Auditory Brainstem Response Test at Different Stimulus Rates in Normal-Hearing Adults Living With HIV

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Abstract

Purpose

The study investigated whether the auditory brainstem response (ABR) at a baseline and at higher repetition rates can detect if neurodegeneration has occurred in adults living with HIV who present with normal behavioral pure-tone thresholds.

Method

An exploratory research design was used. Forty adults with HIV (80 ears, 57.5% female; M_{age} = 26.3 years, *SD* = 3.68) and 20 adults without HIV participated. Phase 1 compared ABR absolute and interwave latencies at a baseline rate. Phase 2 examined the effect of HIV status and category of immunodeficiency on ABR absolute Wave V latency and Wave V latency shift at increased stimulus rates. Analysis included a two-way analysis of variance of the interaction between stimulus rate and HIV status and between CD4+ category and rate, and multiple regression analysis.

Results

In adults living with HIV, the baseline ABR yielded prolonged Wave III and V absolute latencies and interpeak prolongations in 22.5%. Interaural Wave V latency differences were present in 15% of participants. An additional 15% of ears presented with abnormal Wave V at increased rates.

No significant interaction between HIV status and rate in either ear or between CD4+ category and rate was found in either ear ($p > .05$). Although rate and gender contributed significantly to the prediction of Wave V latency of the rate study (left and right, $p < .001$), HIV status did not (left and right, $p > .05$).

Conclusions

Although the interaction of HIV status and CD4+ with rate was not significant, more ears were identified with abnormal results at increased stimulus rates than with the baseline ABR alone. The ABR at increased rates may therefore be a valuable addition for the identification of individuals living with HIV with auditory neural deficiencies.

HIV and AIDS have become more prevalent throughout the world. In 2017, 36.9 million people were living with HIV/AIDS, 1.2 million people were newly infected with the virus, and 1.1 million people died due to the virus (World Health Organization [WHO], 2018). It is estimated that in sub-Saharan Africa, 25.7 million people are living with HIV/AIDS (WHO, 2018). In South Africa, HIV/AIDS occurs alongside unemployment and poverty and is one of the main challenges South African infectious disease health services face (Khoza-Shangase, 2010).

As many as 27.5% of patients with HIV in South Africa present with a hearing loss (van der Westhuizen et al., 2013). The hearing loss can be a direct or indirect cause of the virus (Bankaitis & Schountz, 1998). HIV can affect auditory function due to its neurotropism and the suppression of the immune system. The suppression of the immune system, caused by the HIV infection, results in increased susceptibility to opportunistic diseases and their treatments, which can cause hearing loss (Cohen et al., 2014).

HIV can cause demyelination of subcortical areas in the brain containing auditory structures, resulting in neuropathological changes in the central nervous system (Iacovou et al., 2012; Li et al., 2014). The auditory brainstem response (ABR) test is specifically useful in detecting subtle neural disorders caused by HIV (Matas, Silva, et al., 2010; Santos et al., 2004; Serafini et al., 1998). There are various types of hearing difficulties that can arise from direct effect, neural degradation, and the indirect effect of HIV. Individuals with auditory neural pathology experience symptoms such as tinnitus, aural fullness, and difficulty with speech in noisy situations and can experience sudden or progressive hearing loss (Zapala et al., 2008).

Reyes-Contreras et al. (2002) described histopathological studies showing local demyelination in areas of the brainstem where auditory structures are found. The study suggested that abnormal auditory neurophysiological results are due to the demyelination in adiults living with HIV even in the absence of any clinical neurological manifestations. The study identified the need to assess the integrity of the pontine and midbrain auditory pathways in HIV-positive individuals (Reyes-Contreras et al., 2002). Matas, Santos Filha, et al. (2010) suggested that there is evidence of dysfunction in the synchrony of the generation and transmission of neural impulses along the auditory pathway in the brainstem of patients who are HIV positive. Even in adults living with HIV with normal behavioral hearing thresholds, 57% presented with ABR abnormalities such as prolonged absolute latencies of Wave III and V, and Wave I–III and I–V interpeak latencies were reported (Matas, Santos Filha, et al., 2010). The abnormal findings suggest that adults with HIV are more likely to present with lower brainstem pathology compared to either both lower and upper brainstem pathology or upper brainstem pathology (Matas, Santos Filha, et al., 2010).

The neurological ABR is therefore a useful tool in the early identification of HIV-related neurodegeneration of the auditory system in clinically asymptomatic individuals (Castello et al., 1998; Jalali et al., 2014; Koralnik et al., 1990; Reyes-Contreras et al., 2002). The ABR is specifically useful when using a faster stimulus repetition rate, as there is often subcortical myelin loss that has similar patterns in ABR as other demyelinating diseases, such as multiple sclerosis (Bankaitis, 1995). Bankaitis (1995) investigated the effect of varying ABR stimulus rates on adults with HIV/AIDS who presented with normal pure-tone results in a pilot study. A comparison of the latency of Wave V with the faster click rate (61.1 Hz) showed increased prolongations in patients who were identified as being in the AIDS stage (severely immunocompromised) as compared to individuals who are HIV positive but not severely immunocompromised and control adults.

The ABR at increased stimulus rates has also been found to be particularly sensitive to the identification of disorders resulting in demyelination (Santos et al., 2004). A study composed of normal-hearing participants with multiple sclerosis suggested using a faster stimulus repetition rate as part of a standard auditory test battery, significantly improving the detection of abnormal responses that are dependent on the rate increase (Jacobson et al., 1987; Santos et al., 2004). However, there is no standard auditory neural test battery for individuals with HIV in South Africa. Previous research using increased ABR stimulus repetition rates in normal-hearing adults with HIV has been conducted by Lima and Fukuda (1999). The study made use of a very strict inclusion criteria by the Centers for Disease Control and Prevention; the study only included individuals who had never shown signs of previous infections or had lower-than-normal immunological tests. The study concluded that using a rate of 61.1 Hz is not an efficient method of detecting subtle neurological involvement (Lima & Fukuda, 1999). However, it is not clear how this conclusion was drawn, as there is no way to calculate the true percentage of prevalence of pathology in this population.

The shift in mindset from mortality to morbidity makes the goal of the health care professional clear: to identify hearing disorders as early as possible in individuals who do not yet show any signs of auditory dysfunction by their behavioral pure-tone audiogram yet are at risk of presenting with hearing difficulties in challenging situations that may impact their daily activities (Marin et al., 2009; Peters et al., 2013). The inclusion of ABR at increased stimulus rates to the evoked potential test battery of individuals living with HIV may lead to earlier identification of auditory dysfunction and earlier initiation of habilitation strategies despite normal behavioral pure-tone thresholds. Therefore, the current study aimed to investigate if the ABR can detect whether neurodegeneration has occurred in adults with HIV who presented with normal behavioral pure-tone hearing thresholds.

Materials and Method

The study aim was achieved using an exploratory research design yielding quantitative data conducted in two phases. Phase 1 compared absolute and interwave latencies for ABR at a baseline rate in adults without HIV with adults living with HIV, both of whom presented with normal behavioral pure-tone thresholds. Phase 2 examined the effect of HIV status and category of immunodeficiency on ABR absolute Wave V latency and Wave V latency shift at increased stimulus rates.

The study was approved by the Health Science Ethics Committee under Protocol 41/2018 and by the Faculty of Humanities and departmental ethics committees. All participants provided written informed consent. Data collection took place at the antiretroviral (ARV) clinic and the outpatient clinic of a community-based state hospital in Gauteng, South Africa.

Participants

A sample of 40 normal-hearing adults living with HIV participated in the study (27 women, 13 men). The mean age of the participants living with HIV was 26.30 years (*SD* = 3.68, range: 19–31). A nonprobability purposive sampling technique was used to identify potential participants. All participants with HIV were being treated using first-line ARVs consisting of tenofovir, emtricitabine, and efavirenz. CD4+ cells are one of the categories of the T-lymphocytes present in the bone marrow. CD4+ cells have the purpose to initiate an immune response in response to the presence of a pathogen in the human body. In patients with HIV, the CD4+ count is used to determine the progression of the disease and to monitor the

individual's immune status. CD4+ cell count, lymphocyte count, and the presence of symptoms are used in the classification of stage of HIV infection (Evian, 2000). In addition, all had a lower-than-detectable viral load at the time of testing and a CD4+ count of greater than 200 cells/μl.

No participants were included that were in the severe stages of immunosuppression (Stage 3) to eliminate the possibility of the presence of opportunistic infections or effect of past opportunistic infections adversely affecting ABR wave latencies. The mean CD4+ count was 559.40 cells/μl (*SD* = 220.25, range: 208–1,200). The mean duration on ARVs was 6.68 years (*SD* = 5.10, range: 1–25). Participants with a history of tuberculosis were excluded from the study. A total of 80 ears were analyzed for the test group.

In addition, a sample of 20 adults without HIV with normal behavioral pure-tone thresholds (40 ears, 50% female; M_{age} = 24.3 years, *SD* = 3.51) were recruited. The latest HIV test of the participants documented in the hospital records was required to be negative. An HIV test had to have been performed within 6 months of participation in the study. A nonprobability purposive sampling technique was used to identify potential participants.

Participant Selection

Otoscopy was performed using a Welch Allyn otoscope to ensure no obstructions were present, which could influence electrophysiological tests (Hall, 1992; Langdon & Saenz, 2016). Pure-tone audiometry and acoustic immittance measures were conducted with a GSI 29 Auto Tymp, with supra-aural headphones and a 226-Hz probe tone. Participants were required to present with Jerger Type A tympanograms (middle ear pressure: −100 to 50 daPa; acoustic compliance: 0.3–1.7 ml; ear canal volume: 0.9–2 ml) and present ipsilateral acoustic reflex at 80–95 dB at 1000 Hz (Jerger, 1970; Stach, 2010).

Pure-tone audiometry was conducted from 125 to 8000 Hz. A three-tone pure-tone average (PTA; 500, 1000, and 2000 Hz) was calculated. A normal PTA was classified as ≤ 25 dB HL (Stach, 2010). The mean PTA was 17.65 dB HL (*SD* = 8.84) for the test group with HIV (see Table 1) and 7.03 dB HL (*SD* = 3.41) for adults without HIV. Individuals with a PTA of ≥ 25 dB HL were excluded from the study.

Table 1. Mean and standard deviation of behavioral pure-tone thresholds for adult participants living with the HIV (dB HL; *n* = 80 ears).

Frequency (Hz)	125	250	500	1000	2000	4000	8000	PTA
M (*SD*)	18.00 (10.27)	18.25 (10.47)	18.94 (10.75)	18.06 (9.43)	16.84 (7.59)	17.96 (7.65)	19.50 (9.02)	17.65 (8.84)

Note. PTA = (500 + 1000 + 200 Hz) / 3.

Distortion product otoacoustic emission (DPOAE) measures were conducted to eliminate the possibility of a cochlear hearing loss influencing the ABR results. Inclusion of adults with cochlear pathology, even in the presence of a normal behavioral pure-tone audiometry, may potentially have affected latencies measured during ABR (Cunningham, 2011). DPOAE (65:55 dB SPL stimulus levels) were conducted at the following F2 frequencies (F1/F2 ratio of 1.22): 1000, 2000, 3000, and 5000 Hz. Participants were deemed to have present and normal DPOAE when emission signal-to-noise ratio (SNR) was ≥ 6 dB SPL, noise floor < 0

dB SPL, and an absolute distortion product level fell within the 95% confidence intervals of the means of the equipment, namely, Vivosonic Integrity (Dhar & Hall, 2011; van der Westhuizen et al., 2013).

To further ensure normal-hearing sensitivity, speech reception thresholds were recorded using the South African English Digits-in-Noise Test smartphone application, which was conducted on a Samsung Galaxy S6 device with calibrated earphones (Potgieter et al., 2018). A normal SNR of ≤ −7.50 dB was required to participate in the study. The mean SNR was −9.88 dB (*SD* = 1.27) for adults living with HIV and −10.77 dB (*SD* = 0.70) for adults without HIV.

Data Collection

All data for this study were collected at the ARV clinic or at the outpatient clinic of Tshwane District Hospital. Testing was completed in a room situated away from patient waiting areas to minimize the effect of noise interfering with test results.

ABR measures were conducted with the Vivosonic Integrity V500 system. Calibration was done by using an oscilloscope and measured in dB pe SPL. Clicks were corrected by 35.5 dB and reported in dB nHL. The skin was cleaned prior to electrode placement, and pregelled snap electrodes were placed on both mastoids and the high forehead (Mi-Fz single-channel electrode). ER-3A insert earphones with disposable foam tips were used. Participants were reclined in a chair and asked to close their eyes to minimize interference.

For Phase 1 of the study, a click-evoked ABR was conducted with three separate polarities, namely, rarefaction, condensation, and alternating polarities at 85 dB nHL at a rate of 31.1 Hz. Responses were filtered using 30–3000 Hz and artifact rejection set at a level of 45 μV, with a 15-ms analysis time and a minimum of 2,000 sweeps collected per trace. Impedance values were monitored and kept below 5 kΩ. Repeatability of each trace (at each polarity) was visually confirmed using A and B bin wave displays. The waveforms were analyzed at each polarity.

Phase 2 was completed using the click-evoked ABR measured using alternating stimuli presented at increased rates of 45.1 and 61.1 Hz. Rates were selected as advocated by Ackley et al. (2006). Other parameters remained identical to that used in Phase 1. A minimum of two alternating polarity traces were averaged to ensure repeatability, and Wave V latencies were marked.

Waves were marked independently by two experienced audiologists, and consensus was reached for any differences in marked waves. For both Phase 1 and Phase 2, the left and right ears were tested in a randomized order to minimise bias.

Statistical Method

Data from 40 ears for individuals who were HIV negative (control group) and from a total of 80 ears for the individuals who were HIV positive were analyzed. Left and right ears were analyzed separately to adjust for lack of independence of the data for each ear of the participant group living with HIV, all of which share a single CD4+ count. This approach reduced the chance of a Type I statistical error due to artificial inflation of sample size and (inaccurate) reduction in standard error (*SE*). Latency and amplitude data were described

using descriptive statistics, including the median, *SE*, mean, and standard deviation (*SD*). For the test group, descriptive statistics were also presented with reference to the WHO categorization of immunodeficiency in established HIV infections (see Table 2; WHO, 2007). The WHO classifies CD4+ counts into levels of immunodeficiency, namely, nonsignificant (Stage 0), a CD4+ count at or above 500 cells/μl ($n = 21$); mild (Stage 1), a CD4+ count between 350 and 499 cells/μl ($n = 15$); advanced (Stage 2), a CD4+ count between 200 and 349 cells/μl; and severe (Stage 3), a CD4+ count below 200.

Table 2. World Health Organization immunological classification for established HIV infection.

HIV-associated immunodeficiency	Age-related CD4+ value
	> 5 years (cells/μl)
Not significant (0)	> 500
Mild (1)	350–499
Advanced (2)	200–349
Severe (3)	< 200

In Phase 1 of the study, the control group data at the baseline rate (31.1 Hz) were used to generate an upper limit (viz. the 95th percentile) of absolute latency or interpeak latency with which to compare the results for the group of adults with HIV. In Phase 2 of the study, the alternating ABR data from the control group was used to calculate the 95th percentile for the Wave V latencies measured at increased stimulus rates, namely, 45.1 and 61.1 Hz, and for the Wave V latency shifts from baseline ABR to that at each of the increased stimulus rates. The alternating polarity was used to compare the absolute and interwave latencies of the test group data to the 95th percentile of the control group data.

The Shapiro–Wilk test for normality of distribution was statistically significant ($p < .05$) for Phase 1 data, indicating that the data (absolute and interpeak latencies of Waves I, III, and V) were not normally distributed ($W = 0.931–0.952$, $p < .05$). For Phase 2 data, the Shapiro–Wilk test indicated that the Wave V latencies and Wave V latency shifts at increased stimulus rates with both participant groups and with only participants with HIV were normally distributed ($W = 0.946–0.983$, $p > .05$). The kurtosis value fell between 2 and −2, which is considered acceptable in order to prove normal univariate distribution (George & Mallery, 2010). In addition, skewness was < 0.5, suggesting approximately symmetrical data (Bulmer, 1979). Skewness and kurtosis values and Shapiro–Wilk tests were therefore deemed acceptable for the purpose of the analysis of variance (ANOVA) and regression analysis (Laerd Statistics, 2018).

In Phase 1, the baseline neurological ABR data from the HIV group was analyzed with reference to the group of participants without HIV to identify any delays or prolongations that indicate auditory neural pathology. Those with abnormal neurological ABRs, evident by absolute and interwave latencies > 95th percentile of the control group, were then excluded from the analysis in Phase 2 of the study in order to determine if the increased stimulus rate would identify additional patients with auditory neural pathology not identified in Phase 1 of the study.

In Phase 2, a Cochran–Armitage test of trend was run to determine whether a linear trend exists between the category of immunodeficiency and the number of abnormal Wave V latency shifts and also between the category of immunodeficiency and the number of

abnormal Wave V latencies between the baseline and increased stimulus rates. Two ANOVAs were performed with Wave V latency as the dependent variable. First, a two-way ANOVA was used to determine the interaction between HIV status and stimulation rate and, second, between CD4+ category and rate on Wave V latency of the rate study. The estimated marginal mean, which adjusts for the covariate by reporting the mean of the variable in question, was calculated for the linear interaction of stimulus rate and CD+ category in the left and in the right ear. A multiple linear regression analysis was completed to predict Wave V latency of the rate study from rate, gender, and HIV status. Gender was added as a known bias for ABR latencies. Age of participants was not included due to the restricted age range of the participants in the test group (viz. M = 26.30 years of age, SD = 3.68, range: 19–31), which is unlikely to have an effect on the ABR latencies (Hall, 1992). The multiple regression also allowed determination of the overall fit of the model and the relative contribution of each of the predictors to the total variance explained (Laerd Statistics, 2018). Residual analyses were done to determine the distribution of the residuals and to detect outliers. No outliers were detected. Both the ANOVAs and multiple regression analysis were completed for left and right ears separately.

All statistical analyses were completed using the Statistical Package for the Social Science (SPSS) Version 25 for Windows. An alpha level of .05 was used to indicate significance.

Results

Phase 1

Control Group

Table 3 displays the results of the baseline neurological ABR with reference to the mean, *SD*, and 95th percentile data for right and left ears of the control group. From the data presented in Table 3, the upper limit for absolute and interpeak latencies for the test group were calculated based on the 95th percentiles.

Test Group

Table 4 displays the baseline ABR data for participants with HIV with reference to median, mean, *SD*, and *SE* values of Waves I, III, V of the absolute latencies, I–III, III–V, and I–V for the left and right ears, respectively. Absolute latencies were measured at a median of 1.50–1.54, 3.60–3.70, and 5.50–5.56 ms for Waves I, III, and V, respectively, in the right ear. Absolute latencies for the left ear were measured at a median of 1.52–1.54, 3.70, and 5.50–5.58 ms for Waves I, III, and V, respectively. Delayed Wave III latencies were present in 8.75% (left ear, 7.5%; right ear, 10%) of the participants, and 7.5% (left ear, 5%; right ear, 10%) presented with increased Wave V latency. Equivalent *SE* were found for absolute latencies (*SE* = 0.02–0.04).

Table 3. Baseline neurological auditory brainstem response absolute and interpeak latencies (ms) at a rate of 31.1 Hz for participants without HIV with reference to mean, median, and 95th percentiles using rarefaction, condensation, and alternating polarity for left and right ears (*n* = 40 ears).

Measure	I	III	V	I–III	III–V	I–V
Left (*n* = 20)						
Rarefaction						
M (*SD*)	1.58 (0.16)	3.45 (0.18)	5.22 (0.32)	2.03 (0.17)	1.70 (0.17)	3.89 (0.26)
Mdn (*SE*)	1.62 (0.03)	3.65 (0.03)	5.40 (0.05)	2.00 (0.04)	1.85 (0.04)	3.90 (0.06)
95th percentile	1.57	3.90	5.90	2.59	2.18	4.31
Condensation						
M (*SD*)	1.59 (0.11)	3.66 (0.15)	5.63 (0.22)	2.13 (0.18)	1.90 (0.15)	4.00 (0.22)
Mdn (*SE*)	1.62 (0.03)	3.65 (0.03)	5.40 (0.05)	2.00 (0.04)	1.85 (0.04)	3.90 (0.06)
95th percentile	1.79	3.96	5.96	2.55	2.13	4.43
Alternating						
M (*SD*)	1.56 (0.11)	3.65 (0.15)	5.49 (0.22)	2.06 (0.19)	1.84 (0.16)	3.91 (0.26)
Mdn (*SE*)	1.62 (0.03)	3.62 (0.03)	5.40 (0.05)	2.00 (0.04)	1.85 (0.04)	3.90 (0.06)
95th percentile	1.77	3.93	5.90	2.50	2.03	4.47
Right (*n* = 20)						
Rarefaction						
M (*SD*)	1.53 (0.09)	3.74 (0.16)	5.52 (0.24)	2.25 (0.17)	1.80 (0.10)	3.99 (0.18)
Mdn (*SE*)	1.53 (0.02)	3.77 (0.04)	5.55 (0.05)	2.17 (0.04)	2.20 (0.02)	4.03 (0.04)
95th percentile	1.68	3.94	5.82	2.50	1.85	4.80
Condensation						
M (*SD*)	1.55 (0.09)	3.72 (0.16)	5.50 (0.21)	2.18 (0.17)	1.78 (0.12)	3.96 (0.19)
Mdn (*SE*)	1.53 (0.02)	3.75 (0.04)	5.55 (0.05)	2.20 (0.04)	1.80 (0.02)	4.03 (0.04)
95th percentile	1.68	3.98	5.88	2.50	1.94	4.26
Alternating						
M (*SD*)	1.55 (0.09)	3.72 (0.16)	5.50 (0.21)	2.18 (0.17)	1.78 (0.10)	3.96 (0.18)
Mdn (*SE*)	1.53 (0.02)	3.75 (0.04)	5.55 (0.05)	2.20 (0.04)	1.80 (0.02)	4.03 (0.04)
95th percentile	1.67	3.93	5.80	2.50	1.90	4.20

Note. *SE* = standard error.

Table 4. Baseline neurological auditory brainstem response absolute and interpeak latencies (ms) at a rate of 31.1 Hz for participants living with HIV with reference to mean, median, and 95th percentile using rarefaction, condensation, and alternating polarity (*n* = 80 ears).

Measure	I	III	V	I–III	III–V	I–V
Left ear (*n* = 40)						
Rarefaction						
M (*SD*)	1.54 (0.17)	3.75 (0.21)	5.58 (0.24)	2.21 (0.21)	1.83 (0.23)	4.04 (0.30)
Mdn (*SE*)	1.54 (0.03)	3.70 (0.03)	5.50 (0.04)	2.14 (0.03)	1.87 (0.04)	3.96 (0.05)
95th percentile	1.83	4.20	6.00	2.64	2.39	4.59
Condensation						
M (*SD*)	1.55 (0.13)	3.72 (0.19)	5.63 (0.22)	2.18 (0.23)	1.91 (0.22)	4.08 (0.26)
Mdn (*SE*)	1.52 (0.02)	3.70 (0.03)	5.58 (0.04)	2.18 (0.04)	1.90 (0.03)	4.06 (0.04)
95th percentile	1.80	4.00	6.00	2.50	2.30	4.54
Alternating						
M (*SD*)	1.53 (0.13)	3.74 (0.19)	5.59 (0.21)	2.21 (0.19)	1.84 (0.20)	4.04 (0.26)
Mdn (*SE*)	1.54 (0.02)	3.70 (0.03)	5.58 (0.03)	2.18 (0.03)	1.80 (0.03)	4.01 (0.04)
95th percentile	1.78	4.22	5.94	2.45	2.24	4.48
Right ear (*n* = 40)						
Rarefaction						
M (*SD*)	1.55 (0.17)	3.70 (0.20)	5.56 (0.26)	2.15 (0.19)	1.87 (0.22)	4.01 (0.25)
Mdn (*SE*)	1.50 (0.03)	3.60 (0.03)	5.50 (0.04)	2.16 (0.03)	1.81 (0.03)	4.00 (0.04)
95th percentile	1.90	4.19	6.05	2.51	2.49	4.69
Condensation						
M (*SD*)	1.58 (0.16)	3.74 (0.20)	5.62 (0.21)	2.16 (0.19)	1.89 (0.21)	4.05 (0.21)
Mdn (*SE*)	1.53 (0.03)	3.70 (0.03)	5.56 (0.03)	2.14 (0.03)	1.88 (0.03)	4.03 (0.03)
95th percentile	1.90	4.12	6.00	2.50	2.39	4.53
Alternating						
M (*SD*)	1.55 (0.16)	3.71 (0.19)	5.59 (0.21)	2.16 (0.18)	1.87 (0.19)	4.03 (0.21)
Mdn (*SE*)	1.52 (0.02)	3.70 (0.03)	5.56 (0.03)	2.14 (0.03)	1.83 (0.03)	4.01 (0.03)
95th percentile	1.89	4.12	6.05	2.45	2.38	4.52

Note. *SE* = standard error.

The median I–V interwave latency was measured at 3.96–4.06 ms in the left and right ears. Median absolute and interpeak data from the group with HIV fell within the 95th percentile of the control group. Of the participants with HIV, 3.75% presented with a I–III prolongation (left, 5%; right, 2.5%), 3.75% with a III–V prolongation (left, 2.5%; right, 5%), and 5% with a I–V prolongation (left, 7.5%; right, 2.5%). Six (15%) of the participants presented with asymmetrical interaural Wave V latencies of greater than 0.4 ms (Hood, 1998). In total, nine participants (22.5%) presented with abnormal neurological findings in one or both ears.

Table 5 displays the median, mean, *SD*, and *SE* values of the baseline ABR with reference to the WHO classification of levels of immunodeficiency. The largest median absolute latencies were measured at Wave III (3.89 ms) and Wave V (5.89 ms) in the advanced (Category 2) stage of immunodeficiency, along with the longest median interpeak latencies of Waves I–III and I–V (2.43 and 4.43 ms, respectively) in the left ear. In the right ear, the largest median absolute latencies were measured at Wave III (3.97 ms) and Wave V (5.79 ms) in the advanced (Category 2) stage of immunodeficiency, along with the largest median interpeak latencies of Waves I–III and I–V (2.36 and 4.18 ms, respectively). Only the median absolute

latency of Wave III and Wave V and the interpeak latency of Waves I–III and I–V, in Category 2 of immunodeficiency, fell outside the 95th percentile of the control group.

Table 5. Neurological auditory brainstem response absolute and interpeak latencies (ms) for participants with HIV with reference to World Health Organization classification of levels of immunodeficiency (*n* = 80 ears).

CD4+ category		I	III	V	I–III	III–V	I–V
Left ear (*n* = 40)							
0 (*n* = 21 ears)	*M*(*SD*)	1.54 (0.14)	3.72 (0.18)	5.54 (0.19)	2.17 (0.16)	1.82 (0.18)	4.00 (0.21)
	Mdn(*SE*)	1.52 (0.03)	3.60 (0.04)	5.58 (0.04)	2.18 (0.03)	1.77 (0.04)	3.91 (0.05)
1 (*n* = 15 ears)	*M*(*SD*)	1.54 (0.14)	3.71 (0.15)	5.59 (0.19)	2.17 (0.15)	1.89 (0.22)	4.05 (0.25)
	Mdn(*SE*)	1.57 (0.04)	3.70 (0.04)	5.58 (0.05)	2.14 (0.04)	1.82 (0.06)	4.01 (0.06)
2 (*n* = 4 ears)	*M*(*SD*)	1.50 (0.09)	3.95 (0.29)	5.81 (0.27)	2.48 (0.29)	1.85 (0.19)	4.26 (0.46)
	Mdn(*SE*)	1.49 (0.05)	3.89 (0.14)	5.89 (0.14)	2.43 (0.14)	1.82 (0.09)	4.43 (0.23)
Right ear (*n* = 40)							
0 (*n* = 21 ears)	*M*(*SD*)	1.52 (0.12)	3.66 (0.14)	5.52 (0.18)	2.14 (0.14)	1.85 (0.22)	4.00 (0.19)
	Mdn(*SE*)	1.52 (0.03)	3.60 (0.03)	5.48 (0.04)	2.14 (0.03)	1.82 (0.05)	4.01 (0.04)
1 (*n* = 15 ears)	*M*(*SD*)	1.60 (0.18)	3.74 (0.18)	5.64 (0.19)	2.14 (0.20)	1.90 (0.15)	4.04 (0.20)
	Mdn(*SE*)	1.57 (0.05)	3.70 (0.05)	5.58 (0.05)	2.14 (0.05)	1.87 (0.04)	4.02 (0.05)
2 (*n* = 4 ears)	*M*(*SD*)	1.56 (0.22)	3.92 (0.33)	5.74 (0.35)	2.36 (0.26)	1.82 (0.08)	4.18 (0.32)
	Mdn(*SE*)	1.47 (0.11)	3.97 (0.16)	5.79 (0.17)	2.32 (0.13)	1.80 (0.04)	4.09 (0.16)

Note. *SE* = standard error.

Phase 2

Participants who presented with abnormalities in the neurological ABR examination were excluded from analysis in the rate study. Consequently, the nine participants who presented with abnormal findings in one or both ears during Phase 1 of the study were excluded.

Control Group

Table 6 displays the mean, median, and 95th percentile data for right and left ears separately for the absolute latencies of Wave V measured at increased stimulus rates from the baseline stimulus rate used in Phase 1, as well as the Wave V latency shift from the baseline (31.1 Hz) to increased stimulus rates (45.1 and 61.1 Hz) for participants without HIV. The Wave V absolute latency measured during the baseline ABR was repeated in Table 6 to facilitate calculation of shift from 31.1 Hz to increased stimulus rates. An abnormal shift would therefore be classified as > 95th percentile, between rates of 31.1–45.1, 45.1–61.1, and 31.1–61.1 Hz, while abnormal Wave V latencies was classified as > 95th percentile at rates of 41.1 and 61.1 Hz (see Table 6).

Table 6. Absolute Wave V latencies and Wave V latency shifts (ms) in response to auditory brainstem response at increased stimulus rates in adults without HIV using alternating polarity for left and right ears (*n* = 40).

Measure	Wave V latency			Wave V latency shift		
	V (31.1 Hz)	V (45.1 Hz)	V (61.1 Hz)	31.1–45.1 Hz	45.1–61.1 Hz	31.1–61.1 Hz
Left ear (*n* = 20)						
M (*SD*)	5.49 (0.22)	5.67 (0.23)	5.82 (0.26)	0.17 (0.10)	0.15 (0.13)	0.33 (0.11)
Mdn (*SE*)	5.40 (0.05)	5.67 (0.05)	5.87 (0.06)	0.19 (0.02)	0.11 (0.03)	0.31 (0.03)
5th percentile	5.17	5.23	5.30	0.00	0.00	0.13
95th percentile	5.9	6.07	6.20	0.37	0.47	0.60
Right ear (*n* = 20)						
M (*SD*)	5.50 (0.21)	5.67 (0.18)	5.87 (0.18)	0.16 (0.05)	0.20 (0.09)	0.36 (0.11)
Mdn (*SE*)	5.55 (0.05)	5.70 (0.04)	589 (0.04)	0.05 (0.19)	0.09 (0.20)	0.11 (0.33)
5th percentile	5.00	5.23	5.53	0.10	0.07	0.20
95th percentile	5.80	5.90	6.10	0.23	0.30	0.53

Note. *SE* = standard error.

Test Group

Table 7 displays the mean, median latency of Wave V, and Wave V latency shifts at each of the different stimulus rates using alternating polarity for left and right ears for adults with HIV. The median Wave V latency increased with increased stimulus rate in both ears. When compared to the control group, median latencies fell within the 95th percentile.

Table 7. Absolute Wave V latencies and Wave V latency shifts (ms) in response to auditory brainstem response at increased rates in adults with HIV using alternating polarity for the left and right ears (*n* = 62 ears).

Measure	Wave V latency			Wave V latency shift		
	V (31.1 Hz)	V (45.1 Hz)	V (61.1 Hz)	31.1–45.1 Hz	45.1–61.1 Hz	31.1–61.1 Hz
Left ear (*n* = 31)						
M (*SD*)	5.63 (0.21)	5.70 (0.23)	5.85 (0.26)	0.07 (0.08)	0.15 (0.13)	0.23 (0.14)
Mdn (*SE*)	5.58 (0.04)	5.68 (0.04)	5.84 (0.05)	0.05 (0.01)	0.13 (0.02)	0.21 (0.02)
Right ear (*n* = 31)						
M (*SD*)	5.59 (0.17)	5.69 (0.18)	5.81 (0.19)	0.10 (0.09)	0.12 (0.09)	0.22 (0.10)
Mdn (*SE*)	5.58 (0.03)	5.68 (0.03)	5.84 (0.34)	0.10 (0.15)	0.11 (0.16)	0.21 (0.17)

Note. *SE* = standard error.

Table 8 displays the median, *SE*, mean, and *SD* values of Wave V latency and latency shifts at each of the different stimulus rates with reference to the WHO classification of levels of immunodeficiency for left and right ears separately. The largest Wave V absolute latencies were measured with a stimulus rate of 61.1 Hz; however, the median absolute latencies of Wave V were similar for Stages 0, 1, and 2 of immunodeficiency at each stimulus rate.

Table 8. Absolute Wave V latencies and Wave V latency shifts (ms) of auditory brainstem response at increased stimulus rates with adults with HIV using alternating polarity with reference to World Health Organization classification of levels of immunodeficiency (*n* = 62 ears).

			Wave V latency			Wave V latency shift		
CD4+ category			**V(31.1 Hz)**	**V(45.1 Hz)**	**V(61.1 Hz)**	**31.1–45.1 Hz**	**45.1–61.1 Hz**	**31.1–61.1 Hz**
Left ear (*n* = 31)								
0	(*n* = 19 ears)	*M*(*SD*)	5.62 (0.23)	5.74 (0.26)	5.89 (0.30)	0.09 (0.09)	0.18 (0.15)	0.27 (0.15)
		Mdn(*SE*)	5.58 (0.05)	5.68 (0.06)	5.89 (0.07)	0.05 (0.02)	0.21 (0.03)	0.26 (0.03)
1	(11 = ears)	*M*(*SD*)	5.65 (0.18)	5.71 (0.18)	5.80 (0.16)	0.06 (0.07)	0.10 (0.07)	0.15 (0.07)
		Mdn(*SE*)	5.68 (0.06)	5.68 (0.05)	5.84 (0.05)	0.05 (0.02)	0.06 (0.02)	0.16 (0.02)
2	(*n* = 1 ear)	*M*(*SD*)	5.53	5.53	5.68	0.00	0.15	0.15
		Mdn(*SE*)	5.53	5.53	5.68	0.00	0.15	0.15
Right ear (*n* = 31)								
0	(*n* = 19 ears)	*M*(*SD*)	5.57 (0.18)	5.70 (0.20)	5.81 (0.21)	0.13 (0.10)	0.11 (0.09)	0.24 (0.09)
		Mdn(*SE*)	5.58 (0.04)	5.68 (0.05)	5.84 (0.05)	0.16 (0.13)	0.10 (0.02)	0.26 (0.02)
1	(*n* = 11 ears)	*M*(*SD*)	5.62 (0.15)	5.67 (0.16)	5.80 (0.18)	0.05 (0.06)	0.14 (0.10)	0.19 (0.11)
		Mdn(*SE*)	5.58 (0.05)	5.63 (0.05)	5.74 (0.06)	0.05 (0.02)	0.15 (0.03)	0.16 (0.03)
2	(*n* = 1 ear)	*M*(*SD*)	5.63	5.63	5.84	0.00	0.21	0.21
		Mdn(*SE*)	5.63	5.63	5.84	0.00	0.21	0.21

Note. *SE* = standard error.

Median absolute Wave V latencies at each rate and Wave V latency shifts within the participants living with HIV fell within the 95th percentile of the control group. The number of abnormal Wave V latency shifts (> 95th percentile of control group) did not increase with a decrease in CD4+ counts. In CD4+ Category 0 of immunodeficiency, 14 (five right and nine left ears) absolute Wave V latencies were obtained; 15 were obtained in Category 1 (six right and nine left ears), and four were obtained in Category 2 (two right and two left ears). In CD4+ Category 0 of immunodeficiency, nine (two right and seven left ears) absolute Wave V latencies were obtained; one was obtained in Category 1 (one right ear), and 11 were obtained in Category 2 (six right and five left ears). The Cochran–Armitage test of trend did not indicate a statistically significant linear trend of increased absolute Wave V latency in either the left or right ear ($p > .05$) with lower CD4+ counts. Similarly, the test of trend between CD4+ counts and abnormal Wave V latency shifts was not statistically significant ($p > .05$). Grand averages of the neurological ABR and the rate study for the adults with HIV are presented in Figure 1.

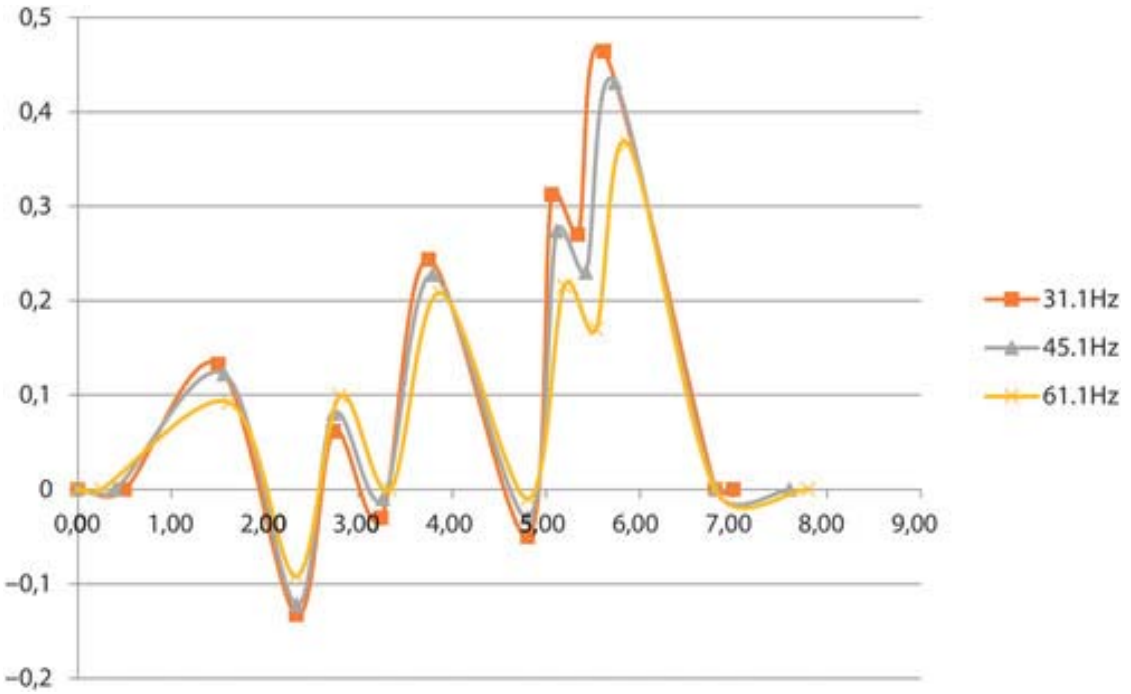

Figure 1. Grand average of the HIV–positive group displaying neurological auditory brainstem response (31.1 Hz) and rate study (45.1 and 61.1 Hz).

A two-way ANOVA was used to determine the interaction between HIV status and stimulus repetition rate, for right and left ears separately, on Wave V latency of the rate study. The interaction was not significant; right: $F(2, 120) = 1.186$, $p = .309$, $\eta_p^2 = .020$; left: $F(2, 120) = 0.513$, $p = .600$, $\eta_p^2 = .008$. An analysis of main effects was subsequently completed, which indicated that rate (right ear: $F = 17.736$, $p < .001$, $\eta_p^2 = .237$; left ear: $F = 11.112$, $p < .001$, $\eta_p^2 = .156$), but not HIV status (right ear: $F = 0.011$, $p = .916$, $\eta_p^2 < .001$; left ear: $F = 2.766$, $p = .099$, $\eta_p^2 = .023$), significantly affected Wave V latency of the rate study. Pairwise comparisons revealed a statistically significant difference in Wave V latency in the left ear measured using a rate of 31.1 and 61.1 Hz (mean increase in Wave V latency of 0.273 ms; 95% CI [0.132, 0.414], $p < .00$) and between a rate of 45.1 and 61.1 Hz (mean increase in Wave V latency of 0.148 ms; 95% CI [0.007, 0.288], $p = .037$) in the left ear, while no statistical difference was measured at rates of 31.1 and 45.1 Hz (mean increase of 0.125 ms; 95% CI [−0.015, 0.266], $p > .05$). In the right ear, pairwise comparisons indicated statistically significant differences in Wave V latency between each rate. A mean increase of 0.128 ms in Wave V latency was measured when rate was increased from 31.1 to 45.1 Hz (CI [0.0.008, 0.249], $p = .032$). A mean increase in Wave V latency of 0.294 ms was measured in right ears between a rate of 31.1 and 61.1 Hz (95% CI [0.174, 0.415], $p < .001$). Mean Wave V latency increased by 0.166 ms between 45.1 and 61.1 Hz stimulus rates (95% CI [0.146, 0.286], $p = .003$).

Within the HIV group, an ANOVA was completed to assess the interaction between CD4+ category and rate. No significant interaction between CD4+ category and rate was measured in either the right ear, $F(4, 84) = 0.214$, $p = .930$, $\eta_p^2 = .010$ (see Figure 2), or the left ear, $F(4, 83) = 0.272$, $p = .895$, $\eta_p^2 = .013$ (see Figure 3). Main effects analysis demonstrated that neither rate nor CD4+ significantly affected Wave V latency (rate right ear: $F = 2.646$, $p = .077$, $\eta_p^2 = .059$; CD4+ category right ear: $F = 0.001$, $p = .999$, $\eta_p^2 < .001$; rate left ear: $F = 1.350$, $p = .265$, $\eta_p^2 = .031$; CD4+ category $F = 0.649$, $p = .525$, $\eta_p^2 = .015$).

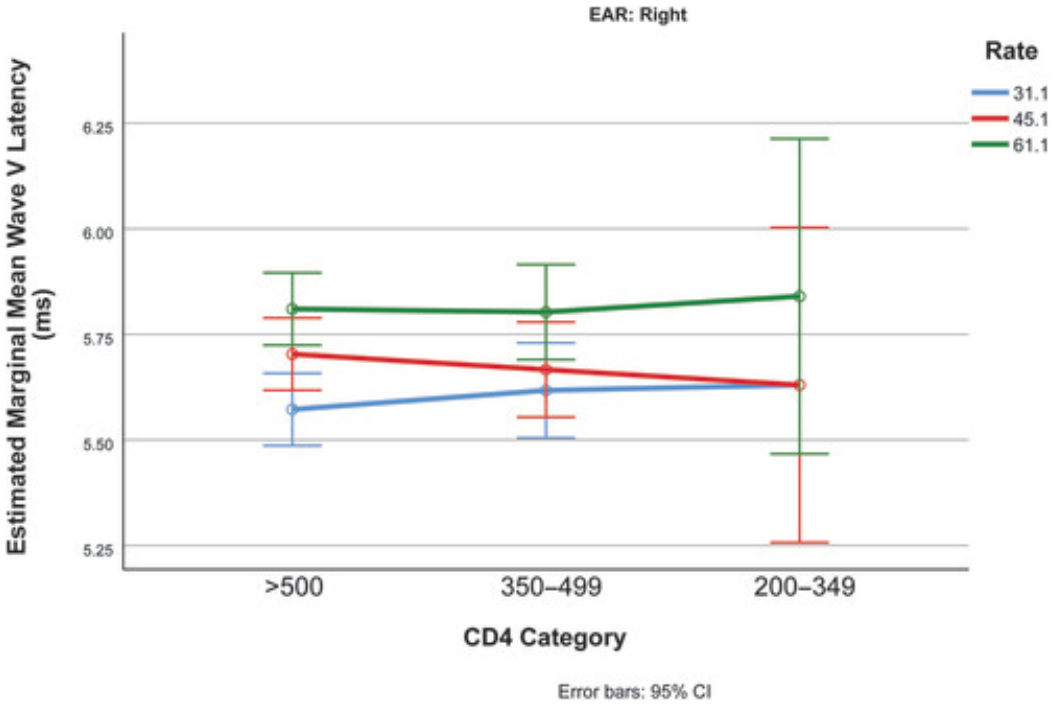

Figure 2. Interaction between stimulus rate and CD4+ category for the right ear. CI = confidence interval.

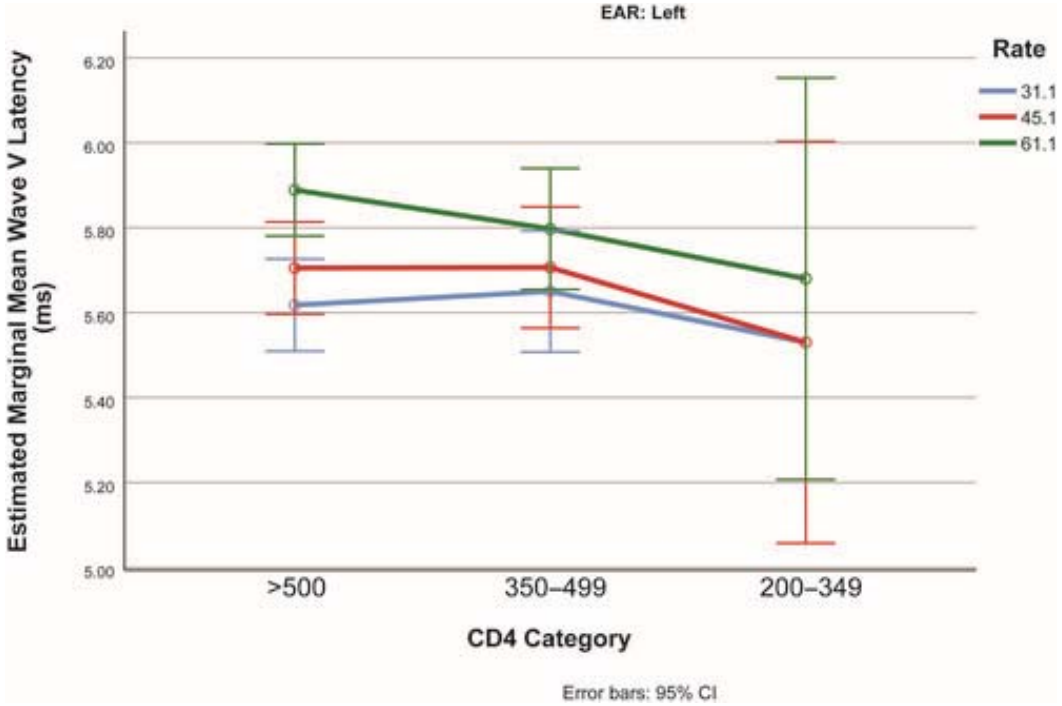

Figure 3. Interaction between stimulus rate and CD4+ category for the left ear. CI = confidence interval.

Finally, a multiple linear regression analysis was completed to predict Wave V latency of the rate study from rate, gender, and HIV status. The regression model statistically significantly predicted the Wave V latency in the right ear, $F(3, 122) = 17.928$, $p < .001$, adj $R^2 = .299$, and in the left ear, $F(3, 122) = 13.483$, $p < .001$, adj $R^2 = .231$. Although rate and gender

contributed highly significantly to the model ($p < .001$), HIV status did not (right, $p = .939$; left, $p = .064$). Regression coefficients are displayed in Table 9.

Table 9. Summary of multiple regression analysis for left and right ears.

Variable	*B*	SE_B	β	*Sig*
Left ear				
Intercept	5.628	0.093		.000
Rate	0.125	0.024	0.402	.000
Gender	−0.141	0.042	−0.262	.001
HIV status	0.084	0.045	0.147	.064
Right ear				
Intercept	5.651	0.077		.000
Rate	0.126	0.020	0.492	.000
Gender	−0.122	0.034	−0.273	.001
HIV status	−0.033	0.038	0.006	.939

Note. B = constant; SE_B = standard error of B; Sig = significance.

Discussion

The ABR has been used in defining the extent of damage to the auditory neural tissue in the brainstem and monitor the speed of the evolution of the lesion caused by the HIV (Matas, Silva, et al., 2010; Serafini et al., 1998). HIV is a viral demyelinating disease that can cause white matter abnormalities, and the use of ARVs can lead to the development of severe inflammatory demyelination (Love, 2006). Studies with adult participants who presented with multiple sclerosis, another demyelinating disease, suggested that the inclusion of faster stimulus repetition rates, when using the ABR, should be part of routine audiological care in adults with demyelinating diseases to identify rate-dependent increased Wave V absolute latencies and latency shifts (Jacobson et al., 1987; Santos et al., 2004). Therefore, this study aimed to investigate whether the ABR and ABR rate study can identify if neurodegeneration has already occurred in adults with HIV who presented with normal behavioral pure-tone hearing thresholds.

The baseline ABR for adults with HIV yielded median absolute latencies and interpeak latencies within the 95th percentile for WHO categories of immunosuppression 0 and 1. However for individuals at an advanced stage of immunodeficiency (WHO Category 2), median absolute latencies of Waves III and V were prolonged when compared to the 95th percentile of the control group. The number of abnormal absolute Wave V latencies did not increase significantly with an increase in immunodeficiency ($p > .05$). Wave V latency was significantly affected by both stimulus rate ($p < .001$) and gender ($p < .001$), but not by HIV status in adults with normal pure-tone audiometric thresholds.

Phase 1: Neurological ABR at Baseline Rate

The baseline neurological ABR indicated equivalent median absolute latencies of normal-hearing adults who are living with HIV when compared to the control group. The median absolute latencies of Waves I, III, and V of participants living with HIV also fell within the 95th percentile of the control group.

Similar median interwave latencies of the baseline ABR in normal-hearing adults living with HIV was found when compared to 95th percentile of the control group data. This correlates with previous studies on normal-hearing adults living with HIV (Lima & Fukuda, 1999; Matas et al., 2015). In contrast to the current study, Bankaitis et al. (1998), Pierelli et al. (1996), and Reyes-Contreras et al. (2002) reported prolonged interwave latencies I–III, I–V of the ABR measurement in individuals who were HIV positive as compared to HIV-negative individuals. It is likely that the current study differs from this finding possibly due to inclusion of participants with a hearing loss in the aforementioned studies, which may have contributed to the prolonged interpeak latencies reported (Hood, 1998).

The current study is in agreement with studies who found that an increased Wave III and V latency is a common phenomenon in individuals with HIV (Bankaitis et al., 1998; Castello et al., 1998; Mata Castro et al., 2000; Matas, Silva, et al., 2010). Delayed Wave III latencies were present in the left and right ears in 8.75% of the study sample; 7.5% presented with increased Wave V latency indicative of the possible neuropathology of the cochlear nucleus, the superior olivary complex, lateral lemniscus, and contralateral inferior colliculus (Hall, 1992). Prolonged Wave I–III interpeak latencies were found in 3.75% of the study sample; 3.75% of participants presented with prolonged interpeak latencies of Waves III–V, and 5% of participants presented with prolonged interpeak latencies of Waves I–V. Matas et al. (2015) suggested that this pattern of I–V and III–V interwave prolongation indicates lower brainstem pathology.

The current study found six individuals with asymmetrical interaural Wave V latencies, the aetiology of which is unknown. Asymmetries in Wave V latencies in adults with HIV has not been reported or evaluated in previous literature. However, asymetrical hearing losses in individuals have been reported in studies investigating vestibular and neuromuscular disorders in individuals with HIV (Heinze et al., 2014; McGuire, 2003). Although the aetiolgy of the asymetries in these patients was not known, it can be the result of a possible underlying oppurtunistic infections that were not documented in the patient records (Heinze et al., 2014). Further research on the aetiology thereof is therefore recommended. The particular participants in the current study were referred to the treating physician for further management.

Baseline ABR With Reference to WHO Categories of Immunodeficiency

Median absolute and interwave latencies of the baseline ABR in Phase 1 of the study were calculated with reference to the WHO classification of levels of immunodeficiency (see Table 5). No difference in median absolute and interwave latencies was found between Stage 0 and Stage 1. However, in Stage 2 of immunodeficiency, the median Wave III and V latencies were prolonged when compared to the 95th percentile of the control group. The delayed Wave III and V latency in adults living with HIV who are in advanced stages of immunodeficiency is indicative of the possible pathology of the lateral lemniscus and the contralateral inferior colliculus (Hall, 1992). Studies investigating individuals with HIV also reported prolonged Wave V latencies in individuals who were in advanced stages of immunodeficiency (Koralnik et al., 1990; Mata Castro et al., 2000; Pierelli et al., 1996). The current study also noted prolongation of Waves I–III and I–V similar to that of Castello et al. (1998), who reported upper brainstem pathology in adults with HIV. In their smaller participant group, Castello et al. (1998) included 11 individuals who were severely immunocompromised with CD4+ counts below 200 cells/µl. No participant in the current study had a CD4+ count below 200 cells/µl. The delayed absolute latencies of Waves III and

V and interpeak latencies in the adults with HIV may indicate early neurological involvement in the advance stage of immunodeficiency in adults with normal audiometric results (Koralnik et al., 1990; Maleßa et al., 1989).

Phase 2: ABR at Increased Stimulus Rates

For the purpose of comparing the rate study of adults living with HIV to individuals without HIV, the 95th percentile for the shift in Wave V latency from baseline to increased stimulus rate, as was measured in the control group, was used. Similarly, the 95th percentile for the absolute Wave V latencies at increased stimulus rates for the control group was compared to that of the adults living with HIV.

Within the adults with HIV, the median absolute Wave V latency at increased stimulus rates fell within the 95th percentile when compared to the control group. There was no significant interaction between HIV status and stimulus repetition rate for either left or right ears on Wave V latency of the rate study ($p > .05$). Similarly, within the adults living with HIV, no significant interaction between CD4+ category and rate was measured in either left or right ears ($p > .05$). With regard to the prediction of Wave V latency, stimulus rate significantly affected Wave V latency ($p < .001$); however, the stage of immunodeficiency (as deduced from CD4+ category) and HIV status did not significantly affect the prediction of Wave V latency ($p > .05$). It is unclear why the category with the lowest CD4+ count presented with the shortest mean Wave V latency (see Figure 3). However, this was based on a single female participant in the CD4+ group. Shorter ABR latencies are typical of females when compared to males (Lima & Fukuda, 1999). The participant's Wave V latency at a rate of 31.1 Hz was measured at 5.53 ms, with a shift to 5.68 ms at the fastest stimulus rate.

The current finding results correlate with previous studies that reported there is no statistically significant increase in Wave V latencies with increased levels of immunosuppression with an ABR rate study (Koralnik et al., 1990; Pierelli et al., 1996). Koralnik et al. (1990) reported abnormal Wave V latency in individuals who had normal audiometric results, who were in Stages 0, 1, and 2 of immunodeficiency.

The 17.5% of ears presented with delayed Wave V latencies with faster stimulus rates are similar to studies done in individuals with multiple sclerosis that advocated for faster rates in the audiometric test battery in patients with demyelinating diseases for the purpose of identification of retrocochlear pathology (Duong et al., 2017). However, an increase in ABR stimulus rate does not appear to be statistically linked to the level of immunosuppression in adults living with HIV with normal audiometric thresholds. Nevertheless, an additional 14 ears with abnormal absolute Wave V latencies were identified with an increase in stimulus rate, compared to the baseline ABR. Although not statistically significant, the additional number of abnormal results with the ABR rate study may be clinically significant. Further assessment of the correlation between individuals identified with abnormal results on ABR at increased stimulus rates, with behavioral outcomes or auditory processing skills, would be of value to confirm clinical value of this finding.

The greatest absolute Wave V latencies were associated with male participants with the greatest immunodeficiency levels (Stage 2). Gender differences in ABR wave latencies have been reported (Lima & Fukuda, 1999). Interestingly, this difference between male and female participants was not measured with individuals with CD4+ levels of greater than or equal to 500 cells/µl in the current study, but only at increased levels of immunodeficiency.

A limitation of the current study was that the researchers made use of CD4+ counts to determine the stage of immunodeficiency. CD4+ counts vary significantly among individuals, populations, sites, and devices (Ying et al., 2016). As CD4+ counts may be influenced by gender, time of day, body mass index, smoking, and exposure to pathogens in the environment, it was hypothesized that the use of viral loads rather than of CD4+ counts would provide a more clear presentation of the virus in the individual (Ying et al., 2016). However, as all participants in the current study were compliant with an ARV treatment regime, their viral loads were undetectable. Larger scale studies incorporating the variables that affect CD4+ count may provide further clarity on this issue. Future research describing the results of the ABR rate study on individuals with HIV with varying viral loads would be of interest.

The CD4+ category that demonstrated the greatest number of abnormal Wave V latencies, namely, those with advanced levels of immunodeficiency, included the smallest number of participants ($n = 8$). Research that focuses on larger numbers of adults with advanced immunodeficiency and the correlation of behavioral measures such as speech testing in adults living with HIV at increased stimulus rates may be of considerable clinical value.

Conclusions

The current study aimed to investigate if the ABR at a baseline rate and also, at higher stimulus rates, can detect whether subtle neurodegeneration has occurred in adults living with HIV who presented with normal behavioral hearing thresholds. Within the adults living with HIV, the neurological ABR yielded prolonged absolute and interpeak latencies in 22.5% of ears, all of whom were in the advanced stage of immunodeficiency. Interaural Wave V latency differences were present in 15% of participants. An additional 17.5% of ears presented with abnormal Wave V latencies at increased stimulus rates. There were no significant interaction between HIV status and rate in the left or right ear, or between CD4+ category and rate in either ear ($p > .05$). Although rate and gender contributed significantly to the prediction of Wave V latency of the rate study ($p < .001$), HIV status did not ($p > .05$). Nevertheless, more ears were identified with abnormal results with the ABR rate study than with the neurological ABR alone. Clinically, the ABR at increased stimulus rates may therefore be a valuable addition to the ABR protocol, for the identification of individuals with auditory neural deficiencies in adults living with HIV, despite presenting with normal behavioral pure-tone audiometric thresholds.

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