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Speech Audiometry Findings from HIV+ and HIV- Adults in the MACS and WIHS Longitudinal Cohort Studies

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Abstract

The purpose of this study was to compare various speech audiometry measures between HIV+ and HIV- adults and to further evaluate the association between speech audiometry and HIV disease variables in HIV+ adults only. Three hundred ninety-six adults from the Multicenter AIDS Cohort Study (MACS) and Women's Interagency HIV Study (WIHS) completed speech audiometry testing. There were 262 men, of whom 117 (44.7%) were HIV+, and 134 women, of whom 105 (78.4%) were HIV+. Speech audiometry was conducted as part of the standard clinical audiological evaluation that included otoscopy, tympanometry, and pure-tone air- and bone-conduction thresholds. Specific speech audiometry measures included speech recognition thresholds (SRT) and word recognition scores in quiet presented at 40 dB sensation level (SL) in reference to the SRT. SRT data were categorized in 5-dB steps from 0–25 dB hearing level (HL) with one category as ≥30 dB HL while word recognition scores were categorized as <90%, 90–99%, and 100%. A generalized estimating equations model was used to evaluate the association between HIV status and both ordinal outcomes. The SRT distributions across HIV+ and HIV- adults were similar. HIV+ and HIV- adults had a similar percentages of word recognition scores <90%, a lower percentage of HIV- adults had 90–99%, but HIV- adults had a higher percentage of 100%. After adjusting for covariables, HIV+ adults were borderline significantly more likely to have a higher SRT than HIV- adults (odds ratio [OR]=1.45, p=0.06). Among HIV+ adults, HIV-related variables (i.e., CD4+ T-cell counts, HIV viral load, and ever history of clinical AIDS) were not significantly associated with either SRT or word recognition score data. There was, however, a

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ceiling effect for word recognition scores, probably the result of obtaining this measure in quiet with a relatively high presentation level. A more complex listening task, such as speech-in-noise testing, may be a more clinically informative test to evaluate the effects of HIV on speech communication.

Keywords

HIV; Speech audiometry; Adults

1. Introduction

Within the last few years there has been increased research on the effects of human immunodeficiency virus (HIV) on hearing impairment among adults (Luque et al, 2014; Maro et al, 2014; Torre et al, 2015; van der Westhuizen et al, 2013). HIV disease has become a chronic health condition leading to concerns of HIV-associated premature aging (Deeks, 2011) and associated comorbidities, including the possibility of earlier onset hearing loss. van der Westhuizen et al (2013) collected pure-tone threshold data from HIV-infected (HIV+) adults and HIV-uninfected (HIV-) adults matched for age, gender, and race and found that HIV+ adults had a significantly higher prevalence of hearing loss compared to HIV- adults. Further, Torre et al (2015) found that HIV+ adults had significantly poorer low-frequency pure-tone averages (LPTA), calculated using 250, 500, 1000, and 2000 Hz and high-frequency pure-tone averages (HPTA), calculated using 3000, 4000, 6000, and 8000 Hz compared to HIV- adults after controlling for age, sex, race, and noise exposure history.

Hearing loss can affect communication; however, there is limited research in speech audiometry measures in HIV+ adults. Maro et al (2014) found that HIV+ adults on antiretroviral therapy (ART) had significantly more self-reported difficulty understanding speech compared to those HIV+ adults not taking ART. In fact, to date, only the single study by Luque et al (2014) included word recognition scores as part of an extensive audiologic battery. HIV+ adults with late stage disease (defined as history of an AIDS-defining opportunistic infection or CD4+ cell count <200 cells/μL) had significantly poorer right ear word recognition scores compared to those with early stage infection (defined as asymptomatic or symptomatic HIV disease with CD4+ cell count >200 cells/μL and no history of AIDS-defining illness) and, also, compared to HIV- control adults. There were, however, no significant group differences for left ear word recognition data.

Higher pure-tone thresholds are associated with poorer word recognition outcomes (e.g., Garstecki & Erler, 1998), but the impact of poorer LPTA and HPTA in HIV+ adults (Torre et al., 2015) on word recognition abilities requires further research. To investigate the effects of HIV infection on the auditory system, especially in those HIV+ adults who are virologically suppressed, the specific aims of this study were to: 1) evaluate speech audiometry results in HIV+ and HIV- adults, and 2) examine the association of speech audiometry with age, sex, race, noise exposure, and, among HIV+ adults, CD4+ cell count and HIV RNA viral load.

2. Material and Methods

The Institutional Review Boards for San Diego State University, The Johns Hopkins Bloomberg School of Public Health, Georgetown University, and Whitman-Walker Health approved all procedures of this study. All participants gave informed consent prior to participating.

2.1 Participants

Participants for this sub-study were recruited from the Baltimore and Washington DC sites of the Multicenter AIDS Cohort Study (MACS) and the Washington D.C. site of the Women's Interagency HIV Study (WIHS). The MACS is an ongoing, prospective study of the natural and treated history of HIV infection among men who have sex with men in the US. Approximately 7,000 men, both HIV+ and HIV-, were recruited beginning in 1984–1985 at four centers across the US (Dudley et al, 1995; Kaslow et al, 1987). The WIHS is a multicenter prospective cohort study that was established in 1994 to study women with or at risk for HIV infection. A total of 3,766 HIV+ and HIV- women were enrolled beginning in 1994–1995 at six centers located throughout the US (Barkan et al, 1998; Bacon et al, 2005). MACS and WIHS participants return every 6 months for a detailed medical history interview, a physical examination, and collection of blood for laboratory testing and storage. Both HIV+ and HIV- adults were recruited during their routine MACS or WIHS study visit. Participants had a screening test using distortion product otoacoustic emissions (DPOAEs) (Torre et al, 2014), and those who did not the pass criteria were referred for clinical testing. Briefly, the screening protocol consisted of DPOAEs measured at 2000, 3000, 4000 and 6000 Hz. Individuals were referred with 2 or more DPOAE nonresponses measured in either ear. A nonresponse was defined by Torre et al. (2014) as the absolute DPOAE level <-15 dB sound pressure level (SPL) or the DPOAE signal-to-noise ratio was $<+6$ dB. Participants were also asked, "Is your hearing excellent, good, a little trouble hearing, moderate trouble, a lot of trouble, or are you deaf?" If participants responded greater than 'moderate' or greater trouble hearing, they were referred for audiologic testing. Of the 515 participants who completed the screening protocol, 396 completed audiologic testing, including 189 who were referred based on DPOAE measures alone. This audiometric testing was completed between August 2008 and October 2012.

2.2 Procedures

Speech audiometry was conducted as part of the standard clinical audiological evaluation that included otoscopy, tympanometry, and pure-tone air- and bone-conduction thresholds (Torre et al, 2015). Speech measures consisted of speech recognition thresholds (SRT), in dB hearing level (HL), and word recognition scores, in percent correct. Spondee words, presented via monitored live voice, were used for SRT testing whereas recorded phonetically balanced word lists were used for word recognition scores. These words were presented at 40 dB above SRT, or 40 dB sensation level (SL) relative to the SRT.

For HIV+ participants, combination ART (cART) use was evaluated at the study visit and was defined using the DHHS/Kaiser Panel definition (DHHS/Henry J Kaiser Family Foundation Panel on Clinical Practices for the Treatment of HIV Infection, 2008). ARTs

were classified as nucleotide reverse transcriptase inhibitors, protease inhibitors, and non-nucleotide reverse transcriptase inhibitors. AIDS-defining conditions including pulmonary tuberculosis were obtained by self-report and conformed to the 1993 CDC definition of AIDS (CDC, 2014).

In the MACS, HIV RNA was measured using the COBAS Ultrasensitive Amplicor HIV-1 monitor assay (Roche Molecular Systems), sensitive to 50 copies HIV RNA/mL. In the WIHS, HIV RNA was measured using COBAS AmpliPrep/COBAS TaqMan HIV-1 Test (Roche Molecular Systems), sensitive to 48 copies HIV RNA/mL. Values were logarithmically ($\log_{10}$) transformed for statistical analysis. CD4+ T-cell counts were measured using standard flow cytometry (Hultin et al, 2007) at each study visit for HIV+ men and women. All laboratory results were collected within one year prior to the hearing testing.

2.3 Statistical Analyses

Speech audiometry data were analyzed using different approaches, as appropriate for the distribution of the data. For both variables, the distributions were skewed and essentially discrete, being limited to a fairly small number of integer values. For SRT the data were grouped into seven response categories, 0 dB HL (2.8%), 5 dB HL (14.1%), 10 dB HL (31.3%), 15 dB HL (26.1%), 20 dB HL (14.2%), 25 dB HL (5.9%), and ≥30 dB HL (5.6%). The word recognition score data were categorized as <90%, 90–99%, and 100%, based on the distribution properties, as described in Results. These two ordinal outcomes were analyzed using standard methods for ordered categorical data. This involves the use of a logistic regression model for the cumulative probabilities, known as a proportional or cumulative odds logistic model. That is, for each ordered category, the probability of having a value less than or equal to this value is modeled. The model assumes that differences between the cumulative probabilities for different values depend only on different intercepts, but not on the independent variables in the model. For this reason the corresponding odds ratios (ORs) for each of the independent variables express the odds of having any given value or lower for a one unit increase in the predictor variable compared with vs. the corresponding odds for the original value of the predictor. For a categorical variable such as HIV status, the OR is the ratio of the odds for having a given value or lower for HIV+ compared with the odds for HIV-. If the OR is greater than one, then cumulative probabilities for HIV+ are predicted to be larger than for HIV-, so that HIV+ tend to have lower values; if the OR is less than one the opposite is true. In the latter case the reciprocal OR, which is the ratio of the odds for having a given value or greater, may be reported instead. The approach used in this paper was to interpret the reciprocal OR; for example, if the OR for HIV status was 0.78, the reciprocal would be 1.28 meaning that HIV+ adults would be 28% more likely to have the greater outcome compared to HIV- adults.

A generalized estimating equations statistical model with working independence was used to examine the relationship between HIV status and both ordinal outcomes for each ear. Two additional, separate models were constructed to examine speech audiometry data for HIV+ participants only. Covariables included in each of the multivariable analyses were sex, age (in decades), race, and reported history of occupational or recreational noise exposure. For

models restricted to HIV+ participants, additional covariables included CD4+ T-cell counts, $\log_{10}$ HIV RNA values, and ever having had an AIDS-defining condition. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for predictors of each model. Computations were performed using SAS, Version 9.3.

3. Results

Three hundred ninety-six adults completed speech audiometry testing. There were 262 men (mean age=55.3 years, SD=8.9 years), of whom 117 (44.7%) were HIV+, and 134 women (mean age=45.3 years, SD=8.8 years), of whom 105 (78.4%) were HIV+. The proportion of HIV+ participants within this sample was consistent with the entire MACS and WIHS. The socio-demographic characteristics of the study participants, stratified by HIV status and sex, are presented in Table 1. Three hundred and three participants (76.5%) reported their hearing to be ‘good’ or ‘excellent’; there was no statistical difference by HIV status. The distribution for word recognition score data included percent correct for both ears; however, five participants (two HIV+ women and two HIV- men and one HIV- woman) have word recognition score data for one ear. HIV+ men were younger than HIV- men, but this was not true for women; and overall HIV+ participants were more likely to be female and of black race compared to the HIV- participants. Among HIV+ participants, men and women had similar CD4+ cell counts, but men had a higher proportion with full virologic suppression and higher CD8+ cell counts. Lastly, more HIV+ women had had at least one AIDS-defining condition compared to men.

The distributions for the SRT data are shown for HIV+ and HIV- participants in Figure 1. The distributions were similar by HIV status, although HIV+ adults had a median SRT of 10 dB HL while the HIV- adults had a median SRT of 15 dB HL. The distributions of the word recognition scores for HIV+ and HIV- adults are shown in Figure 2a. Because of the skewness of the distribution, percentages ≤84% were combined into one group. There were more HIV+ adults in the 92% and 96% groups whereas the other groups had similar rates between HIV+ and HIV- adults. The categorization of the word recognition score data (<90%, 90–99%, and 100%) by HIV status is shown in Figure 2b. The proportions of HIV+ and HIV- adults with <90% were similar; HIV- adults had a lower proportion with 90–99%, but a higher proportion of 100% correct.

After multivariable adjustment, HIV status achieved borderline significance, such that HIV+ adults were 45% more likely to have a higher SRT (OR=1.45, 95% CI=0.99–2.13, p=0.06, the reciprocal of the OR estimated by the logistic model) compared to HIV- adults. For comparison, the ORs for a ten-year increase in age and male gender, the two most highly significant predictors, were 1.82 (95% CI: 1.47–2.27) and 1.56 (95% CI: 1.02–2.44). The HIV-related variables (i.e., CD4+ T-cell counts, HIV viral load, and ever history of AIDS-defining illness) were not significantly associated with SRT data. There was no statistically significant association of HIV status with word recognition score categories nor were there any significant associations between HIV-related variables and word recognition score categories.

4. Discussion

Adjusted SRT scores were slightly higher in HIV+ adults compared with HIV- adults. This difference achieved only borderline significance; however, most of the participants, whether HIV+ and HIV-, had SRT values ≤25 dB HL. This finding may be clinically meaningful, since HIV+ adults were 6 years younger on average than HIV- adults, yet had slightly higher SRT values suggesting that HIV+ adults may experience hearing loss earlier in mid-life. HIV status was not associated with word recognition score data and, lastly, no HIV-related disease or treatment variables were associated with SRT data or word recognition score categories.

Stimuli used for speech audiometry have greater acoustic complexity compared to pure-tone audiometry and allow for a better assessment of communication skills in adults. Word recognition scores in the current study demonstrated ceiling effects, suggesting that this procedure in quiet might have been too easy a task. It has been demonstrated that even in older adults, speech audiometry performance in quiet is good, provided the speech level permits audibility of high frequency information (Gordon-Salant, 2005). The word recognition scores from the current study and those from Luque et al (2014) were similar, although Luque et al (2014) reported significantly poorer word recognition score data for HIV+ adults in association with late stage HIV disease. Both studies employed speech testing in quiet using the clinically agreed-upon standard of 25 words per list (or, a “half-list”), with comparable word recognition score ceiling effects (>96%). There were differences in presentation level during word recognition score testing since the current study used 40 dB SL (re: SRT) whereas Luque et al (2014) tested at 50 dB HL or higher if needed to ensure audibility at 4000 Hz. Additional differences were that the current study used a slightly larger sample size, participants were slightly older, and none had advanced HIV disease. Although Luque et al (2014) found significant word recognition score differences, there was only a mean 1–1.3% difference for the late stage HIV disease group compared to the early stage and control groups. From a clinical perspective, this difference is inconsequential; HIV+ participants did not even miss one more word per word list.

It is likely that the hearing deficits, such as self-reported difficulty understanding speech and higher gap detection thresholds (Maro et al, 2014), among HIV+ adults may be indicative of central auditory involvement. This could reflect the neurocognitive side effects of HIV from persistent infection and inflammation. Prior to availability of cART, it was reported that about 60% of patients with advanced HIV infection showed signs of neurological dysfunction during the course of HIV infection (Levy et al, 1985). Moreover, it is becoming evident that despite cART, HIV persists within the central nervous system (Heaton et al, 2011). This could be a result of incomplete viral suppression such that low levels of HIV in the central nervous system may result in neural damage. Alternatively, persistent brain injury related to HIV may have occurred prior to the initiation of cART. It therefore seems reasonable to hypothesize that central nervous system damage may play a role in the central auditory processing deficits of HIV+ adults.

The limitations of word recognition testing in quiet, such as ceiling effects, are recognized, even in those with hearing loss. Word recognition is a simpler listening task that most likely

does not represent a daily listening environment. However, since word recognition testing is a routine part of the standard audiological test battery, it was important to evaluate these data in an effort to differentiate peripheral from retrocochlear deficits in HIV+ adults. The addition of speech testing with background noise would have been advantageous in two ways: first, speech-in-noise testing is more representative of real-life communication; and second, these measures require central auditory processing because of the complexity of the auditory input. These word recognition scores were collected within very active University clinics, so including additional measures (e.g., speech-in-noise testing) would have added an additional time burden and thus were not feasible.

5. Conclusions

The current study showed a borderline statistically significant association between HIV status and two speech audiometry tests included in standard audiologic evaluations. In HIV+ adults only, there were also no statistical significant associations with speech audiometry measures, regardless of disease severity. In this sample of MACS/WIHS participants, there was no statistically significant association between HIV status and cochlear function (Torre et al, 2014), although HIV+ adults in these studies did have poorer hearing (Torre et al, 2015). Taken together, the available data suggest that hearing loss in HIV+ may result from either peripheral auditory neural problems or more central auditory processing disorders. Future research should examine measures of auditory neural function and central auditory processing, such as speech-in-noise testing.

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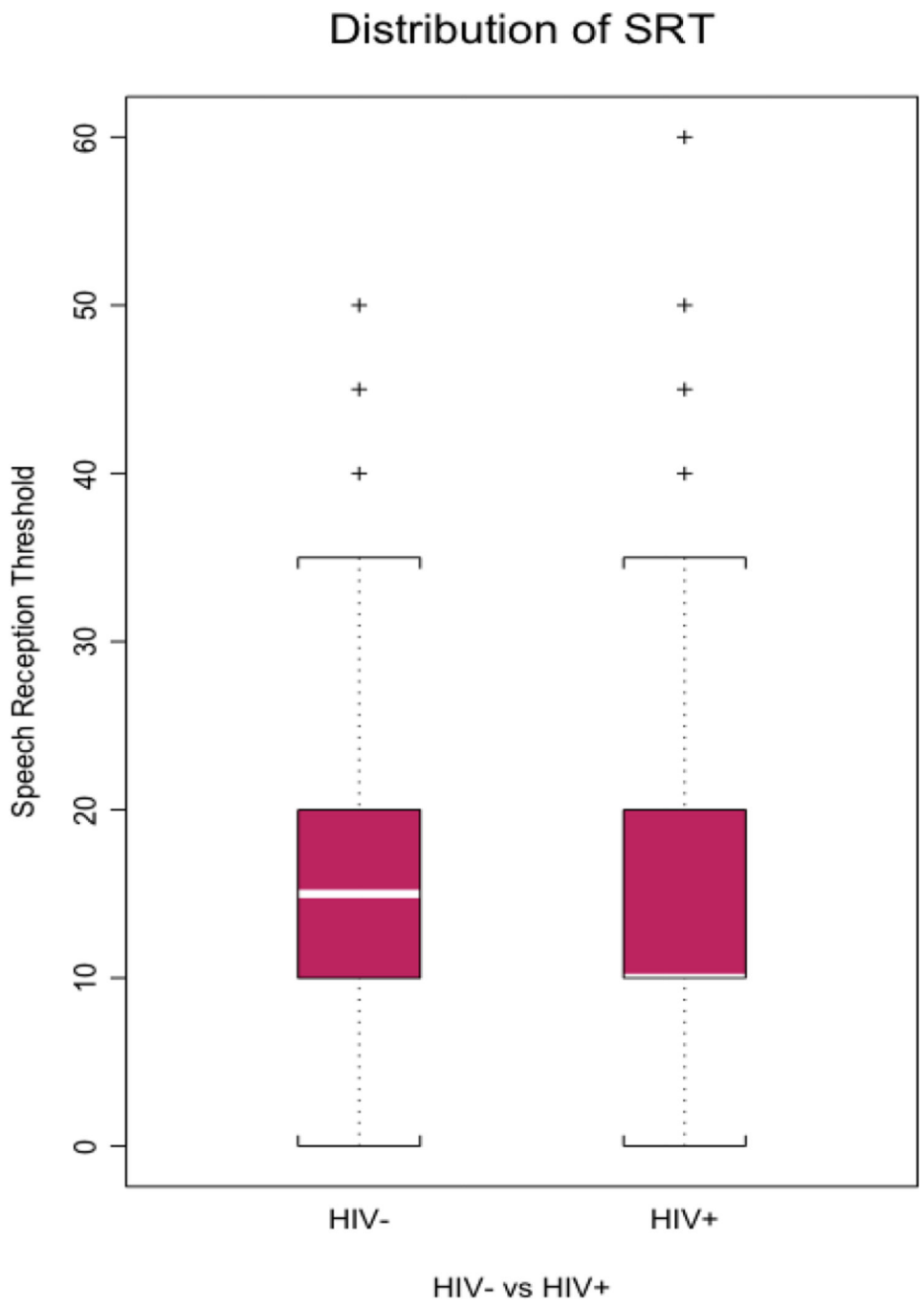
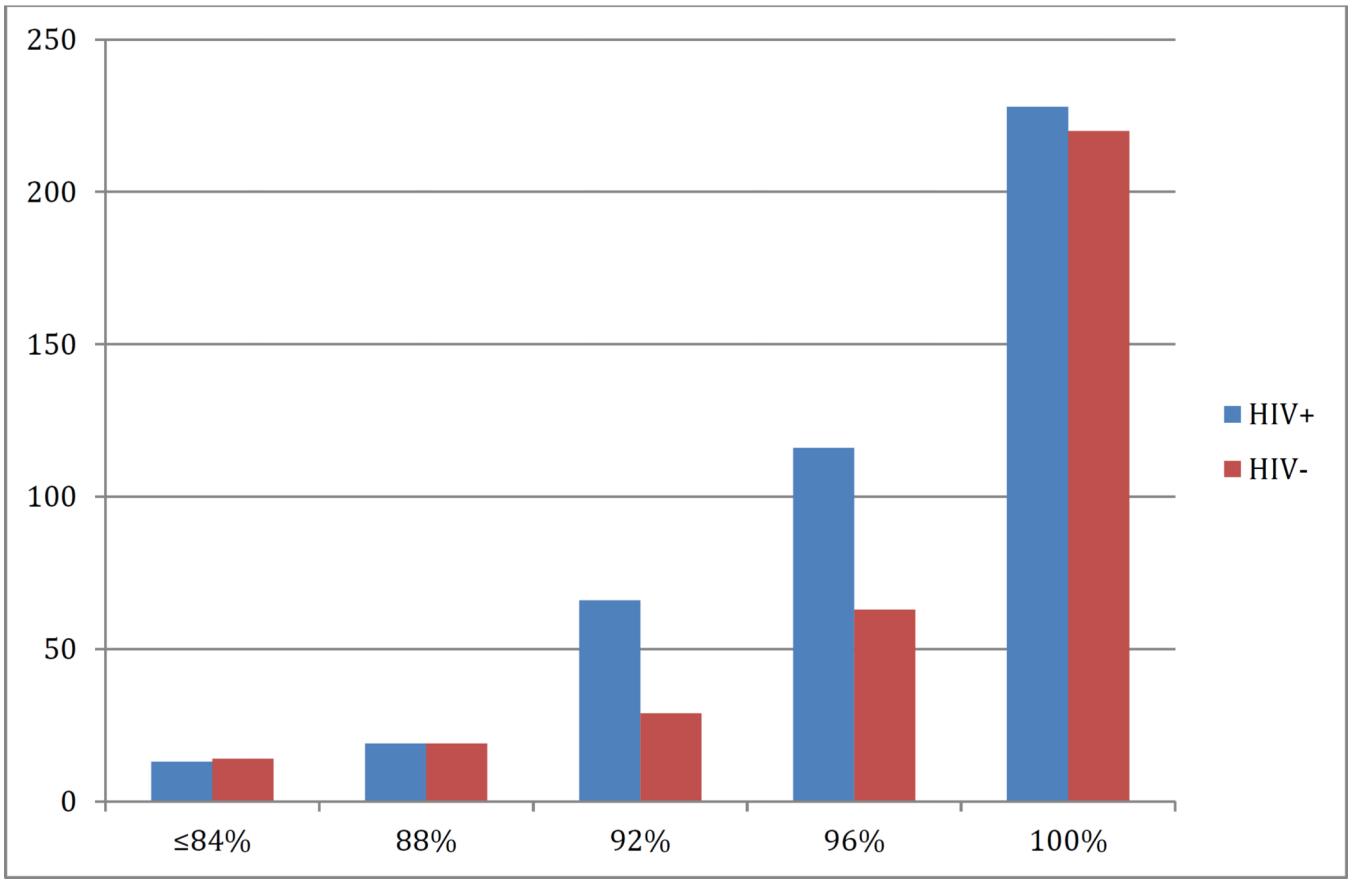


Figure 1.

The distributions of speech recognition threshold scores stratified by HIV status are shown. White lines indicate median data, boxes are the 25th and 75th percentiles, whiskers are values outside of the middle 50% of the distribution (the interquartile range), and plus signs represent extreme values or “outliers”.

a.



b.

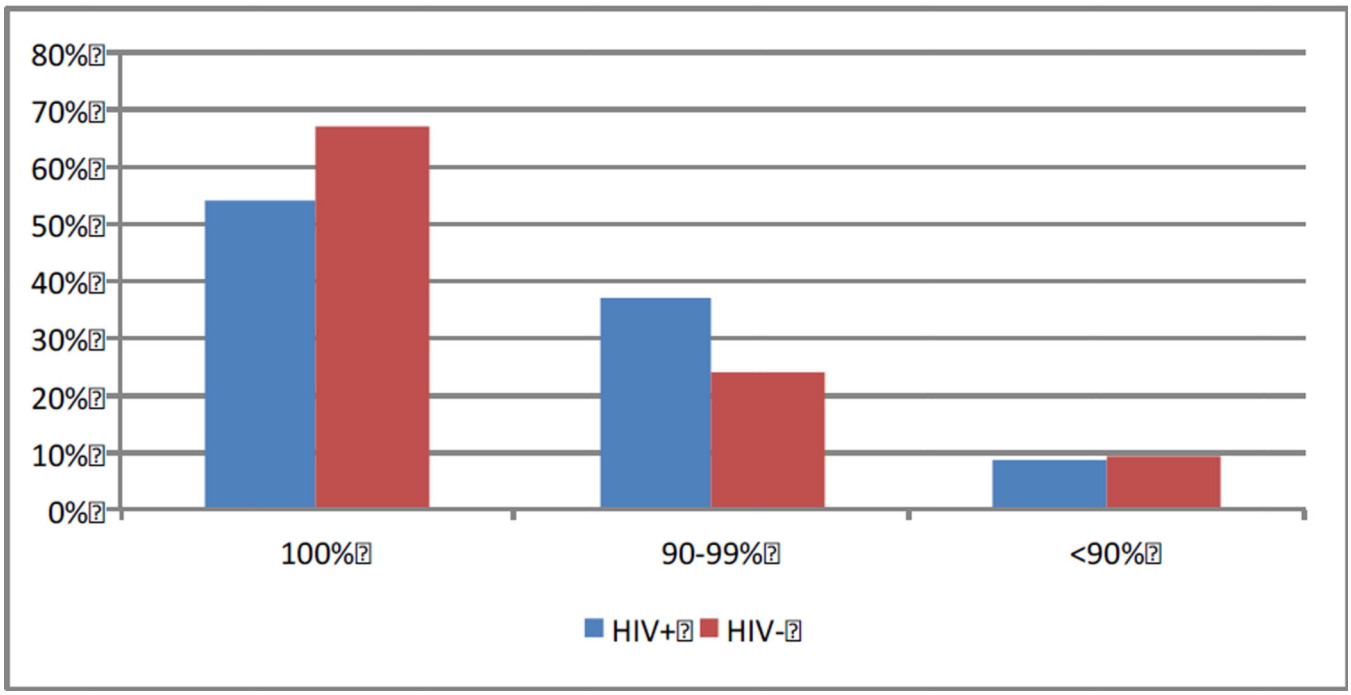


Figure 2.

a. The distributions of WRS for HIV+ (blue) and HIV- (red) participants are shown.

b. The percentages for HIV+ (blue) and HIV- (red) participants for the three word recognition score categories, <90%, 90–99%, and 100%, are shown.

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Table 1

Demographic characteristics of participants, stratified by HIV status and sex.

	HIV+			HIV-			
	Men (n=117)	**Women (n=105)**	**All HIV+ (n=222)**	**Men (n=145)**	**Women (n=29)**	**All HIV- (n=174)**	***P* Value[a]**
Age, mean (SD), yrs	52.3 (7.9)	46.3 (8.0)	49.5 (8.5)	57.8 (9.0)	41.7 (10.5)	55.1 (11.0)	**<0.001**
Race, n (%)							**<0.001**
Non-black	56 (47.9)	18 (17.1)	74 (33.3)	117 (80.7)	9 (31.0)	126 (72.4)	
Black	61 (52.1)	87 (82.9)	148 (66.7)	28 (19.3)	20 (69.0)	48 (27.6)	
Occupational noise exposure, n (%)	31 (26.5)	14 (13.3)	45 (20.3)	35 (24.1)	3 (10.3)	38 (21.8)	0.70
Non-occupational noise exposure, n (%)	63 (53.8)	55 (52.4)	118 (53.2)	91 (62.8)	19 (65.5)	110 (63.2)	0.06
SRT median (IQR)	15 (10,20)	10 (10,15)	10 (10,20)	15 (10,20)	5 (5,10)	15 (10,15)	0.61
Word recognition score, categorized, n (%)							
100%	156 (66.7)	72 (34.6)	228 (51.6)	191 (66.3)	29 (50.9)	220 (63.8)	**<0.001**
90–99%	66 (28.2)	116 (55.8)	182 (41.2)	71 (24.7)	21 (36.8)	92 (26.7)	
<90%	12 (5.1)	20 (9.6)	32 (7.2)	26 (9.0)	7 (12.3)	33 (9.6)	
Ever AIDS, n (%)	19 (16.2)	40 (38.1)	59 (26.6)				
Current CD4+ cell count, mean (SD), cells/μL,	603 (287)	549 (305)	577 (296)				
Log_{10} HIV RNA, (median IQR), copies/mL	1.6 (1.6, 1.6)[b]	1.9 (1.7, 3.1)	1.7 (1.6, 2.5)				

Abbreviations: Ever AIDS, ever diagnosed with AIDS; IQR, Interquartile range; SD, standard deviation.

[a]Comparisons between all HIV+ and all HIV- participants.

[b] 1.6 denotes a plasma HIV RNA value of <50 copies/ml, or undetectable by the assay used.