet environment away from distractions and to refrain from utilizing any performance aids or seeking help from others. All data collected at Emory and SDSU were collected in-person.

Outcome Measures

A pure-tone average (PTA) was calculated from 0.5, 1, 2, and 4 kHz thresholds for each ear, from which a better ear and worse ear PTA was defined. Hearing loss was defined as a better ear or worse ear PTA >25 dB. The outcome of DDT was percent correct for each ear.

Statistical Analyses

Worse ear and better ear PTA and DDT percent correct are presented as medians and interquartile ranges due to the skewness of the distributions. Linear models (PROC GLM and PROC REG; SAS, Version 9.4) were used to examine how HIV serostatus relates to PTA and DDT and the association between cognitive outcomes (global and domain-specific SSs) and DDT while adjusting for age, sex, race, and years of education. HIV by cognitive outcome interaction terms were included in all models to test the moderating role of HIV serostatus in the cognition and DDT association.

Global and domain-specific cognitive performance were examined as continuous SSs and as dichotomous variables of impaired versus non-impaired, with impairment defined as a SS more than 1 standard deviation below the mean (i.e., $SS < 7$). In all analyses, PTA was evaluated separately for the better and worse ear and DDT were evaluated separately for each ear (i.e., DDT-right and DDT-left).

Results

One hundred and two participants (67 PWH and 35 PWOH) completed baseline pure-tone threshold testing. Table 2 summarizes the demographic characteristics and cognitive status of the study participants by HIV status. On average, participants were 69 years old (range: 60–91 years) with 15 years of education. PWH were younger, more likely to be male, and had fewer years of education compared to PWOH. Further, PWH had higher percentages of Black and Hispanic adults, whereas the majority of PWOH were non-Hispanic White. PWH and PWOH did not differ on global or domain-specific SSs, rates of global or domain-specific impairment, or rate of MCI. For example, 31.4% (11 of 35) of PWOH and 31.3% (21 of 67) of PWH were defined as having global cognitive impairment. This confirms that both globally impaired and unimpaired individuals were enrolled in this study. PWH had a median duration of HIV disease of 28 years.

PWH had similar median worse ear PTAs compared to PWOH but and significantly lower (i.e., better) better ear PTAs compared to PWOH (Table 3), although this difference was not significant after adjusting for demographic covariates (age, sex, race, and years of education). PWH also had a lower percentage (44.8%, 30 of 67) of worse ear hearing loss compared to PWOH (57.1%, 20 of 35), although this difference was also not statistically significant ($X^2(1)=1.41$, $p=0.23$). However, a significantly lower percentage (28.4%) of PWH had better ear hearing loss compared to PWOH (51.4%; $X^2(1)=5.29$, $p=0.02$). In the analyses with PWH only, none of the HIV disease severity variables were associated with any of the hearing outcomes.

Since DDT was conducted at a presentation level 50 dB above the participant's SRT, some presentation levels would have been uncomfortably loud (e.g., 95–110 dB), therefore the assessment was not completed. As a result, 61 PWH and 29 PWOH had DDT data; median DDT percent correct in the right ear was slightly higher (i.e., better) than median DDT percent correct in the left ear in both PWH and PWOH. DDT percent correct was similar between PWH and PWOH (Table 3). There was no association between HIV status and DDT in the right ear or the left ear in the unadjusted model and adjusted models.

All HIV by cognitive domain score interaction terms were not statistically significant and therefore removed from the final models. Global cognitive impairment was significantly associated with lower DDT-left percent correct (DDT-left; $F[1,77]=16.22$, $p<0.05$) while marginally associated with lower DDT-right percent correct (DDT-right; $F[1,77]=3.58$, $p=0.06$) in models adjusting for demographic covariates and HIV status (Table 4). The adjusted mean DDT-left was 89.2% in those without global impairment and 70.4% in those with global impairment. For DDT-right, the adjusted mean for those with global impairment was 90.2% and 82.7% for those without global impairment.

Verbal fluency impairment, learning impairment, and working memory impairment were significantly associated with lower DDT-left and lower DDT-right in adjusted models (Table 4). The adjusted means for DDT-left and DDT-right were 8%–18% lower in those with impairments in those domains compared to those without impairment. Executive function and processing speed impairment significantly related to lower DDT-right and showed a trend association with lower DDT-left. Delayed recall and motor domains were not associated with DDT-left or DDT-right.

When examining continuous SSs, global SS was significantly and positively associated with DDT-left ($F[1,77]=15.79$, $p<0.05$) and DDT-right ($F[1,77]=12.42$, $p<0.05$) after adjusting for demographic covariates and HIV status. Verbal fluency, executive function, processing speed, learning, and working memory SSs were significantly and positively associated with DDT-left and DDT-right (Figure 1). DDT performance in either ear was not significantly associated with the other cognitive domains.

Discussion

Given the high rates of hearing problems reported in PWH and the potential accelerated aging effects that are emerging among PWH, more research is needed on hearing in this population. In the current study, a group PWOH that included a significant number of people with MCI diagnosis had symmetrical hearing loss such that slightly over 50% had worse ear and better ear hearing loss. Conversely, PWH had more asymmetrical hearing loss, with fewer participants having better ear hearing loss as compared to the worse ear hearing loss. The reason for this asymmetry is not known at this time and requires additional study.

The prevalence of hearing loss in the current study is higher than what has been reported in PWH [2,3]. Around 50% of PWH and PWOH had worse ear hearing loss while others have reported hearing loss between 14% [2] and 17.6% [3] among PWH. This is likely due to participant age; all participants in the current study were 60 years, whereas in other studies, mean ages were in the 30s [2] or 40s [3]. Given that the prevalence of hearing loss increases with age [14], this difference was not unexpected.

Prevalence of hearing loss did not differ by HIV serostatus. The lack of an association between HIV status and hearing loss is consistent with some research [3,4], but not with other research [1,2]. Although the adjusted models in the current study, included age, sex, race, and years of education, noise exposure (either occupational or recreational) was not included in the models. PWOH in this sample were significantly older than PWH, it is

possible that PWOH also had more occupational noise exposure than PWH resulting in a higher prevalence of worse ear and better ear hearing loss. Sample sizes in the current study may not be large enough to detect relatively small differences between groups.

There was no difference in central auditory processing between PWH and PWOH who were matched on cognitive impairment status. Others have used different measures of central auditory processing [4,22,23], the current study is the first to evaluate DDT in PWH. Others have used central auditory processing measures including speech in noise testing and gap detection. For speech in noise testing, researchers either only tested PWH [22] or compared young adults living with HIV with those young adults who were perinatally HIV exposed, but uninfected [23]. In the latter study, results were similar to those in the current study such that the ability to identify speech in noise was similar between the two groups [23]. Gap detection thresholds were similar between PWH and PWOH [4] suggesting that central auditory processing may be spared the effects of HIV, although more research is needed in this area.

Certain types of hearing loss are known to herald the development of cognitive problems; this has been examined in mostly PWOH populations. Hearing loss has been shown to predict decline in global cognitive measures as well as learning and memory [24,25] and age-related hearing loss was identified as the largest potentially modifiable risk factor for dementia by the Lancet Commission on Dementia Prevention, Intervention and Care [26]. Central auditory processing impairment has also been found among those with clinical or biological evidence of early-stage Alzheimer's disease [27,28]. In light of the higher rates of cognitive impairment and some evidence of accelerated aging in PWH, the question of how hearing ability could potentially signal current or incipient cognitive decline is particularly important. In this sample, a majority of participants met criteria for cognitive impairment in at least one domain and over 30% of both PWH and PWOH were defined as having global cognitive impairment. In the current study, there was poorer performance on a measure of central auditory processing in both ears related to poorer global cognitive function although only a statistical trend with DDT-right. A study of young men with HIV in China also showed a relationship between poorer central auditory processing and worse cognition; those with cognitive impairment had poorer speech in noise outcomes [22]. However, cognition was assessed using a singular global cognitive screen, the brief Montreal Cognitive Assessment. This study further informs these prior findings by including a PWOH group and examining whether this relationship is driven by specific cognitive domains.

Poorer central auditory processing performance in both ears was associated with working memory, verbal fluency, learning and executive function and processing speed impairment. Although the associations between DDT-left and executive function and processing speed were statistical trends. Most of the domains that related to central auditory processing performance were higher-order cognitive domains regulated by frontal lobe function. This is likely due to the multi-tasking component of the DDT that involves frontal-regulated executive processes. Central auditory processing also related to the hippocampal-based learning domain. Learning is one of the earliest domains impacted in Alzheimer's disease. Given the evidence of central auditory processing deficits in early-stage Alzheimer's disease

[27,28], it is possible that this relationship is driven by a subset of the sample with early-stage Alzheimer's pathogenesis.

The relationship between central auditory processing and cognition did not differ by HIV serostatus. It is possible that this relationship may be more impactful among PWH given the higher frequency of cognitive impairment in this population. Although this higher prevalence of cognitive deficits in PWH was not found in the current sample, meta-analytic studies report that frontal-based executive function is among the most commonly and severely impaired domain among PWH [9,29,30]. The high rates of executive function deficits and the current findings suggest that communication ability may be compromised among PWH.

There are some limitations in the current study. While certain cognitive domains and central auditory processing appear to be related, it is not clear if it is a casual relationship. If longitudinal studies show that DDT deficits precede cognitive impairment, then interventions for DDT such as dichotic interaural intensity difference training [31] may reduce the risk of cognitive decline. Further, this was an older sample, and many had cognitive impairment. While the focus of the study was older people, it is acknowledged that the study would have broader applicability if people across the age spectrum were included. Including a younger, unimpaired sample of PWH and PWOH as a reference cohort may better elucidate the relationships between aging, cognition, and central auditory processing. The lack of an assessment for substance use is another limitation since substance use impacts cognition. As mentioned previously, noise exposure is a risk factor for hearing loss that ideally should be accounted for in analyses; those data were not available. The current study did have smaller sample sizes compared to other studies [1,3], but the current study did include comprehensive neurocognitive and audiological assessments on all participants. Lastly, DDT data were not collected on all participants because the presentation level would have been uncomfortably loud for those with more hearing loss.

Conclusions

The current study provides novel data on peripheral hearing and central auditory processing comparisons in older PWH and PWOH and how central auditory processing relates to cognitive function. There were higher rates of hearing impairment (about 50%) than prior studies of hearing sensitivity among PWH likely due to the older sample in this study. These rates did not significantly differ between PWH and PWOH. There were no differences in central auditory processing between PWH and PWOH. Regardless of HIV serostatus, poorer central auditory processing was significantly associated with global cognition and the specific domains of working memory, verbal fluency, learning and executive function and processing speed. Measuring central auditory processing together with standard audiology evaluations provides more accurate evaluation of communication ability and can provide valuable insights for future treatment. It is hoped that this type of research will enable more comprehensive, multi-modal assessment methods for persons aging with HIV, and more accurately reflect targets for interventions.

Acknowledgments

Funding for this project was supported by NIA R01 AG062387 and P30AI050409 (Emory Center for AIDS Research)

References

1. Torre P III, Hoffman HJ, Springer G, Cox C, Young MA, Margolick JB, et al. Hearing loss among HIV-seropositive and HIV-seronegative men and women. *JAMA Otolaryngol–Head Neck Surg* 2015; 141:202–210. [PubMed: 25541676]
2. Van der Westhuizen Y, Swanepoel DW, Heinze B, Hofmeyr LM. Auditory and otological manifestations in adults with HIV/AIDS. *Int J Audiol* 2013; 52:37–43. [PubMed: 23043519]
3. Luque AE, Orlando MS, Leong UC, Allen PD, Guido JJ, Yang H, et al. Hearing function in patients living with HIV/AIDS. *Ear Hear* 2014; 35:e282–e290. [PubMed: 25127320]
4. Maro II, Moshi N, Clavier OH, MacKenzie TA, Kline-Schoder RJ, Wilbur JC, et al. Auditory impairments in HIV-infected individuals in Tanzania. *Ear Hear* 2014; 35:306–317. [PubMed: 24441742]
5. Niemczak CE, Cox C, Grigoryan G, Springer G, Fellows AM, Torre P III, et al. Gap detection responses modelled using the Hill equation in adults with well-controlled HIV. *Int J Audiol* 2022; 1–10.
6. Wei J, Hou J, Su B, Jiang T, Guo C, Wang W, et al. The Prevalence of Frascati-Criteria-Based HIV-Associated Neurocognitive Disorder (HAND) in HIV-Infected Adults: A Systematic Review and Meta-Analysis. *Front Neurol* 2020; 11:581346. [PubMed: 33335509]
7. Wang Y, Liu M, Lu Q, et al. Global prevalence and burden of HIV-associated neurocognitive disorder: A meta-analysis. *Neurology* 2020; 95:e2610–e21. [PubMed: 32887786]
8. Grant I. Neurocognitive disturbances in HIV. *Int Rev Psychiatry* 2008; 20:33–47. [PubMed: 18240061]
9. Heaton RK, Franklin DR, Ellis RJ, McCutchan JA, Letendre SL, Leblanc S, et al. HIV-associated neurocognitive disorders before and during the era of combination antiretroviral therapy: differences in rates, nature, and predictors. *J Neurovirol* 2011; 17:3–16. [PubMed: 21174240]
10. Woods SP, Moore DJ, Weber E, Grant I. Cognitive neuropsychology of HIV-associated neurocognitive disorders. *Neuropsychol Rev* 2009; 19:152–168. [PubMed: 19462243]
11. Petersen KJ, Metcalf N, Cooley S, Tomov D, Vaida F, Paul R, et al. Accelerated brain aging and cerebral blood flow reduction in persons with human immunodeficiency virus. *Clinical Infect Dis: official publication Infect Dis Soc Am* 2021; 73:1813–1821.
12. Sheppard DP, Iudicello JE, Morgan EE, Kamat R, Clark LR, Avci G, et al. Accelerated and accentuated neurocognitive aging in HIV infection. *J Neurovirol* 2017; 23:492–500. [PubMed: 28321696]
13. Tan IL, Smith BR, Hammond E, Vornbrock-Roosa H, Creighton J, Selnes O, et al. Older individuals with HIV infection have greater memory deficits than younger individuals. *J Neurovirol* 2013; 19:531–536. [PubMed: 24078559]
14. Cruickshanks KJ, Wiley TL, Tweed TS, Klein BEK, Klein R, Mares-Perlman JA, et al. Prevalence of hearing loss in older adults in Beaver Dam, Wisconsin: The epidemiology of hearing loss study. *Am J Epidemiol* 1998; 148:879–886. [PubMed: 9801018]
15. Katz J, Chasin M, English KM, Hood LJ, Tillery, editors. *Handbook of clinical audiology*. Philadelphia, PA: Wolters Kluwer Health; 2015.
16. Tremblay K, Pinto A, Fischer M, Klein BEK, Klein R, Levy S, et al. Self-reported hearing difficulties among adults with normal audiograms: The Beaver Dam offspring study. *Ear Hear* 2015; 36:e290–299. [PubMed: 26164105]
17. Shinn J, Long A, Rayle C, Bush M. Primary auditory symptoms in patients with normal peripheral hearing sensitivity: redefining hearing loss. *Hear Bal Comm* 2016; 14:44–49.
18. Hurley RM, Musiek FE. Effectiveness of three central auditory processing (CAP) tests in identifying cerebral lesions. *J Am Acad Audiol* 1997; 8:257–262. [PubMed: 9272747]

19. American Speech-Language-Hearing Association. Guidelines for Manual Pure-Tone Audiometry. 2005. Available from www.asha.org/policy.
20. Cysique LA, Franklin D Jr, Abramson I, Ellis RJ, Letendre S, Collier A, et al. Normative data and validation of a regression based summary score for assessing meaningful neuropsychological change. *J Clin Exper Neuropsychol* 2011; 33:505–22. [PubMed: 21391011]
21. Kohli M, Fisher A, Sun-Suslow N, Heaton A, Dawson M, Marquie J, et al. Concurrent validity and reliability of teleneuropsychological evaluations among people with and without HIV. *J Int Neuropsychol Soc* 2023; 29(2):193–204. [PubMed: 36510855]
22. Zhan Y, Fellows AM, Qi T, Clavier OH, Soli SD, Shi X, et al. Speech in noise perception as a marker of cognitive impairment in HIV infection. *Ear Hear* 2018; 39:548–554. [PubMed: 29112532]
23. Torre III P, Russell JS, Smith R, Hoffman HJ, Lee S, Williams PL, et al. Words-in-noise test performance in young adults perinatally HIV infected and exposed, uninfected. *Am J Audiol* 2020; 29:68–78. [PubMed: 32004075]
24. Lin FR, Yaffe K, Xia J, Xue QL, Harris TB, Purchase-Helzner E, et al. Hearing loss and cognitive decline in older adults. *JAMA Intern Med* 2013; 173:293–299. [PubMed: 23337978]
25. Armstrong NM, An Y, Ferrucci L, Deal JA, Lin FR, Resnick SM. Temporal sequence of hearing impairment and cognition in the Baltimore longitudinal study of aging. *J Gerontol. Series A, Biol Sci Med Sci* 2020; 75:574–580.
26. Livingston G, Sommerlad A, Orgeta V, Costafreda SG, Huntley J, Ames D, et al. Dementia prevention, intervention, and care. *Lancet* 2017; 390(10113): 2673–2734. [PubMed: 28735855]
27. Gates GA, Beiser A, Rees TS, D’Agostino RB, Wolf PA. Central auditory dysfunction may precede the onset of clinical dementia in people with probably Alzheimer’s disease. *J Am Geriatr Soc* 2002; 50: 482–488. [PubMed: 11943044]
28. Gates GA, Anderson ML, McCurry SM, Feeney MP, Larson EB. Central auditory dysfunction as a harbinger of Alzheimer dementia. *Arch Otolaryngol Head Neck Surg* 2011; 137:390–395. [PubMed: 21502479]
29. Cysique LA, Maruff P, Brew BJ. The neuropsychological profile of symptomatic AIDS and ADC patients in the pre-HAART era: a meta-analysis. *J Int Neuropsychol Soc: JINS* 2006; 12:368–382. [PubMed: 16903129]
30. Reger M, Welsh R, Razani J, Martin DJ, Boone KB. A meta-analysis of the neuropsychological sequelae of HIV infection. *J Int Neuropsychol Soc: JINS* 2002; 8:410–24. [PubMed: 11939699]
31. Musiek FE, Shinn J, Hare C. Plasticity, auditory training, and auditory processing disorders. *Sem Hear* 2002; 23:263–276.

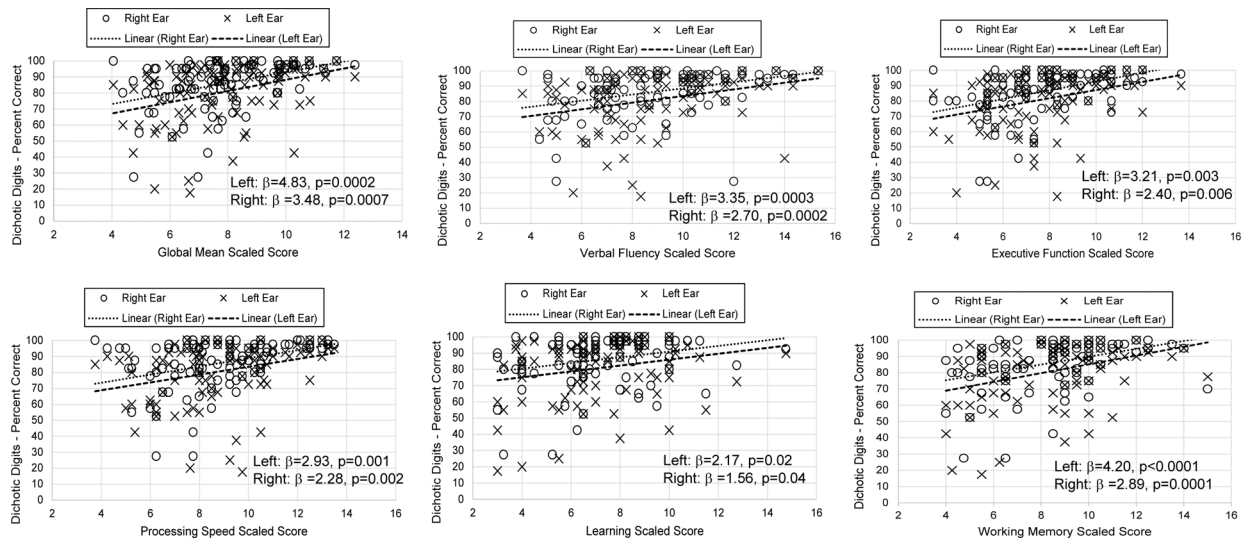


Figure 1. Dichotic digits percent correct as a function of domain-specific cognitive function scaled scores for left and right ears.

Table 1.

HIV Neurobehavioral Research Program Neuropsychological Test Battery

<u>Verbal Fluency</u>	<u>Executive Functioning</u>
Controlled Oral Word Association Test (FAS) ¹	Wisconsin Card Sorting Test
Category Fluency (Animals/Actions) ¹	Trail Making Test (Part B)
<u>Speed of Information Processing</u>	Stroop Color-Word trial ¹
WAIS-III Digit Symbol	<u>Learning</u>
WAIS-III Symbol Search ¹	HVLT-R (Immediate Recall) ¹
Trail Making Test (Part A)	BVMT-R (Immediate Recall)
Stroop Color trial*	<u>Memory</u>
<u>Attention/Working Memory</u>	HVLT-R (Delayed Recall) ^{1,2}
WAIS-III Letter-Number Sequencing ¹	BVMT-R (Delayed Recall) ²
Paced Auditory Serial Addition Task ¹	<u>Motor</u>
	Grooved Pegboard (average of Dominant and non-dominant hand trials)

¹ Assessments administered remotely at UCSD.

² HVLT-R and BVMT-R delayed recall was assessed 25 minutes after learning trials.

HVLT-R = Hopkins Verbal Learning Test-Revised; BVMT-R = Brief Visuospatial Memory Test-Revised.

Table 2.

Demographics and clinical characteristics stratified by HIV status.

Characteristic	PWH (n=67)	PWoH (n=35)	Test Statistic (t-test or Chi ²)	p-value
Age (years), Mean (SD); Range	66.6 (4.7); 60–80	72.9 (7.0); 61–91	5.42	<0.0001
Male, n (%)	47 (70.2)	18 (51.4)	3.49	0.06
Race/Ethnicity				
Hispanic, n (%)	6 (9.0)	1 (2.9)		
Non-Hispanic White, n (%)	31 (46.3)	26 (74.3)	5.99 [†]	0.01
Non-Hispanic Black, n (%)	30 (44.7)	8 (22.8)		
Other, n (%)	1 (1.3)	0 (0.0)		
Education (years), Mean (SD)	14.4 (3.1)	16.2 (3.1)	2.89	<0.01
Cognitive Functioning				
Global, Mean SS (SD)	7.9 (1.9)	8.0 (1.6)	0.20	0.84
Verbal Fluency, Mean SS (SD)	8.6 (2.7)	9.0 (2.4)	0.80	0.43
Executive Function, Mean SS (SD)	7.5 (2.3)	8.0 (1.8)	1.15	0.25
Processing Speed, Mean SS (SD)	8.8 (2.2)	9.3 (2.4)	1.20	0.23
Learning, Mean SS (SD)	7.5 (2.6)	7.1 (1.9)	-0.81	0.42
Delayed Recall, Mean SS (SD)	7.7 (2.7)	6.7 (2.1)	-1.94	0.06
Working Memory, Mean SS (SD)	8.4 (2.5)	8.4 (2.2)	0.07	0.95
Motor, Mean SS (SD)	6.0 (2.7) ²	5.6 (2.2) ³	-0.79	0.43
MCI, Yes (%)	45 (67.2)	24 (68.6)	0.02	0.89
HAND, Yes (%)	21 (31.3)			
HIV Variables				
Duration of HIV disease (years), Median (IQR)	28 (20.0, 32.5)	--	--	--
Current CD4 count, Median (IQR) ⁴	624 (499, 812)	--	--	--
Nadir CD4 count, Median (IQR) ⁵	140 (34, 339)	--	--	--
AIDS, n (%) ⁶	40 (59.7)	--	--	--

[†] Due to the small number of Hispanic participants, only a comparison between non-Hispanic white and black participants was completed.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

- 2 with missing data
- 3 1 with missing data
- 4 13 with missing data
- 5 5 with missing data
- 6 4 with missing data

MCI = mild cognitive impairment; HAND = HIV-associated neurocognitive disorder; SS = Scaled Score; IQR = Interquartile Range

Hearing outcomes (peripheral hearing sensitivity and central auditory processing) stratified by HIV status.

Table 3.

Hearing Outcome	PWH (n=67)	PWoH (n=35)	Chi ²	p-value
<u>Peripheral Hearing Sensitivity</u>				
Worse ear PTA, in dB, Median (IQR)	25.0 (20.0, 37.5)	26.3 (22.5, 46.3)	2.92	0.09 [/]
Better ear PTA, in dB, Median (IQR)	20.0 (16.3, 26.3)	26.3 (20.0, 41.3)	6.84	<0.01 [/]
Worse ear hearing loss, n (%)	30 (44.8)	20 (57.1)	1.41	0.23
Better ear hearing loss, n (%)	19 (28.4)	18 (51.4)	5.29	0.02
<u>Central Auditory Processing</u>				
Dichotic Digits – Right, % correct, Median (IQR)	90.0 (80.0, 97.5)	95.0 (85.0, 97.5)	2.06	0.15 [/]
Dichotic Digits – Left, % correct, Median (IQR)	87.5 (72.5, 95.0)	90.0 (80.0, 92.5)	0.11	0.74 [/]

[/] Kruskal-Wallis test

Table 4.

The adjusted dichotic digits testing percent correct for the left and right ear stratified by cognitive function impairment.

Cognitive Function Variable	Dichotic Digits Testing – Left Percent Correct		
	Impaired	Not Impaired	F-statistic p-value *
Global	70.4	89.2	16.22 0.0001
Verbal Fluency	72.0	85.1	5.92 0.01
Executive Function	76.6	84.9	3.59 0.06
Processing Speed	74.8	84.2	3.05 0.08
Learning	78.1	86.2	3.90 0.05
Delayed Recall	79.3	85.5	1.69 0.20
Working Memory	70.0	88.5	16.49 0.0001
Motor	81.1	84.7	0.54 0.46
Cognitive Function Variable	Dichotic Digits Testing – Right Percent Correct		
	Impaired	Not Impaired	F-statistic p-value *
Global	82.7	90.2	3.58 0.06
Verbal Fluency	78.4	90.1	7.47 <0.01
Executive Function	81.1	90.6	7.72 <0.01
Processing Speed	80.5	89.4	4.31 <0.05
Learning	83.3	91.6	6.56 0.01
Delayed Recall	86.1	89.0	0.60 0.44
Working Memory	80.8	90.9	6.90 0.01
Motor	86.9	88.8	0.24 0.63

* p-values corresponding to models adjusted for age, sex, race, years of education, and HIV status.