

COMPARISON OF N1P2 CORTICAL AUDITORY EVOKED POTENTIAL AND NARROW-BAND CHIRP AUDITORY STEADY STATE POTENTIAL IN HEARING THRESHOLD DETECTION IN ADULTS

Contributions:

A Study design/planning
B Data collection/entry
C Data analysis/statistics
D Data interpretation
E Preparation of manuscript
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Abstract

Background: Various auditory evoked potential techniques have been explored as a means of objectively predicting the behavioral audiogram in groups of subjects who cannot provide reliable or accurate behavioral results. The tone-evoked auditory brainstem response (ABR) cannot differentiate between severe and profound SNHL, whereas the auditory steady state response (ASSR) can provide threshold information in a frequency-specific manner at intensity levels of 120 dB SPL. The cortical auditory evoked potential (N1P2 CAEP) has shown advantages over the ABR and ASSR.

Objectives: To assess the ability of the N1P2 cortical auditory evoked potential (CAEP) to estimate the hearing threshold level at different frequencies, in normal hearing adults and adults with different degrees of sensorineural hearing loss (SNHL); and to compare it to the auditory steady state response (ASSR).

Methods: This study included 90 subjects (180 ears), grouped into 6 groups according to the degree of hearing obtained by pure tone audiometry (PTA). Hearing threshold was then measured using N1P2 CAEP and ASSR.

Results: N1P2 CAEP and ASSR were highly correlated to PTA at all frequencies. However, N1P2 CAEP predicted behavioral thresholds more accurately than ASSR at all frequencies, especially at 500 and 1000 Hz in the normal hearing group and for all degrees of SNHL. N1P2 CAEP was equally accurate at all frequencies and predicted behavioral thresholds better at more severe degrees of SNHL at 1, 2, and 4 kHz.

Conclusion: The N1P2 CAEP can be reliably used as an objective method for estimating the behavioral hearing threshold, yielding more accurate results than the ASSR, especially at lower frequencies and with more severe degrees of hearing loss. We therefore recommend using the N1P2 CAEP in estimating the behavioral threshold in difficult-to-test adults.

Key words: chirp • sensorineural hearing loss • hearing threshold • auditory steady state response • N1P2

PORÓWNANIE SŁUCHOWYCH POTENCJAŁÓW KOROWYCH N1P2 I POTENCJAŁU STANU USTALONEGO GENEROWANEGO WĄSKOPASMOWYM BODŹCEM TYPU CHIRP W ROZPOZNANIU PROGU SŁYSZENIA U OSÓB DOROSŁYCH

Streszczenie

Wstęp: Różne metody pomiaru słuchowych potencjałów wywołanych przeanalizowano pod kątem obiektywnego przewidywania audiogramu behawioralnego u pacjentów, w przypadku których nie jest możliwe uzyskanie wiarygodnych lub dokładnych wyników behawioralnych badań słuchu. Badanie słuchowych potencjałów wywołanych pnia mózgu (ABR) nie pozwala na rozróżnienie ciężkiego i głębokiego niedosłuchu odbiorczego (SNHL), podczas gdy badanie potencjałów wywołanych stanu ustalonego (ASSR) może dostarczać informacji o progu słyszenia w zależności od częstotliwości przy poziomach intensywności 120 dB SPL. Słuchowe potencjały korowe (N1P2 CAEP) wykazały przewagę nad ABR i ASSR.

Cele: Ocena badania słuchowych potencjałów korowych N1P2 (CAEP) pod kątem jego zdolności szacowania poziomu progu słyszenia dla różnych częstotliwości u dorosłych z prawidłowym słuchem i dorosłych z niedosłuchem odbiorczym o różnym stopniu nasilenia (SNHL), a także porównanie tego badania z badaniem potencjałów wywołanych stanu ustalonego (ASSR).

Metoda: W badaniu wzięło udział 90 osób (180 uszu) podzielonych na 6 grup według stopnia niedosłuchu zdiagnozowanego w badaniu audiometrii tonalnej (PTA). Następnie zmierzono próg słyszenia za pomocą N1P2 CAEP i ASSR.

Wyniki: CAEP i ASSR były silnie skorelowane z PTA na wszystkich częstotliwościach. Jednak badanie CAEP przewidywało progi behawioralne dokładniej niż ASSR dla wszystkich częstotliwości, zwłaszcza dla częstotliwości 500 i 1000 Hz, u osób ze słuchem prawidłowym i pacjentów

z SNHL w zakresie wszystkich stopni niedosłuchu. CAEP były równie dokładne dla wszystkich częstotliwości i lepiej przewidywały progi behawioralne w zakresie ciężkiego i głębokiego stopnia SNHL dla 1 kHz, 2 kHz i 4 kHz.

Wnioski: Badanie N1P2 CAEP może być stosowane jako rzetelna obiektywna metoda szacowania behawioralnego progu słyszenia, która daje dokładniejsze wyniki niż ASSR, szczególnie dla niższych częstotliwości i w przypadku ciężkiego i głębokiego stopnia niedosłuchu. Dlatego zalecamy stosowanie CAEP do szacowania progu behawioralnego u dorosłych pacjentów, w przypadku których nie jest możliwe uzyskanie wiarygodnych lub dokładnych wyników behawioralnych badań słuchu.

Słowa kluczowe: bodziec *chirp* • niedosłuch odbiorczy • próg słyszenia • reakcja słuchowa stanu ustalonego • N1P2

Introduction

Various auditory evoked potential techniques have been explored as a means of objectively predicting the behavioral audiogram in groups of subjects who cannot provide reliable or accurate behavioral results [1]. One of the most important and clinically useful aspects of the N1P2 cortical auditory evoked potential (CAEP) is that responses in adults can be observed close to threshold, and therefore CAEP can be used as an objective estimator of auditory threshold. The use of the N1P2 CAEP response as an electrophysiological measure in estimating hearing sensitivity is well established, suggesting that threshold estimation in adults is accurate to within 10–20 dB [2]. The N1P2 CAEP has advantages over the tone-evoked auditory brainstem response (ABR) [2] and the auditory steady state response (ASSR) [1].

N1P2 is an auditory late response (ALR), referring to cortical evoked responses with a latency of about 50 to 500 ms. An ALR waveform as recorded clinically usually consists of gently sloping and broad waves in contrast to the sharp and narrow-peaked waves characterizing the shorter latency responses. The first negative voltage component, labeled N1, occurs in the 90 to 150 ms region, with an average latency of about 100 ms. It is followed by a positive wave labeled P2 that normally appears between 160 and 200 ms [3].

N1 and P2 are thought to have multiple generators in Heschl's gyrus (auditory cortex) and have latencies of 100–160 ms and 160–270 ms respectively, depending on the sensation level of the stimulus [4]. The N1P2 response is considered an obligatory exogenous evoked (or event-related) potential; that is, it does not involve cognitive processing although it is affected by arousal level [5]. Although the most significant clinical limitation of the N1P2 response as an audiological tool is its late maturation, extending into the late teenage years, the technique remains viable in older children and adults [5].

The N1P2 CAEP remains a valuable clinical tool for adults who are unable to participate or reliably respond in conventional/standard audiometric procedures [6]. Obvious client groups include adults pursuing medicolegal compensation for alleged occupational hearing loss, patients with suspected nonorganic hearing loss, and adults with marked learning difficulties or dementia [7].

Lightfoot and Kennedy [2] identified a mean audiometric/electrophysiological threshold difference of 6.5 dB, after correction. That is better than most estimates of adult ABR accuracy. Individuals exaggerating their audiometric thresholds often give better responses than honest subjects, especially for stimulus levels that are audible but below their volunteered thresholds. This is thought to be associated with heightened cortical arousal level for these

stimuli, which are seen as a threat. As with the ABR, the accuracy of threshold prediction increases for individuals with a recruiting hearing loss, with the steeper input-output response function seen in such cases yielding larger amplitude responses than non-recruiting or normally hearing individuals at stimulus levels just above their threshold [4].

One of the advantages of the N1P2 response is the almost ideal frequency specificity it provides, allowing steeply sloping or notched audiometric contours to be resolved. Unlike the ABR, the morphology of the N1P2 response is every bit as clear for low frequencies as for high. Response amplitude does decline at frequencies above about 3 kHz, although the threshold prediction at 8 kHz is found to be no worse than at lower frequencies. In addition to the excellent frequency specificity and good threshold precision, other advantages over the ABR include testing the integrity of a greater proportion of the auditory nervous system and the ability to employ speech-based stimuli [4]. The N1P2 response is less affected by muscle activity and is more frequency-specific than the ABR [8].

The ASSR is an increasingly popular technique for estimating hearing threshold [9]. Overall, the N1P2 CAEP is found to provide responses closer to threshold than the ASSR. The N1P2 CAEP demonstrates a closer relationship of evoked potential threshold with behavioral hearing levels compared to the 40 Hz ASSR. However, this alone does not demonstrate an accuracy advantage. Because the N1P2 CAEP demonstrates significantly lower variance in results than the ASSR, this gives it an overall clinical advantage [1].

The ABR cannot differentiate between severe and profound SNHL, whereas the ASSR can provide threshold information in a frequency-specific manner at intensity levels of 120 dB SPL. ASSR measurement can facilitate the assessment of patients with severe to profound degrees of SNHL. The steady tonal stimuli used in ASSR permit higher outputs to be realized than do typical evoked response test systems. As an option, multiple frequencies and/or two ears can be tested simultaneously. The most important advantage is that the spectrum of the response is predicted precisely by that of the stimulus spectrum without the need for subjective interpretation of the recorded response [10]. This intensity stimulation advantage uniquely qualifies the ASSR for investigation of residual hearing in young and difficult-to-test cochlear implant candidates [11].

ASSR can differentiate normal hearing conditions from hearing loss or differentiate mild from moderate hearing loss, except at 500 Hz. The difference between ASSR and behavioral thresholds decreases as frequency increases. ASSR has difficulties in discriminating mild hearing loss from normal hearing, especially at low frequencies [12]. This could be the result of poorer neural synchronization

and higher ASSR thresholds for 500 Hz under normal hearing conditions. Moreover, the difference between ASSR and behavioral thresholds decreases as the severity of hearing loss increases and this could be related to recruitment [12]. The configuration of the SNHL does not affect the ASSR thresholds and ASSR can accurately reflect the flat and sloping configurations of hearing loss. The configuration of hearing loss does not affect ASSR thresholds, but the difference between behavioral and ASSR thresholds is greater at 500 Hz in both configurations [13].

Rationale

The N1P2 CAEP shows advantages over previous frequency-specific evoked potentials in hearing threshold estimation in adults. This was the reason for examining N1P2 application in the current study to assess hearing thresholds, and was why we compared them with ASSRs rather than ABRs. Thus, the N1P2 CAEP could be a better tool for hearing threshold detection in adults where no reliable behavioral threshold can be obtained. This study was carried out on Egyptian participants and investigated the ability of the N1P2 to reflect the behavioral threshold audiogram (compared to the recently used ASSR).

Aim of the work

To assess the ability of the N1P2 cortical auditory evoked response potential to estimate the hearing threshold level at different frequencies, both in adults with normal hearing thresholds and adults with different degrees of sensorineural hearing loss, and to make a comparison with auditory steady state responses.

Subjects and methods

The present study comprised 90 subjects (180 ears). They included adults of both genders with ages of 20–50 years. Patients were recruited from the Audiology Unit outpatient clinic (otorhinolaryngology department) of Kasr Al-Ainy Hospital, Cairo University, in the period April 2017 to April 2019. The study was approved by the Medical Research ethics committee and the Otolaryngology department council of the Faculty of Medicine, Cairo University. Informed consent was signed by all subjects for participation in the study.

The exclusion criteria were: conductive hearing loss; unilateral hearing loss; neurological disorders; retrocochlear hearing loss; central auditory processing disorders; any speech or language disorders; cognitive disorders; and infants and children.

The subjects in the study were chosen to have flat audiograms. This made it easy to divide the cases into subgroups with different degrees of hearing level, and to compare the accuracy of the test across frequencies with similar thresholds. Subjects were grouped into 6 groups according to PTA hearing threshold level (HTL) averages of 500, 1000, and 2000 Hz [14] (plus 4000 Hz to include the Arabic language high frequency components in speech, to match the tested Egyptian patients). Thus, Group 1: 40 normal hearing ears with PTA average up to 25 dBHL; Group 2: 30 mild SNHL ears with PTA average of 26–40 dBHL; Group 3:

30 moderate SNHL ears with PTA average of 41–55 dBHL; Group 4: 30 moderately severe SNHL ears with PTA average of 56–70 dBHL; Group 5: 26 severe SNHL ears with PTA average of 71–90 dBHL; and Group 6: 24 profound SNHL ears with PTA average above 91 dBHL.

All subjects were submitted to the following tests.

Detailed history taking, including personal, present, past, and family history.

Otologic examination, including otoscopy and tuning fork tests. A) Audiometric assessment in a sound-treated room (Amplisilence model E) using a pure tone audiometer (Itera II, Madsen Otometrics) calibrated according to ISO standards. This included pure tone audiometry (PTA) – air conduction 250–8000 Hz and bone conduction 500–4000 Hz. B) Speech audiometry including speech reception threshold (SRT) using Arabic spondaic words [15], and Word discrimination score using Arabic phonetically balanced (PB) words [16].

Immittancemetry using a Madsen Zodiac 901 middle ear analyzer (GN Otometrics, Denmark) calibrated to ISO standards. Acoustic reflexes were tested at frequencies of 500–4000 Hz. This included: A) Single frequency tympanometry with a 226 Hz probe tone; all subjects had bilateral type A tympanograms reflecting normal middle ear function; B) Acoustic reflex thresholds using pure tones at frequencies of 500, 1000, 2000, and 4000 Hz, both ipsilaterally and contralaterally.

Narrow band CE-Chirp ASSR using auditory evoked potentials: two-channel Eclipse EP 25 device (Interacoustics, Assens, Denmark).

The ASSR signal was recorded with the non-inverting electrode placed on the high forehead, the inverting electrode on each mastoid, and the ground electrode on the low forehead. Electrode impedance was maintained below 3 k Ω during testing. The EEG was continuously monitored to ensure the subject was relaxed (by online display of each channel simultaneously). During a recording session, the actual rejection level was modified by manually increasing or decreasing the rejection limits as needed from within the recording screen. For optimum recordings, the EEG level was low enough that a 20 μ V rejection threshold setting could be applied while ensuring that brief periods of increased EEG level would be rejected. However, for non-optimum recording situations, a setting of 40 μ V was needed during data acquisition. Stimuli were narrow-band CE-chirp signals delivered to each ear ipsilaterally by an insert earphone (EAR3A) at a rate of 40 Hz, with a bandwidth of 1 ± 0.5 octave. Stimuli were 1-octave-wide chirps with center frequencies of 0.5, 1, 2, and 4 kHz. An algorithm combining phase and response magnitude was used to automatically detect the minimum level of response. The ASSR measurement started at 60 dB nHL for normal hearing subjects and slight and mild SNHL subjects, and started at 100 dB nHL for testing more severe degrees of SNHL; intensity levels were manipulated to determine ASSR threshold at each carrier frequency. Following a clear response, the stimulus intensity was decreased in 10 dB steps. If there was no response the stimulus intensity was

increased in 5 dB steps. The algorithm stopped the recording in either channel if the critical test value reached a level of significance, leaving the recording to continue in the remaining channel. The algorithm also stopped the recording if no significant response was found after 6 minutes, leading to a 'no-response' decision. Stimuli were presented using the multiple auditory steady state response technique. Simultaneous searching for thresholds was possible because each frequency was controlled independently. Near threshold, each frequency was tested separately to ensure correct thresholds. Green colour: a response was detected with a confidence level of 95% or higher based on statistical analysis of the EEG. ASSR response detection algorithms rely on the SNR of the response to determine if a true neural response has occurred. Red colour: no significant response is present based on statistical measures. The recording session was finished when at least one 'response-present' and one 'no-response' condition had been reached for all test frequencies at both ears with single frequency testing. ASSR thresholds were defined as the lowest intensity where a response was present, and a no-response was obtained at 5 dB lower. Converting ASSR thresholds to estimated audiograms (in dB_{HL}) was performed by selecting the available pre-programmed correction factor table (for awake adults, 40 Hz insert phone, as recommended by the Interacoustics instrument and included in the v1.2.3 software – the pre-programmed correction factors varied from 0 to 20 dB according to frequency and intensity).

Hearing threshold estimation using N1P2 CAEP for recording the N1P2 response for tone burst frequencies of 500, 1000, 2000, and 4000 Hz from two channels of Neuro-Audio (Neurosoft Ltd, Russia). After cleaning the skin, surface electrodes were positioned with the non-inverting electrode placed on Cz, inverting electrode on the right or left mastoid (M1 and M2), with ground electrode on the low forehead (Fpz). Electrode impedance was maintained below 5 k Ω during testing. All subjects were asked to remain quietly seated but awake and read a magazine. They were informed that the test was automatic. Tone burst stimuli had 10 ms linear rise/fall times at 1 kHz and above (20 ms at lower frequencies) and 60 ms plateau time. Stimuli were delivered to each ear ipsilaterally by an insert earphone EAR-3A-10 Ω , presented at 25 dBSL (25 dB above the threshold established from the subject's PTA) at 1.1 pulse/sec. A total of 250 sweeps were collected for each trace. (The necessary number of stimulus repetitions is ≤ 200 , but varies depending on the size of the response and background noise; confident detection may require as few as 20 to 50 signals at high intensity levels for a very quiet and normal hearing patient [3], or as many as 500 to 1000 [17].)

N1P2 morphology was evaluated and waveforms were judged based on visual inspection of the recordings. Descending intensities in steps of 10 dB and ascending intensities of 5 dB were used up to the minimum threshold of automatic response detection. For the N1P2 response, N1 was defined as the first robust negativity in the waveform in the latency range 100–160 ms, and P2 was defined as the positive waveform following N1 in the latency range 160–270 ms.

The time taken to perform the N1P2 test was about 1 to 1.5 hours, while ASSR took about 1 hour. The patients were tested in two sessions. There was no difference in time between males and females. The long duration of the tests is the main limitation of this study.

Statistical methods

Data were coded and entered using SPSS (Statistical Package for the Social Sciences) v.25. Data was summarized using mean, standard deviation, median, minimum and maximum for quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Data were checked for normality using a Shapiro–Wilk test and normality plots, and were found to be not normally distributed. Comparisons between quantitative variables were done using the non-parametric Kruskal–Wallis and Mann–Whitney tests. For comparison of paired measurements within each patient, the non-parametric Wilcoxon signed rank test was used [18]. For comparing categorical data, a Chi square (χ^2) test was performed. An Exact test was used instead when the expected frequency was less than 5 [19]. Correlations between quantitative variables were done using a Spearman correlation coefficient when the variables were not normally distributed [20]. *P*-values less than 0.05 were considered statistically significant.

Results

This study was a diagnostic nonrandomized prospective type study using a sample size of 180 ears of 90 patients; 40 were normal healthy ears and 140 had SNHL. This number of cases was adopted after using the Medcalc 19 program by setting alpha error significance of 0.05%, 95% confidence level, and 80% power. The sample size for this study was calculated from the monthly prevalence of SNHL in our outpatient clinic of nearly 78%, according to our data. The relevant equations are set out in Machin D et al. [21]. The sample size is suitable for testing Pearson correlations according to the equations of Hulley et al. [22] with an expected correlation coefficient $r \geq 0.3$ at a minimum sample size of 85.

From our sample size of 180 ears there were 30 ears with mild hearing loss, 30 with moderate hearing loss, 30 with moderately severe hearing loss, 26 with severe hearing loss, and 24 with profound hearing loss. The study sample included 43 females (48%) and 47 males (52%), with a mean age of 39.5 years $\pm$ 10.3 ranging from 20 to 50 years.

All subjects underwent an N1P2 CAEP test using tone burst stimuli and an ASSR test using a narrow-band CE-Chirp stimulus. Figures 1 (a,b,c,d) and 2 (a,b,c,d) show examples of N1P2 traces for electrophysiologic threshold detection in this study at 500, 1000, 2000, and 4000 Hz in the right and left ears of one of the normal hearing subjects (male, 22 years), while Figures 1e and 2e show the estimated ASSR audiogram test result of the same ears.

Figures 3 a,b,c,d and 4 a,b,c,d show examples of N1P2 traces for electrophysiologic threshold detection at 500, 1000, 2000, and 4000 Hz in one of the moderately severe SNHL subjects in this study (female, 45 years) in the right and

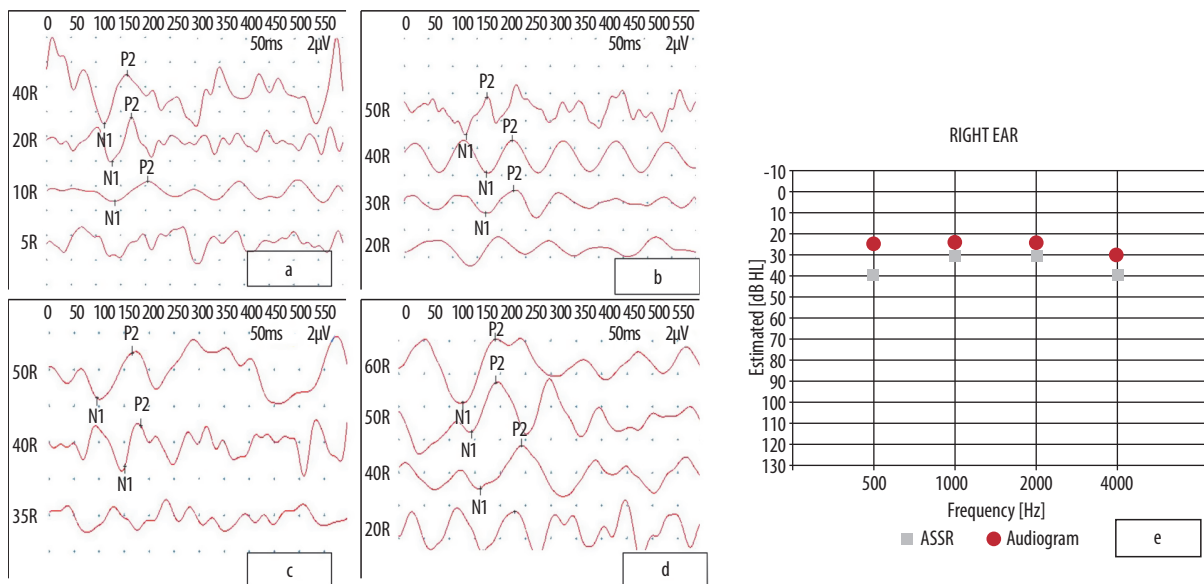


Figure 1. (a,b,c,d) Examples of N1P2 traces in the right ear (at 500, 1000, 2000, and 4000 Hz respectively) in a subject from the normal hearing group (male, 22 years). (e) Estimated hearing levels in dB HL (at 500, 1000, 2000, and 4000 Hz) from ASSR evoked potentials in the same ear (red circles). The grey squares are the uncorrected electrophysiologic ASSR thresholds

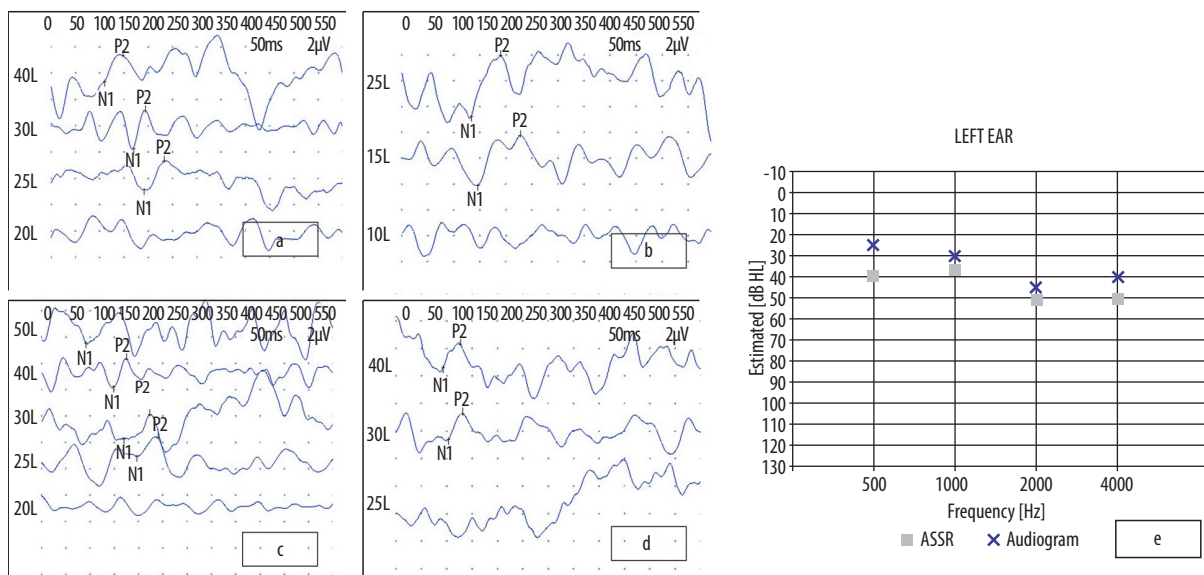


Figure 2. (a,b,c,d) As for Figure 1 except for the left ear (blue crosses)

left ears, and Figure 5 shows the estimated ASSR audiogram test result for the same ears.

Results of the behavioral PTA threshold, the electrophysiologic threshold of N1P2, and the estimated audiogram based on ASSR (after application of the available pre-programmed correction factor table selected in the instrument) at different frequencies using air conduction in the normal hearing subgroup in the right and left ears are shown in Figures 6–11. The figures show results for the normal hearing subgroup, the mild, moderate, moderately severe, severe, and profound hearing loss subgroups respectively.

Table 1 shows a comparison between the behavioral PTA threshold minus the electrophysiologic N1P2 threshold and the behavioral PTA threshold minus the estimated ASSR audiogram threshold in both ears using air conduction in the normal hearing subgroup. There was a statistically significant difference in comparison between the behavioral PTA threshold minus the electrophysiologic N1P2 threshold and the behavioral PTA threshold minus the estimated ASSR audiogram threshold at 1000 Hz in the right ear and 500 Hz in left ear using air conduction in the normal hearing subgroup.

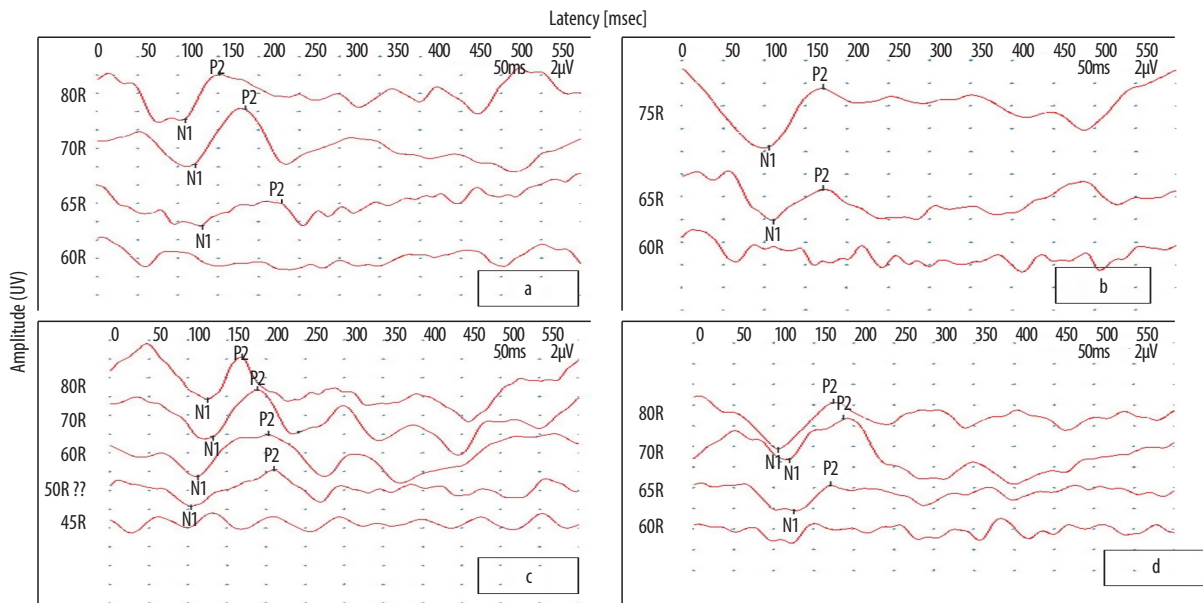


Figure 3. (a,b,c,d) Examples of N1P2 traces in the right ear (at 500, 1000, 2000, and 4000 Hz respectively) in a subject from the moderately severe SNHL group (female, 45 years)

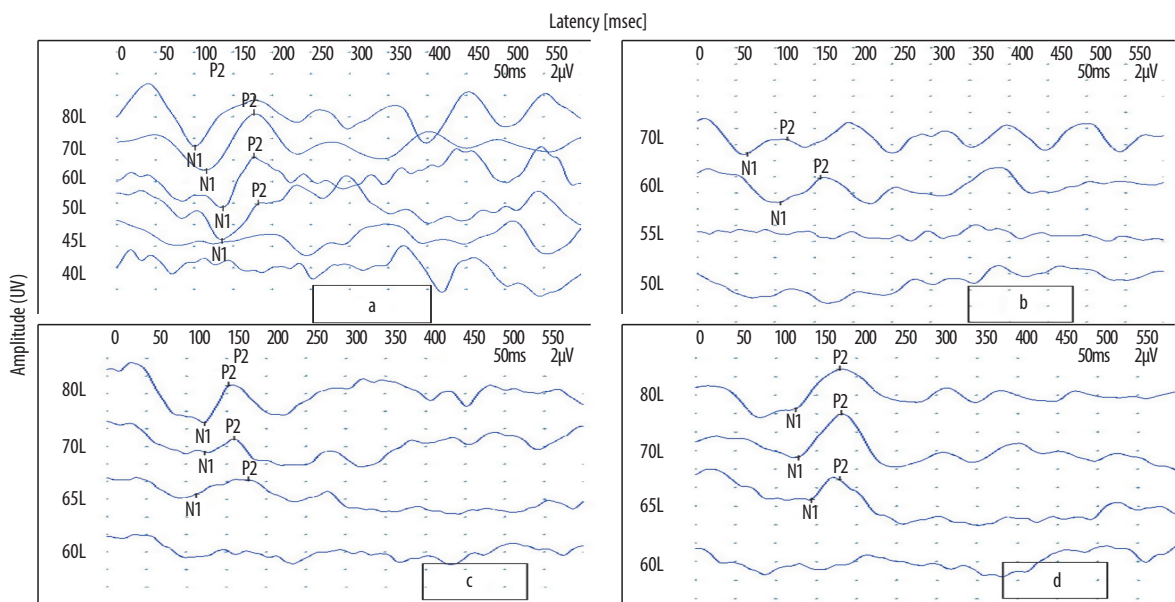


Figure 4. (a,b,c,d) Examples of N1P2 traces in the left ear (at 500, 1000, 2000, and 4000 Hz respectively) in a subject from the moderately severe SNHL group (female, 45 years)

There was no significant difference in comparison among the different frequencies regarding the *behavioral PTA threshold minus the electrophysiologic N1P2 threshold* using air conduction in the normal hearing subgroup ($Z = 1.646, p = 0.649$; $Z = 0.734, p = 0.865$) in the right and left ears respectively.

There were significant differences in comparison among the different frequencies regarding the *behavioral PTA threshold minus the estimated ASSR audiogram threshold* in both ears using air conduction in the normal hearing subgroup ($Z = 29.24, p = 0.001$; $Z = 9.443, p = 0.024$) in the right and left ears respectively. A post hoc test revealed a significant

difference ($p < 0.05$) between 4000 and 2000 Hz, 500 and 2000 Hz, and 1000 and 2000 Hz in the right ear. The *behavioral PTA threshold minus the estimated ASSR audiogram threshold* was significantly smaller at 2000 Hz than at other frequencies, and this was found in all groups. Comparing 4000 and 500 Hz in the left ear, the 4 kHz *behavioral PTA threshold minus the estimated ASSR audiogram threshold* was significantly less than that at 500 Hz.

Table 2 shows a comparison between the *behavioral PTA threshold minus the electrophysiologic N1P2 threshold* and the *behavioral PTA threshold estimated from ASSR levels*

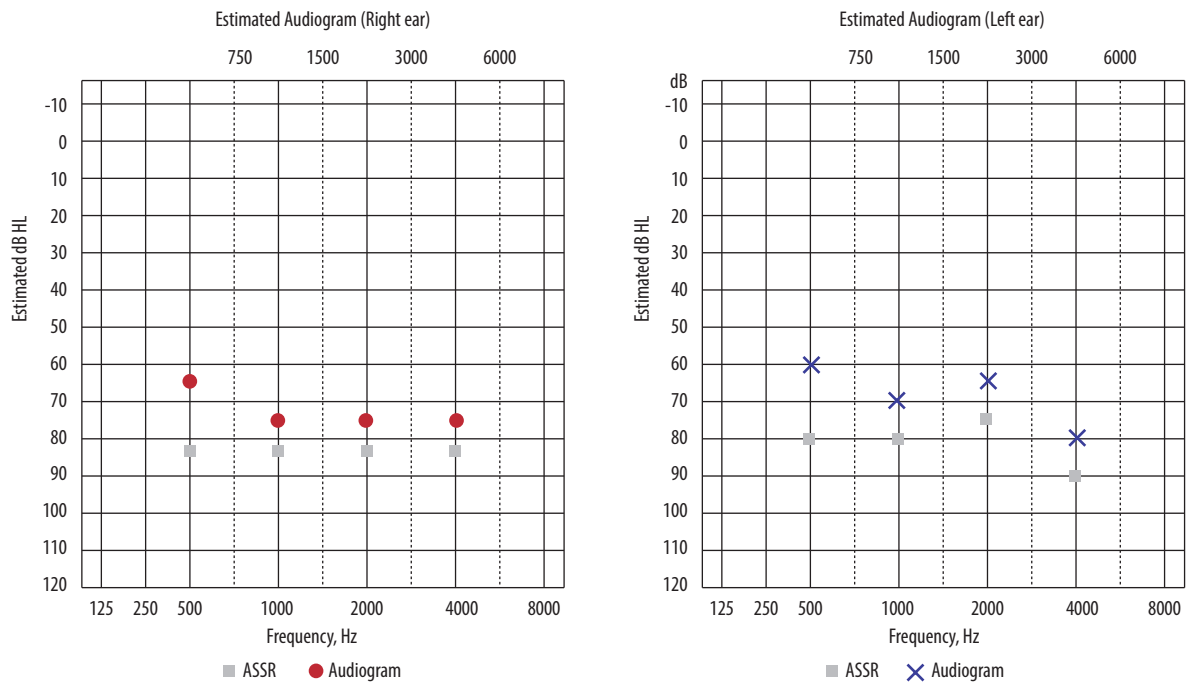


Figure 5. Estimated hearing levels (dBeHL) from ASSR evoked potentials in the right and left ears of a subject from the moderately severe SNHL group. The grey squares represent uncorrected electrophysiologic ASSR thresholds

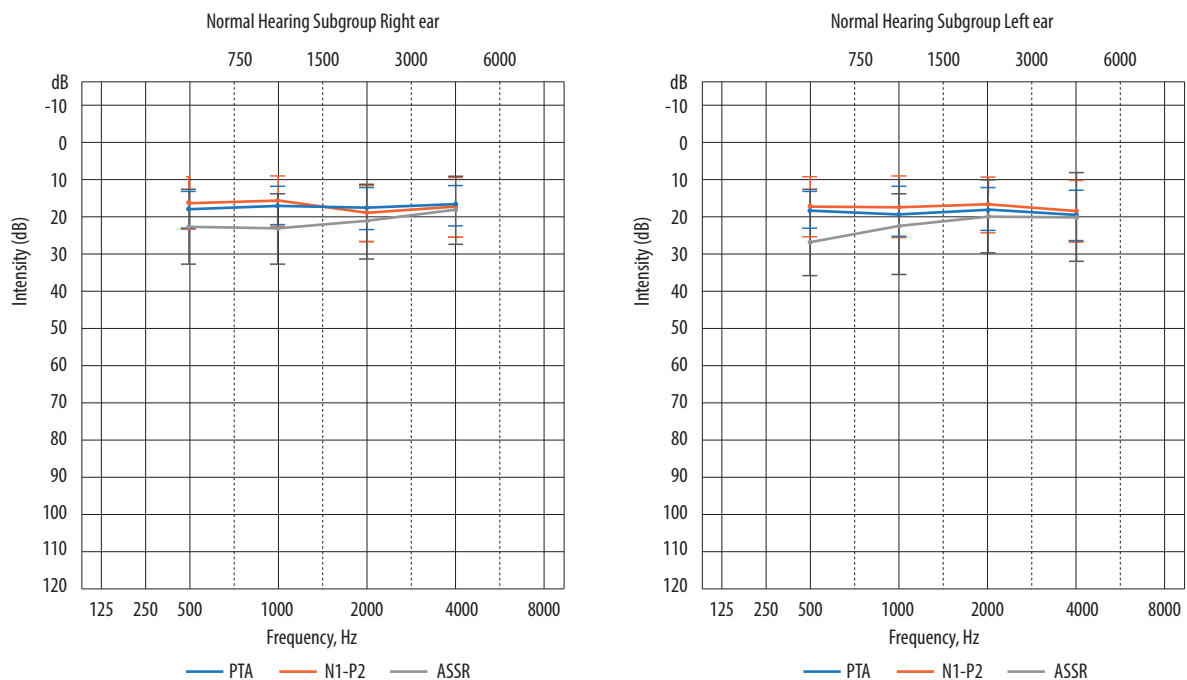


Figure 6. Normal hearing group results for right and left ears. Blue line is the behavioral PTA threshold, orange line is the physiologic threshold of N1P2, and grey line is the estimated audiogram based on the ASSR pre-programmed correction factor table selected by the instrument

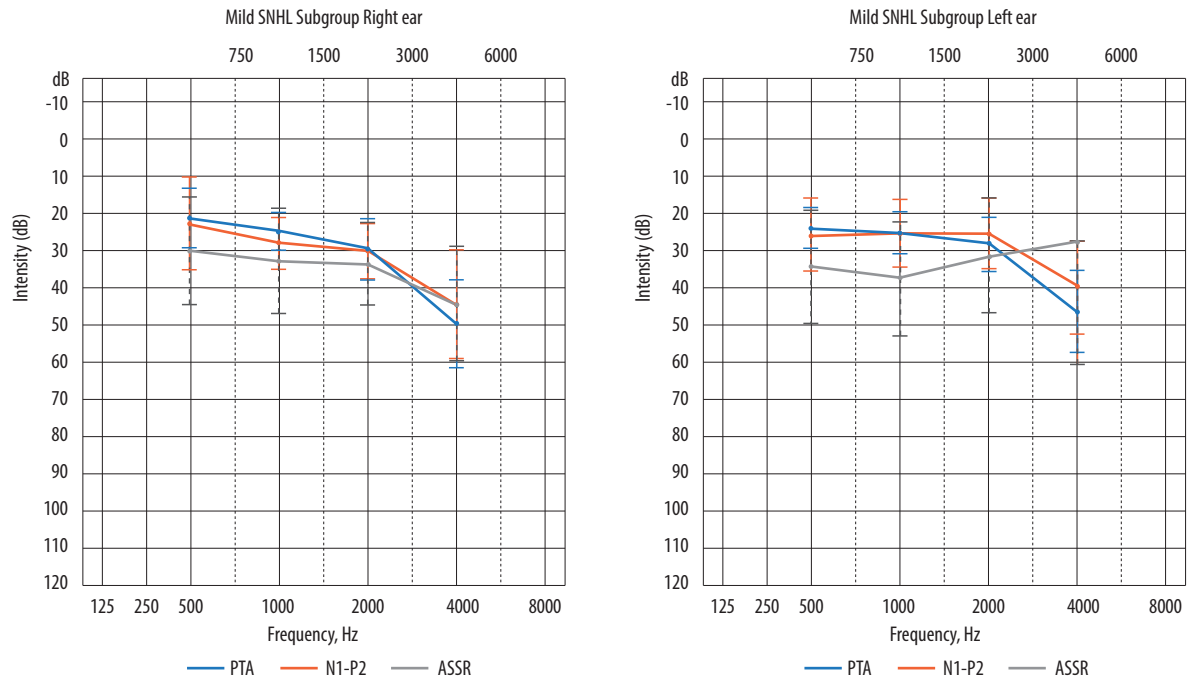


Figure 7. Mild SNHL subgroup results for right and left ears. Key as per Figure 6

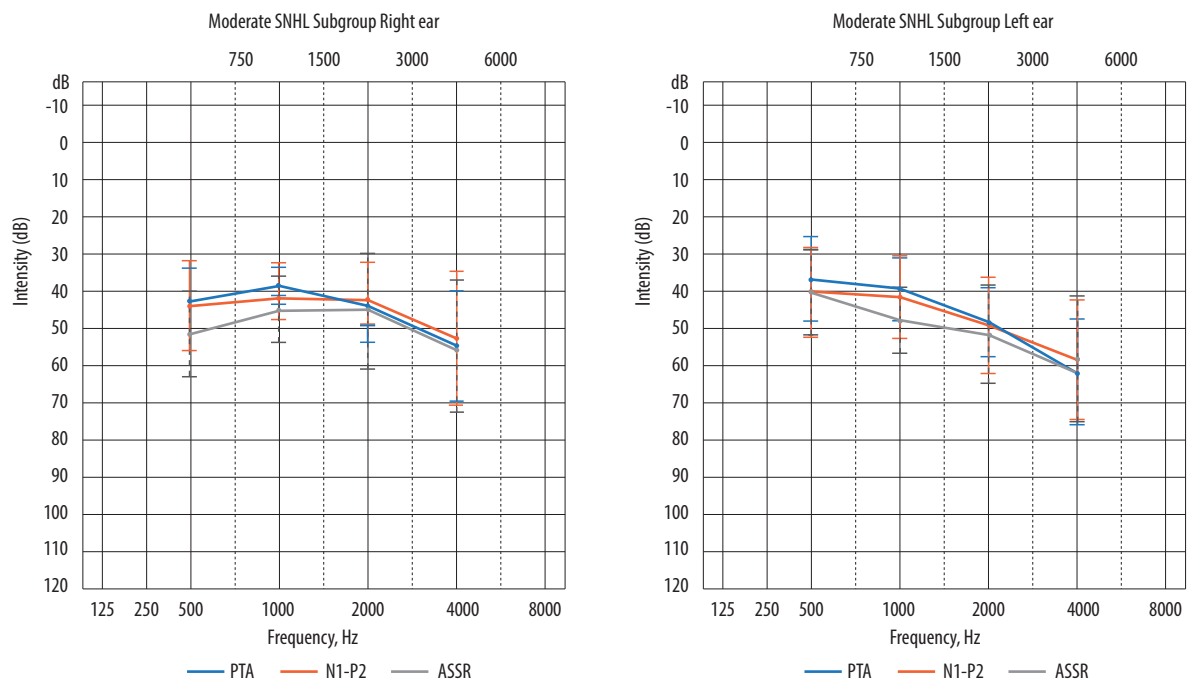


Figure 8. Moderate SNHL subgroup results for right and left ears. Key as per Figure 6

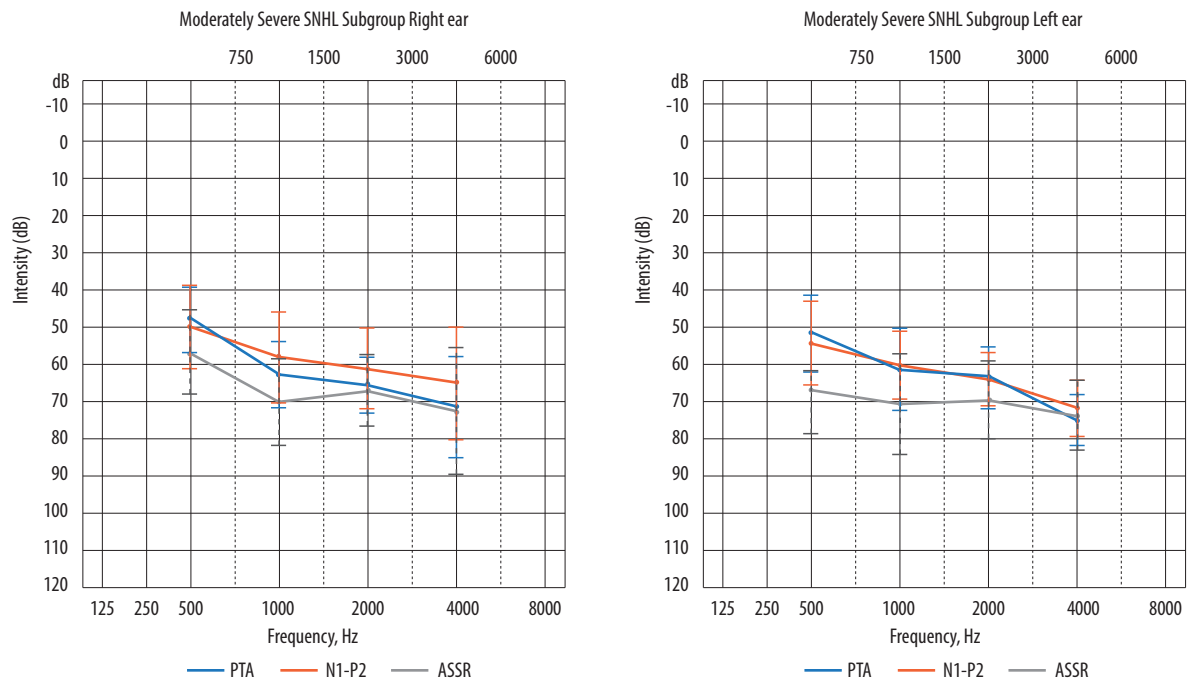


Figure 9. Moderately severe SNHL subgroup results for right and left ears. Key as per Figure 6

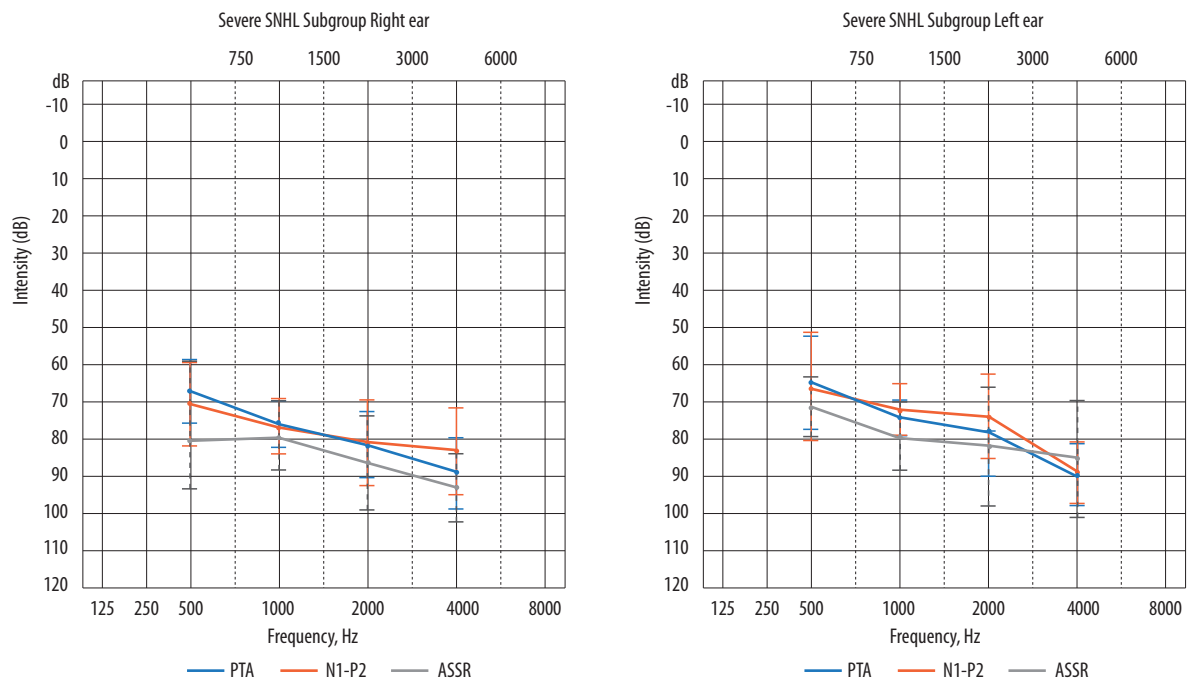


Figure 10. Severe SNHL subgroup results for right and left ears. Key as per Figure 6

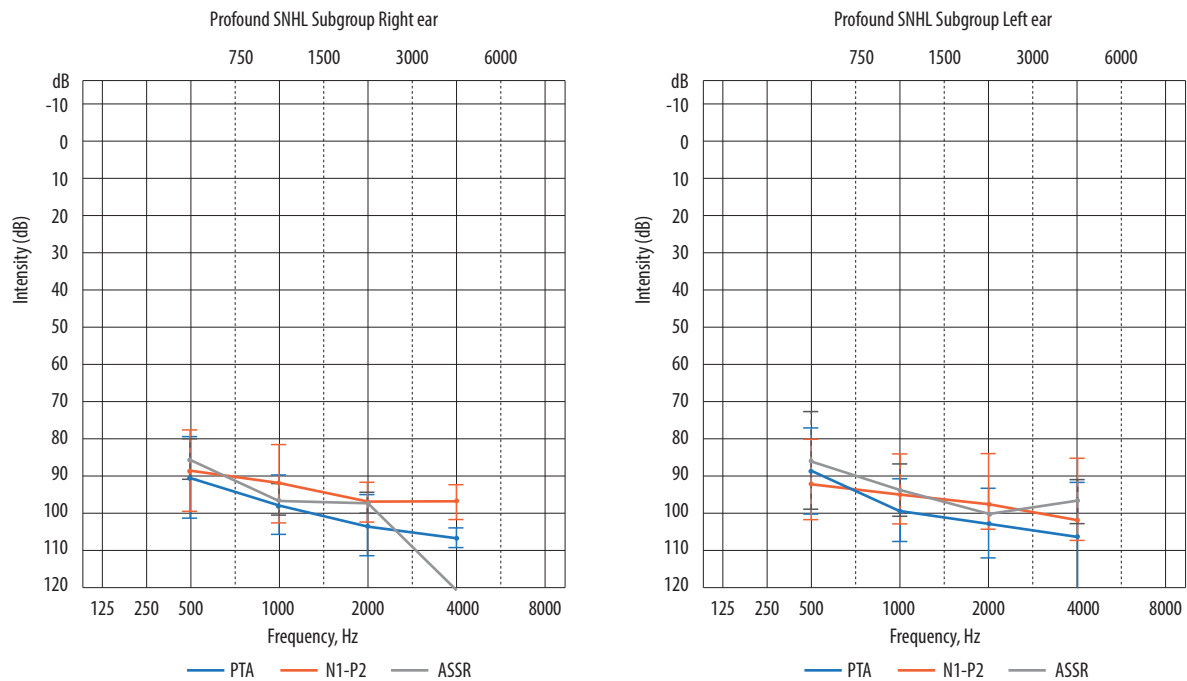


Figure 11. Profound SNHL subgroup results for right and left ears. Key as per Figure 6

Table 1. Comparison of the differences between *the behavioral PTA minus the physiologic N1P2 threshold* and *the behavioral PTA minus the estimated ASSR audiogram threshold* in both ears using air conduction in the normal hearing subgroup

Normal hearing group													
PTA – N1P2 †												Z* value	p value
PT – ASSR ‡												Z* value	p value
Freq.													
(Hz)													
MeanSDMedianMin.Max.													
MeanSDMedianMin.Max.													
right (n = 20)	500	–1.75	8.93	–5	–15	15	4.75	11.29	7.5	–15	25	–1.909	0.056
	1000	–1.25	9.01	0	–15	20	6.25	10.11	5	–10	25	–3.447	0.001
	2000	1.25	9.44	0	–15	25	3.5	10.77	0	–10	20	–0.956	0.339
	4000	1	6.61	0	–10	15	1.25	7.41	0	–10	15	–0.245	0.807
left (n = 20)	500	–1	9.4	0	–15	15	9	10.21	10	–15	25	–2.829	0.005
	1000	–2.25	10.94	–5	–15	20	3	13.8	2.5	–20	30	–0.955	0.34
	2000	–1.25	9.3	–5	–15	20	2.5	11.87	0	–15	25	–0.945	0.344
	4000	–1.25	5.1	–2.5	–5	15	–0.75	10.29	–5	–20	25	–0.035	0.972

* Z of Wilcoxon signed rank test

† behavioral PTA minus physiologic N1P2 threshold

‡ behavioral PTA minus estimated ASSR audiogram threshold

at different frequencies using air conduction in the mild SNHL subgroup.

There was a statistically significant difference in comparison between behavioral PTA threshold, the electrophysiologic threshold of N1P2 difference, and the *behavioral PTA threshold*

minus the estimated ASSR audiogram threshold at 1000 Hz in the left ear using air conduction in the mild SNHL subgroup.

There were significant differences in comparison among the different frequencies regarding the behavioral PTA threshold, the electrophysiologic threshold of

Table 2. Comparison between the *behavioral PTA minus physiologic N1P2 threshold* and *behavioral PTA minus estimated ASSR audiogram threshold* in both ears using air conduction in the mild SNHL subgroup

Mild hearing loss group													
	PTA – N1P2 †						PTA – ASSR ‡					Z* value	P value
	Freq.	Mean	SD	Median	Min.	Max.	Mean	SD	Median	Min.	Max.		
	(Hz)												
Right (n = 14)	500	1.43	8.42	2.5	–15	15	8.93	15.09	10	–15	35	–1.464	0.143
	1000	3.21	5.41	0	–5	15	8.21	12.95	5	–10	40	–0.988	0.323
	2000	0.36	6.64	0	–10	15	3.93	9.64	0	–5	25	–1.030	0.303
	4000	–5.36	8.87	–5	–20	10	–5.36	12.78	–7.5	–20	15	–0.154	0.877
Left (n = 16)	500	1.88	8.14	0	–15	15	10.63	15.9	7.5	–10	40	–1.642	0.101
	1000	0.94	7.35	0	–15	15	12.5	16.93	5	–10	55	–2.300	0.021
	2000	–2.81	10.8	–2.5	–25	15	3.44	13.13	0	–15	35	–1.552	0.121
	4000	–6.25	6.95	–5	–20	0	–2.5	14.72	–2.5	–25	25	–0.543	0.587

* Z of Wilcoxon signed rank test

† behavioral PTA minus physiologic N1P2 threshold

‡ behavioral PTA minus estimated ASSR audiogram threshold

N1P2 difference using air conduction in the mild SNHL subgroup ($Z = 7.896$, $p = 0.048$; $Z = 8.959$, $p = 0.030$) in the right and left ears respectively. A post hoc test revealed a significant difference ($p < 0.05$) between 4000 and 1000 Hz in the right ear, between 4000 and 1000 Hz, and 4000 and 500 Hz in the left ear. At 4000 Hz, the behavioral PTA threshold and the electrophysiologic threshold of N1P2 difference was significantly greater than the 1000 Hz behavioral PTA threshold, the electrophysiologic threshold of N1P2 difference in both ears, and 500 Hz behavioral PTA threshold, the electrophysiologic threshold of N1P2 difference in the left ear.

There were significant differences in comparison among the different frequencies regarding the behavioral PTA threshold minus the estimated ASSR audiogram threshold in both ears using air conduction in the mild SNHL subgroup ($Z = 28.688$, $p < 0.001$; $Z = 8.147$, $p = 0.043$) in the right and left ears respectively. A post hoc test revealed that there was a significant difference ($p < 0.05$) between 4000 and 2000 Hz, 1000 and 2000 Hz, and 500 and 2000 Hz in the right ear. The *behavioral PTA threshold minus the estimated ASSR audiogram threshold* was significantly smaller at 2000 Hz than it was at other frequencies, and this was found in all groups. Comparing 4000 and 500 Hz, and 4000 and 1000 Hz in the left ear, the *behavioral PTA threshold minus the estimated ASSR audiogram threshold* difference was significantly smaller at 4000 Hz than it was at other frequencies.

Table 3 shows a comparison between the *behavioral PTA threshold minus the electrophysiologic N1P2 threshold* and *behavioral PTA threshold minus the estimated ASSR audiogram threshold* in both ears using air conduction in the mild SNHL subgroup.

There was statistically significant difference in comparison between the *behavioral PTA threshold minus the electrophysiologic N1P2 threshold* and the *behavioral PTA threshold minus the estimated ASSR audiogram threshold* at 500 Hz in the right ear using air conduction in the moderate SNHL subgroup.

There was no significant differences in comparison among the different frequencies regarding the PTA – N1P2 difference in the right ear using air conduction in the moderate SNHL subgroup ($Z = 5.924$, $p = 0.115$); but in the left ears the differences were statistically significant ($Z = 8.008$, $p = 0.046$). A post hoc test revealed that there was a significant difference ($p < 0.05$) between 4000 and 500 Hz in the left ear (for 4000 Hz the difference PTA – N1P2 was significantly less than the difference PTA – N1P2 for 500 Hz).

There were significant differences in comparison among the different frequencies regarding the *behavioral PTA threshold minus the estimated ASSR audiogram threshold* in both ears using air conduction in the moderate SNHL subgroup ($Z = 33.592$, $p < 0.001$; $Z = 8.733$, $p = 0.033$) in the right and left ears respectively. A post hoc test revealed a significant difference ($p < 0.05$) between 4000 and 2000 Hz, 1000 and 2000 Hz, and 500 and 2000 Hz in the right ear. The *behavioral PTA threshold minus the estimated ASSR audiogram threshold* was significantly smaller at 2000 Hz than it was at other frequencies. Comparing 4000 and 1000 Hz in the left ear, at 4000 Hz the difference of *behavioral PTA threshold minus the estimated ASSR audiogram threshold* was significantly less than the 1000 Hz difference of *behavioral PTA threshold minus the estimated ASSR audiogram threshold*.

Table 4 shows a comparison between the *behavioral PTA threshold minus the electrophysiologic N1P2 threshold* and the *behavioral PTA threshold minus the estimated ASSR*

Table 3. Comparison between the *behavioral PTA minus physiologic N1P2 threshold* and the *behavioral PTA minus estimated ASSR audiogram threshold* in both ears using air conduction in the moderate SNHL subgroup

Moderate hearing loss group													
	PTA – N1P2 †						PTA – ASSR ‡					Z* value	P value
	Freq. (Hz)	Mean	SD	Median	Min.	Max.	Mean	SD	Median	Min.	Max.		
Right (n = 14)	500	1.07	6.56	0	–5	10	8.93	8.81	10	–10	25	–2.516	0.012
	1000	3.21	4.64	5	–5	15	6.43	7.95	5	–5	20	–1.565	0.118
	2000	–1.79	8.46	–2.5	–15	15	1.43	9.69	0	–15	20	–0.952	0.341
	4000	–2.14	8.02	–5	–15	15	0	12.56	0	–20	25	–0.773	0.439
Left (n = 16)	500	3.75	5.32	2.5	0	20	3.75	9.4	7.5	–10	15	–0.319	0.750
	1000	2.33	6.51	0	–5	15	7.81	8.94	5	–5	25	–1.593	0.111
	2000	1.87	6.55	0	–10	20	2.5	10.33	5	–20	20	–0.202	0.840
	4000	–3.44	10.76	–5	–20	20	–3.75	10.57	–2.5	–20	15	–0.259	0.796

* Z of Wilcoxon signed rank test

† behavioral PTA minus physiologic N1P2 threshold

‡ behavioral PTA minus estimated ASSR audiogram threshold

Table 4. Comparison between the *behavioral PTA minus physiologic N1P2 threshold* and *behavioral PTA minus estimated ASSR audiogram threshold* in both ears using air conduction in the moderately severe SNHL subgroup

Moderately severe hearing loss group													
	PTA – N1P2 †						PTA – ASSR ‡					Z* value	P value
	Freq. (Hz)	Mean	SD	Median	Min.	Max.	Mean	SD	Median	Min.	Max.		
Right (n = 16)	500	1.88	5.12	0	–10	10	8.75	10.57	7.5	–5	25	–2.121	0.034
	1000	–4.69	6.7	–2.5	–20	5	7.5	11.25	7.5	–15	25	–2.909	0.004
	2000	–4.38	9.11	–5	–25	10	1.56	9.44	2.5	–15	20	–1.677	0.094
	4000	–6.56	8.7	–5	–20	15	0.94	10.36	0	–20	25	–2.037	0.042
Left (n = 14)	500	3.21	7.5	5	–10	15	15	10.74	15	0	30	–2.722	0.006
	1000	–1.07	9.03	0	–20	10	10	10.38	10	–15	20	–2.535	0.011
	2000	0.36	6.03	0	–10	10	6.07	11.12	10	–15	25	–1.501	0.133
	4000	–2.5	5.46	–2.5	–10	5	–0.77	9.76	0	–20	10	–0.405	0.685

* Z of Wilcoxon signed rank test

† behavioral PTA minus physiologic N1P2 threshold

‡ behavioral PTA minus estimated ASSR audiogram threshold

audiogram threshold in both ears using air conduction in the moderately severe SNHL subgroup. There was a statistically significant difference in comparison between the *behavioral PTA threshold minus the electrophysiologic N1P2 threshold* and the *behavioral PTA threshold minus the estimated ASSR audiogram threshold* at 500, 1000, and 4000 Hz in the right ear and for 500 and 1000 Hz in the left ear using air conduction in the moderately severe SNHL subgroup.

There was no significant difference in comparison among the different frequencies regarding the *behavioral PTA threshold minus the electrophysiologic N1P2 threshold* in the left ear using air conduction in the moderately severe SNHL subgroup ($Z = 4.693$, $p = 0.200$); but in the right ears the differences were statistically significant ($Z = 12.592$, $p = 0.006$). A post hoc test revealed a significant

difference ($p < 0.05$) between 4000 and 500 Hz in the right ear. The behavioral PTA threshold minus the electrophysiologic N1P2 threshold was significantly smaller at 4000 Hz than it was at 500 Hz).

There were significant differences in comparisons among the different frequencies regarding the PTA – ASSR difference in both ears using air conduction in the moderately severe SNHL subgroup ($Z = 38.135$, $p < 0.001$; $Z = 12.98$, $p = 0.005$) in the right and left ears respectively. A post hoc test revealed a significant difference ($p < 0.05$) between 4000 and 2000 Hz, 500 and 2000 Hz, and 1000 and 2000 Hz in the right ear. The ASSR – PTA threshold difference was significantly smaller at 2000 Hz than it was at other frequencies. Comparing 4000 and 500 Hz in the left ear, the 4000 Hz PTA – ASSR difference was significantly less than the 500 Hz PTA – ASSR difference.

Table 5 shows a comparison between the *behavioral PTA threshold minus the electrophysiologic N1P2 threshold* and *PTA – ASSR* in both ears using air conduction in the severe SNHL subgroup. There was a statistically significant difference in comparison between *behavioral PTA threshold minus the electrophysiologic N1P2 threshold* and *PTA – ASSR threshold difference* at 500 and 4000 Hz in the right ear and 1000 and 2000 Hz in the left ear using air conduction in the severe SNHL subgroup.

There was no significant difference in comparison among the different frequencies regarding the *PTA – N1P2 difference* in both ears using air conduction in the severe SNHL subgroup ($Z = 6.016$, $p = 0.111$; $Z = 2.560$, $p = 0.465$) in the right and left ears respectively.

There was no significant difference in comparison among the different frequencies regarding the *behavioral PTA threshold minus the estimated ASSR audiogram threshold* in the left ear using air conduction in the severe SNHL subgroup ($Z = 38.854$, $p = 0.544$), but in the right ears the differences were statistically significant ($Z = 2.138$, $p < 0.001$). A post hoc test revealed a significant difference ($p < 0.05$) between 1000 and 2000 Hz, 4000 and 2000 Hz, and 500 and 2000 Hz in the right ear (the *ASSR – PTA threshold difference* was significantly smaller at 2000 Hz than it was at other frequencies).

Table 6 shows a comparison between the *PTA – N1P2 difference* and the *behavioral PTA threshold minus the estimated ASSR audiogram threshold difference* in both ears

Table 5. Comparison between the *behavioral PTA minus physiologic N1P2 threshold* and *behavioral PTA minus estimated ASSR audiogram threshold* in both ears using air conduction in the severe SNHL subgroup

Severe hearing loss group												Z* value	P value
PTA – N1P2 †						PTA – ASSR ‡							
Freq. (Hz)	Mean	SD	Median	Min.	Max.	Mean	SD	Median	Min.	Max.			
Right (n = 14)	500	3.57	7.45	2.5	–5	25	13.21	13.67	10	–10	40	–2.502	0.012
	1000	0.71	5.14	0	–10	10	3.21	8.68	2.5	–10	25	–1.081	0.28
	2000	–0.71	8.29	0	–20	15	5.36	11	5	–15	20	–1.912	0.056
	4000	–5	10.61	–5	–20	15	3.93	8.59	2.5	–10	20	–2.076	0.038
Left (n = 12)	500	–0.42	8.11	0	–15	10	6.67	11.35	5	–20	25	–1.612	0.107
	1000	–2.92	5.42	0	–15	5	5	9.05	2.5	–10	20	–2.532	0.011
	2000	–4.17	5.57	–5	–15	5	4.17	12.22	5	–15	25	–2.572	0.01
	4000	–0.42	4.98	0	–5	10	–1.25	11.88	0	–20	15	–0.322	0.748

* Z of Wilcoxon signed rank test

† behavioral PTA minus physiologic N1P2 threshold

‡ behavioral PTA minus estimated ASSR audiogram threshold

Table 6. Comparison between the *behavioral PTA minus physiologic N1P2 threshold* and *behavioral PTA minus estimated ASSR audiogram threshold* in both ears using air conduction in the profound SNHL subgroup

Profound hearing loss group													
PTA – N1P2 †												Z* value	P value
PTA – ASSR ‡													
	Freq. (Hz)	Mean	SD	Median	Min.	Max.	Mean	SD	Median	Min.	Max.		
Right (n = 12)	500	−1.5	7.84	−2.5	−10	10	2.86	11.85	5	−15	15	−0.707	0.48
	1000	−6.5	4.12	−7.5	−10	0	1.43	7.48	0	−10	10	−1.633	0.102
	2000	−7.86	6.36	−10	−15	0	−2.86	9.06	0	−15	10	−0.447	0.655
	4000	−5.56	7.68	0	−20	0	0	0	0	0	0	0.000	1.000
Left (n = 12)	500	4.44	7.68	0	−5	20	1.25	8.76	0	−10	20	−1.289	0.197
	1000	−1.25	7.44	−5	−10	10	−2.5	11.02	−5	−15	20	−0.730	0.465
	2000	−4	6.15	−2.5	−15	5	−1.88	6.51	0	−10	10	0.000	1.000
	4000	−2.5	8.02	0	−20	5	−2.5	8.8	0	−20	5	0.000	1.000

* Z of Wilcoxon signed rank test

† behavioral PTA minus physiologic N1P2 threshold

‡ behavioral PTA minus estimated ASSR audiogram threshold

using air conduction for the profound SNHL subgroup. There was no statistically significant difference in comparison between the *behavioral PTA threshold minus the electrophysiologic N1P2 threshold* and the *behavioral PTA threshold minus the estimated ASSR audiogram threshold* at different frequencies using air conduction in the profound SNHL subgroup in both ears.

There was no significant difference in comparison among the different frequencies regarding the PTA – N1P2 difference in both ears using air conduction in the profound SNHL subgroup ($Z = 3.49, p = 0.322$); ($Z = 5.727, p = 0.126$) in the right and left ears respectively.

There was a significant difference in comparison among the different frequencies regarding the *behavioral PTA threshold minus the estimated ASSR audiogram threshold* in the right ears using air conduction in the profound SNHL subgroup ($Z = 18.449, p < 0.001$). A post hoc test revealed a significant difference ($p < 0.05$) between 4000 and 2000 Hz, 500 and 2000 Hz, and 1000 and 2000 Hz in the right ear. That is, the *behavioral PTA threshold minus the estimated ASSR audiogram threshold* was significantly larger at 2000 Hz than it was at other frequencies, and this was found in all groups.

There were statistically significant differences among the different groups of the study regarding *behavioral PTA threshold minus the electrophysiologic N1P2 threshold* at 1000 Hz in the right ear using air conduction. With further analysis, a post hoc test showed that statistically significant differences were found between hearing losses for the profound and mild ($p = 0.005$), profound and moderate ($p = 0.002$), moderately severe and mild ($p = 0.038$), moderately severe and moderate groups ($p = 0.016$), with smaller differences for the more severe degrees of hearing loss. But there were no statistically significant differences in *behavioral PTA threshold minus the electrophysiologic N1P2 threshold* in the left ear using air conduction among the different groups.

Also, there were no statistically significant differences in the *behavioral PTA threshold minus the estimated ASSR audiogram threshold* in the right or left ear using air conduction among the different groups.

There was a statistically significant difference in comparison between PTA – N1P2 threshold difference and *behavioral PTA threshold minus the estimated ASSR audiogram threshold* at 500, 1000, 2000, and 4000 Hz in the right ear and 500, 1000, and 2000 Hz in the left ear using air conduction in all subjects.

The mean difference of *behavioral PTA threshold minus electrophysiologic N1P2 threshold* was -0.5 to 1.7 dB compared to -1.9 to 8.2 dB difference between estimated ASSR audiogram thresholds and behavioral thresholds, depending on the test frequency. N1P2 CAEP thresholds were significantly closer to the behavioral hearing thresholds than estimated ASSR audiogram thresholds in all studied subjects at all frequencies using air conduction, where ASSR thresholds exceeded N1P2 CAEP levels by approximately 7 dB at 500 Hz in both ears and were less pronounced at 4000 Hz.

Figures 13–18 show box and whisker charts of the difference *behavioral PTA threshold minus electrophysiologic N1P2 threshold* and the difference *behavioral PTA threshold minus electrophysiologic N1P2 threshold* in the right and left ears of the studied groups.

Table 7 shows that there was a statistically significant correlation between the behavioral PTA threshold at 1, 2, and 4 kHz and the difference *behavioral PTA threshold minus electrophysiologic N1P2 threshold* – i.e. as the PTA threshold decreased at 1, 2, and 4 kHz, the difference was greater. Behavioral PTA thresholds and electrophysiologic N1P2 thresholds were highly correlated, and behavioral PTA thresholds and estimated ASSR audiogram thresholds were highly correlated at all frequencies.

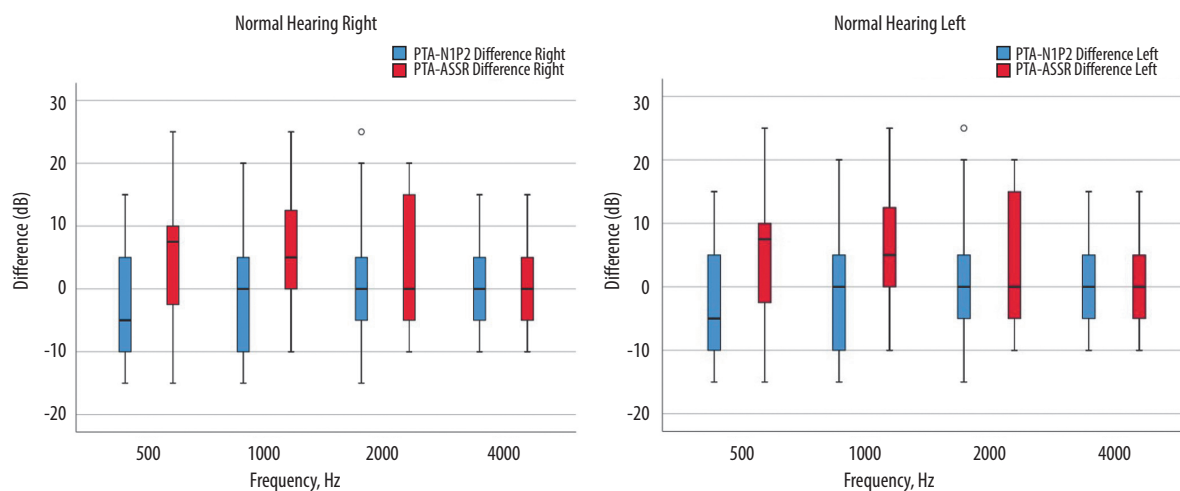


Figure 13. Box and whisker charts of the difference (behavioral PTA threshold minus electrophysiologic N1P2 threshold) for the right and left ears of the normal hearing group

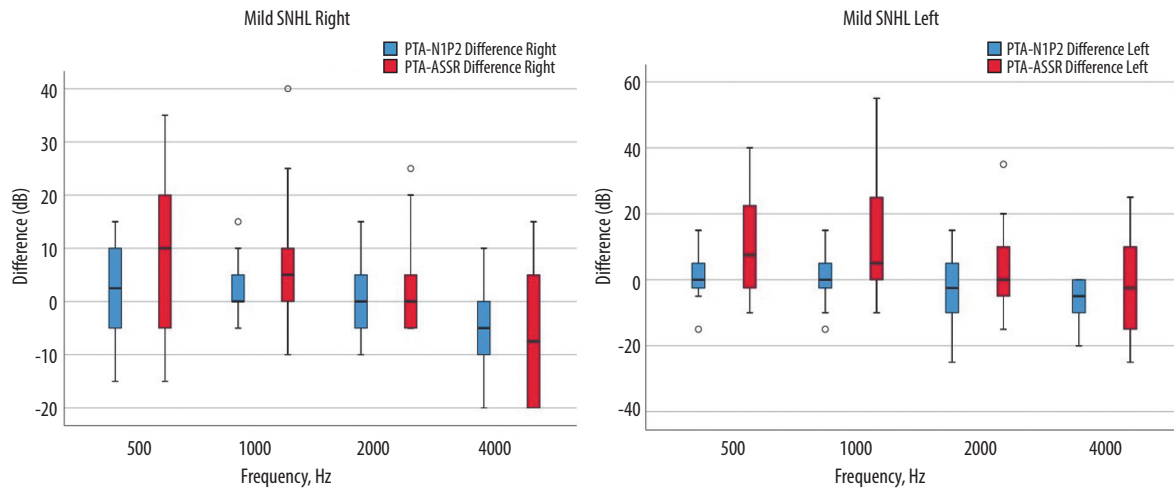


Figure 14. As per Figure 13, but for the mild SNHL group

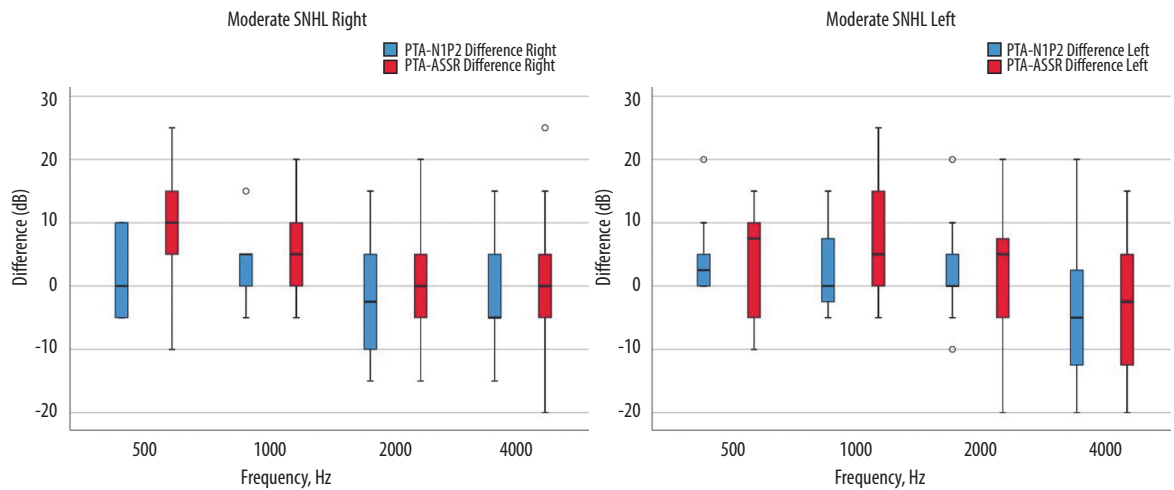


Figure 15. As per Figure 13, but for the moderate SNHL group

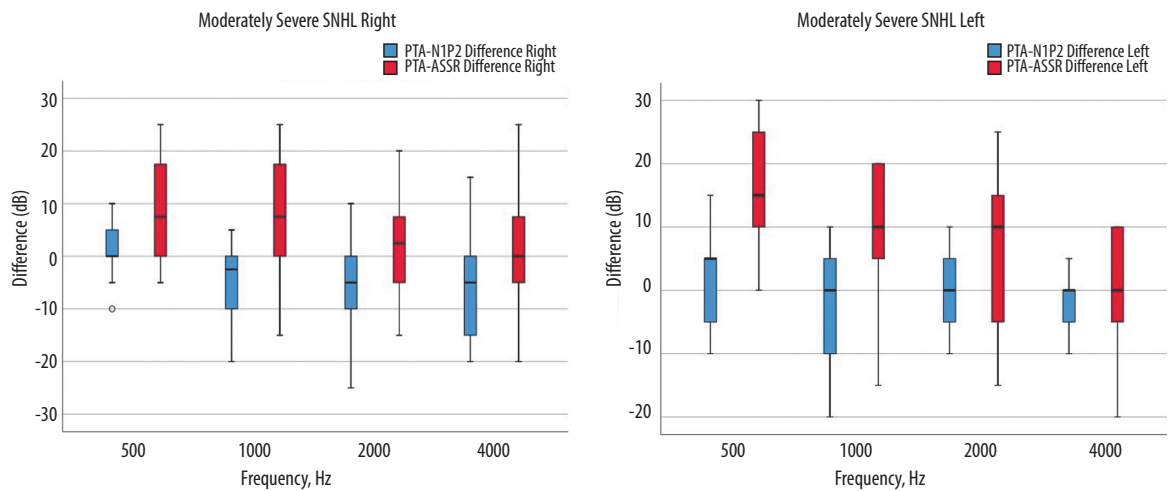


Figure 16. As per Figure 13, but for the moderately severe SNHL group

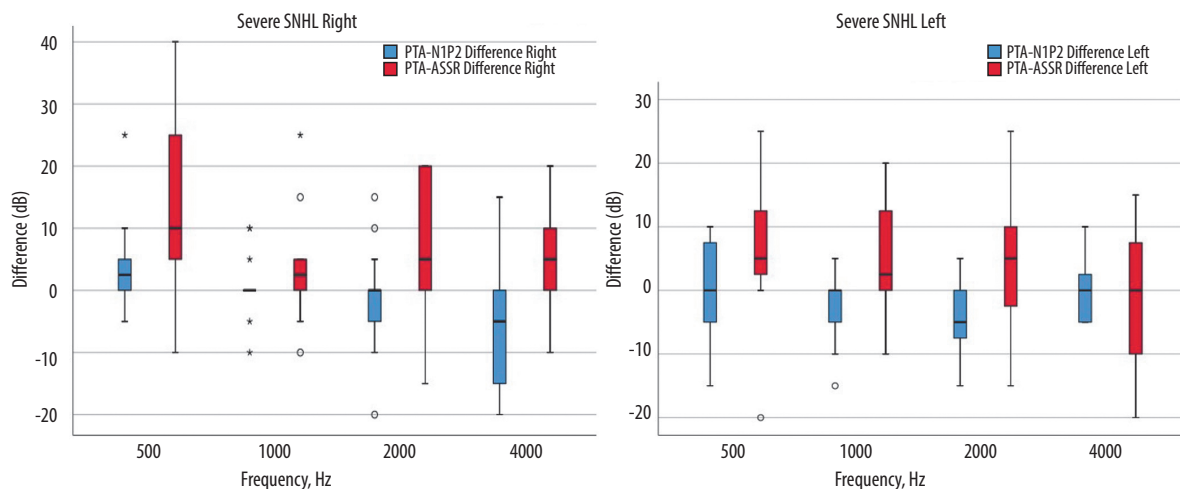


Figure 17. As per Figure 13, but for the severe SNHL group

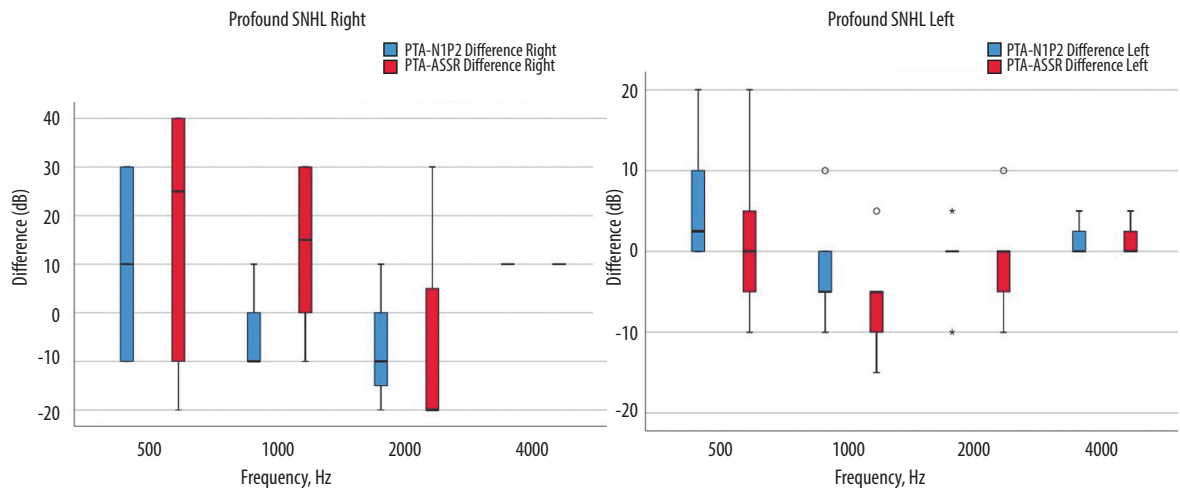


Figure 18. As per Figure 13, but for the profound SNHL group

Table 7. Pearson correlation coefficient (r) between PTA behavioral thresholds against $PTA \text{ minus } N1P2$ and $PTA \text{ minus } ASSR$ and against $N1P2 \text{ threshold}$ and $ASSR \text{ threshold}$ at 4 different frequencies in all the studied subjects

Behavioral threshold	PTA – N1P2		PTA – ASSR	
	r	p	r	p
PTA 500 Hz	0.088	0.309	0.006	0.945
PTA 1000 Hz	–0.243	0.005	0.07	0.425
PTA 2000 Hz	–0.187	0.033	0.033	0.714
PTA 4000 Hz	–0.192	0.032	–0.022	0.814

Behavioral threshold	N1P2 threshold		ASSR threshold	
	r	p	r	p
PTA 500 Hz	0.954	<0.001	0.835	<0.001
PTA 1000 Hz	0.960	<0.001	0.875	<0.001
PTA 2000 Hz	0.941	<0.001	0.891	<0.001
PTA 4000 Hz	0.923	<0.001	0.855	<0.001

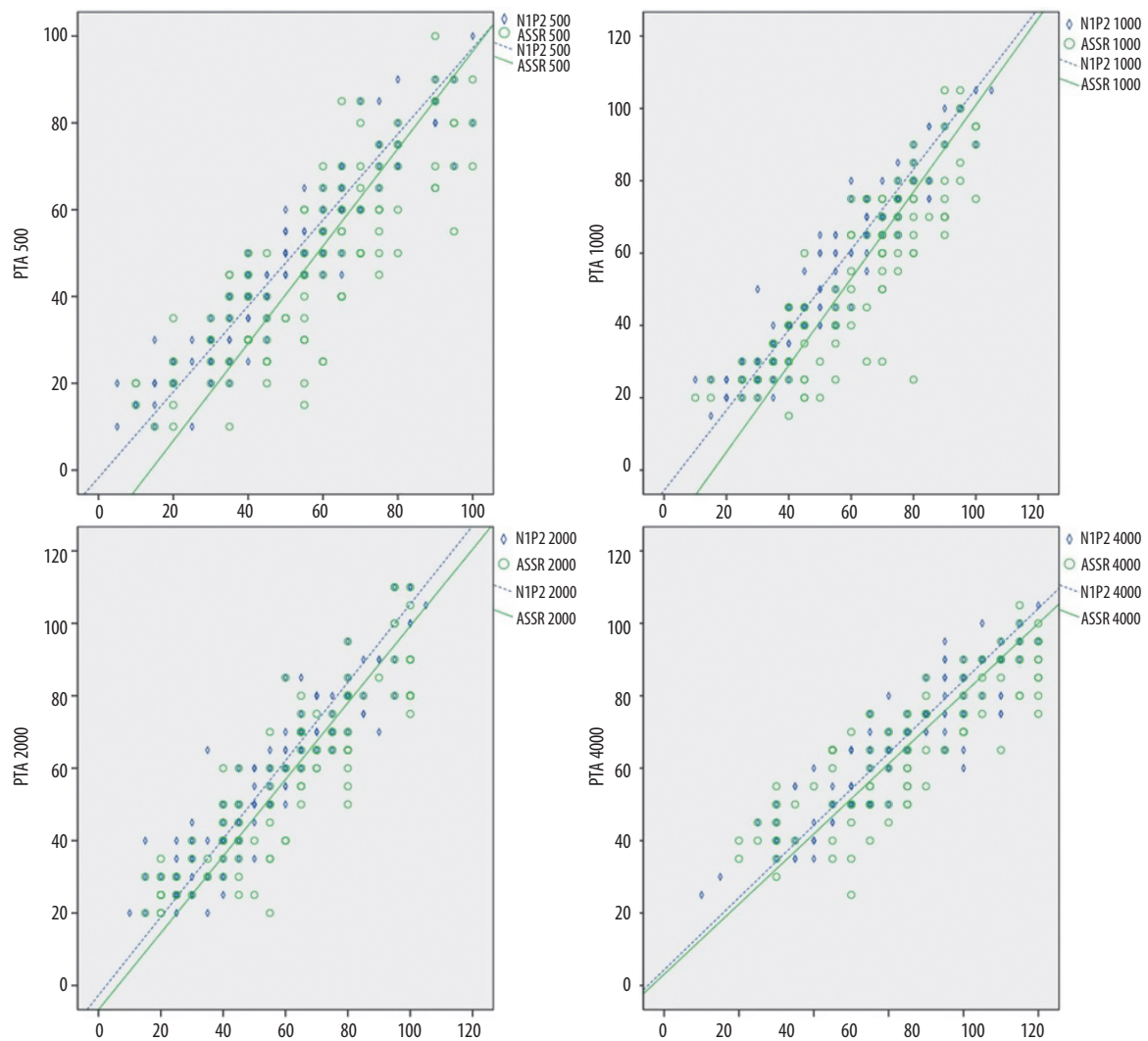


Figure 12. Distributions of physiologic N1P2 thresholds and estimated ASSR audiogram thresholds (x-axis) versus behavioral PTA thresholds (y-axis) for 500 Hz (top left), 1000 Hz (top right), 2000 Hz (bottom left), and 4000 Hz (bottom right). The blue diamonds are N1P2 thresholds; the green circles are ASSR thresholds. The lines are linear regressions for prediction of thresholds from physiologic N1P2 (blue) and estimated ASSR audiogram thresholds (green)

Linear regression analysis was used to relate estimated ASSR audiogram thresholds and N1P2 data to behavioral thresholds, and scatterplots of data are shown in Figure 12a–d. The relationships between the behavioral PTA thresholds and the estimated ASSR audiogram thresholds in dBHL are described by regression equations (Table 8, which relate behavioral PTA thresholds to physiologic thresholds obtained by N1P2 and the estimated ASSR audiogram thresholds at 500, 1000, 2000, and 4000 Hz). Both behavioral PTA thresholds and the physiologic N1P2 thresholds were compared at each frequency and every degree of hearing level. Data in statistical analyses was used to get a regression equation for the final correction to predict the behavioral threshold from the physiological N1P2 threshold. The slope of the electrophysiologic N1P2 thresholds regression suggests that there is a better way to estimate the ASSR audiogram thresholds than one-to-one correspondence with

behavioral PTA thresholds. Greater correction factors are required to predict behavioral PTA thresholds from estimated ASSR audiogram thresholds than from electrophysiologic N1P2 thresholds. The regression slopes are similar across test frequencies for the electrophysiologic N1P2 only. There is a wider dispersion of data for estimated ASSR audiogram thresholds than for N1P2.

There was no statistically significant correlation between age and the difference *behavioral PTA threshold minus electrophysiologic N1P2 threshold* or between age and the *behavioral PTA threshold minus estimated ASSR audiogram threshold*.

Discussion

Various auditory evoked potential techniques have been explored as a means of objectively predicting the behavioral

Table 8. R-square values and regression equations relating N1P2 CAEP thresholds with behavioral thresholds and those relating ASSR thresholds with behavioral thresholds at 500, 1000, 2000, and 4000 Hz

Frequency	R-square values		Regression equations: $y = b + (m \times x)$	
	N1P2	ASSR	N1P2	ASSR
500 Hz	0.911	0.697	$y = 2.11 + 0.92 \times x$	$y = 3.57 + 0.78 \times x$
1000 Hz	0.922	0.765	$y = 0.65 + 1.02 \times x$	$y = 2.85 + 0.94 \times x$
2000 Hz	0.885	0.793	$y = 3.67 + 0.97 \times x$	$y = 6.18 + 0.85 \times x$
4000 Hz	0.852	0.731	$y = 12.67 + 0.87 \times x$	$y = 19.29 + 0.72 \times x$

audiogram in groups of subjects who cannot provide reliable or accurate behavioral results. Malingerers, and physically or mentally disabled persons, may all fall within these groups [1].

The aim of this study was to estimate the hearing threshold level at different frequencies using the N1P2 cortical auditory evoked response potential in adult subjects with either normal hearing or sensorineural hearing loss, and to compare the abilities of N1P2 and ASSR to estimate the behavioral hearing threshold levels.

This study revealed that in the normal hearing subgroup, mild, moderate, moderately severe, and profound SNHL subgroups, the mean *behavioral PTA minus electrophysiologic N1P2 threshold* was significantly less than the *behavioral PTA minus the estimated ASSR audiogram threshold* (Tables 1–5). But in the profound SNHL subgroup, this study revealed that the mean difference of PTA – ASSR was comparable to the mean PTA – N1P2 CAEP difference at all frequencies using air conduction in the profound SNHL subgroup in both ears (Table 6).

Therefore, N1P2 CAEP was better than ASSR in predicting behavioral thresholds at all frequencies, especially at 500 and 1000 Hz in the normal hearing subgroup, at 1000 Hz in the mild SNHL subgroup, at 500 Hz in right ears in the moderate SNHL subgroup, at 500, 1000, and 4000 Hz in the right ear and 500 and 1000 Hz in the left in the moderately severe SNHL subgroup.

In comparison to these results, Yeung and Wong [23] found that the mean difference between CERA and behavioral thresholds at 500, 1000, 2000, and 4000 Hz for normal hearing subjects were 9.2, 9.1, 11.3, and 12.1 dB respectively. On examining 10 ears of 5 normal hearing subjects, Dabbous et al. [24] found that, using ASSR, the mean PTA – ASSR thresholds difference in the right ear was 9, 10, 9, and 7 dB for air conduction at frequencies of 500, 1000, 2000, and 4000 Hz respectively; while in the left it was 9, 10, 8, and 9 dB for air conduction. Their average difference was higher than the current study because in the current study we used the instrument pre-programmed correction factor table for adults to automatically get the estimated ASSR audiogram (in dBHL), while they used the electrophysiological ASSR hearing threshold without applying a correction to convert from electrophysiological hearing threshold to estimated psychoacoustic hearing threshold (estimated ASSR audiogram).

Moreover, N1P2 CAEP was equally accurate at all frequencies in the normal hearing subgroup, in the severe SNHL subgroup, and in the profound SNHL subgroup. N1P2 CAEP was better in predicting the behavioral thresholds at 500 Hz than at 4000 Hz in the mild SNHL subgroup in the left ear using air conduction, and in the moderate SNHL subgroup and in the moderately severe SNHL subgroup. N1P2 CAEP threshold detection ability was better at low frequencies than high frequencies in the mild SNHL subgroup, however the difference did not exceed 15 dB.

The difference *behavioral PTA minus estimated ASSR audiogram threshold* was smaller at 2000 Hz than it was at other frequencies, and this was found in all groups. That is, ASSR was better at high frequencies.

In comparison to these results for mild to moderate sensorineural hearing losses, Yeung and Wong [23] found that the mean PTA – CAEP threshold difference was 7.1, 8.3, 4.7, and –2.6 dB at frequencies of 500, 1000, 2000, and 4000 Hz respectively, and the mean PTA – ASSR threshold differences were 12.9, 14.3, 12.3, and 2.4 dB at frequencies of 500, 1000, 2000, and 4000 Hz respectively.

In comparison to these results, Yeung and Wong [23] found in moderately severe to severe sensorineural hearing losses that the mean PTA – CAEP threshold difference was 5.5, 8.6, 8.2, and –2.9 dB at frequencies of 500, 1000, 2000, and 4000 Hz respectively, and the mean PTA – ASSR threshold difference was 11.3, 14.6, 9.3, and –0.71 dB at frequencies of 500, 1000, 2000, and 4000 Hz respectively.

In agreement with our results, Yeung and Wong [23] found for profound sensorineural hearing loss that the mean PTA – CAEP threshold difference was –2, 2.1, 5.9, and –9.4 dB at frequencies of 500, 1000, 2000, and 4000 Hz respectively, and the mean PTA – ASSR threshold difference was 1.5, 2.9, 4.4, and 1.7 dB at frequencies of 500, 1000, 2000, and 4000 Hz respectively.

Comparing different frequencies

N1P2 CAEP results

Our results show that N1P2 CAEP was better at 500 Hz than at 4000 Hz in the mild, moderate, and moderately severe SNHL subgroups. That is, the N1P2 CAEP is generally better at low frequencies than at high.

In accordance with our results, Tomlin et al. [1] found that N1P2 CAEP response thresholds to 500 Hz stimuli were on average 3 dB lower than those obtained to 4000 Hz tone bursts. They stated that this slight low-frequency advantage was consistent with the observations of Wunderlich and Cone-Wesson [25] and Jacobson et al. [26]: low frequency tones result in a greater spread of activity along the basilar membrane, with contribution from both the apical and basal turns of the cochlea. In contrast, high frequency stimuli activate only the basal nerve fibers [26]. The tonotopic arrangement of the basilar membrane is maintained in the auditory cortex, and as the low frequency reception areas are more superficial to the scalp than the higher frequency regions the distance between sites of generation and recording are reduced, resulting in relatively higher response amplitudes [25,26]. But, in contrast with our results, Yeung and Wong [23] found that the mean threshold differences for CAEP were smaller at 4000 Hz than at lower frequencies (500 and 1000 Hz) in those with hearing impairment.

ASSR results

We found that ASSR predicted the behavioral thresholds better at higher than lower frequencies. The difference was smallest at 2000 Hz and 4000 Hz in normal, mild SNHL, moderate SNHL, moderately severe SNHL groups and was least at 2000 Hz only in the severe SNHL and profound SNHL groups.

Ghannoum et al. [27] also found that the differences were almost equal at all frequencies in the normal hearing and moderate SNHL group; and was least at 2000 Hz and 4000 Hz in the mild SNHL group and least at 2000 Hz in the slight SNHL group.

In agreement with our results, Yeung and Wong [23] found that the mean threshold differences for ASSR were smaller at 4000 Hz than at lower frequencies (500 and 1000 Hz) in those with hearing impairment.

Also results of Herdman and Stapells [28] and Hsu et al. [29] revealed that the correlation between ASSR thresholds and behavioral PTA thresholds was weaker at 0.5 kHz than at higher frequencies. The ASSR thresholds were closest to behavioral PTA thresholds at 4 kHz.

Ishida et al. [30] also found that the PTA – ASSR threshold difference was significantly larger for 500 Hz and significantly smaller for 4000 Hz compared with 1000 and 2000 Hz. Results for 500 Hz were subject to high EEG noise and sub-optimum stimulus parameters [28,31,32].

Results of the present study revealed that behavioral PTA and electrophysiologic N1P2 thresholds were highly correlated, and behavioral PTA and estimated ASSR audiogram thresholds were highly correlated at all frequencies. However, the mean difference of *behavioral PTA minus the electrophysiologic N1P2 threshold* was significantly less than the difference of *behavioral PTA minus the estimated ASSR audiogram threshold* in all subjects at all frequencies using air conduction, where estimated ASSR audiogram thresholds exceeded electrophysiologic N1P2 thresholds levels by approximately 7 dB at 500 Hz in both ears and less pronounced at 4000 Hz.

Our r coefficients between estimated ASSR audiogram thresholds and behavioral PTA thresholds ranged from 0.83 for 500 Hz to 0.891 for 2000 Hz. Higher values, ranging from 0.923 at 4000 Hz to 0.960 at 1000 Hz, were obtained between behavioral PTA thresholds and electrophysiologic N1P2 thresholds (Table 7).

The slope of the electrophysiologic N1P2 thresholds regression (Figure 13) suggests that ASSR gives a better than one-to-one correspondence with behavioral PTA thresholds. That is, greater correction factors are required to predict behavioral PTA thresholds from estimated ASSR audiogram thresholds than from electrophysiologic N1P2 thresholds. The regression slopes are similar across test frequencies for electrophysiologic N1P2 thresholds only.

The r^2 values for the regression equations (Table 8) relating the electrophysiologic N1P2 CAEP thresholds with behavioral PTA thresholds showed a stronger relation than those relating behavioral PTA thresholds with estimated ASSR audiogram thresholds – i.e. ASSR thresholds predict the behavioral PTA thresholds less accurately than the electrophysiologic N1P2 CAEP.

In accordance with our results, Tomlin et al. [1] found significant strong correlations between behavioral hearing levels and both ASSR and N1P2 CAEP thresholds. The N1P2 CAEP however, was found to be a more robust measure for determining behavioral hearing thresholds in awake adults. Pearson r coefficients, reflecting the relationship between ASSR and behavioral thresholds, were around 0.84 for 500 Hz and 0.85 for 4000 Hz. Even higher coefficients (0.95 at 500 Hz and 0.96 at 4000 Hz) were obtained for the comparison between behavioral thresholds and N1P2 CAEP thresholds.

Biagio et al. [33] found that the N1P2 CAEP correlation with behavioral thresholds was 0.85, compared to 0.75 for ASSR. They stated that the N1P2 CAEP technique, however, had been used for at least three decades and offers an accurate tool for estimating hearing thresholds in adult populations for whom reliable behavioral testing may not be possible or may be questioned. They concluded that the N1P2 CAEP was clinically more effective (accurate) than the single stimulus 40 Hz ASSR technique to estimate behavioral audiometric thresholds in adults exposed to occupational noise. That is, visualization of the response is simpler in ASSR since the equipment itself performs statistical analyses that are easy to view. They stated that the N1P2 CAEP may be the objective measure of choice in adults exposed to occupational noise but, unlike the ASSR, requires interpretation of responses by experienced clinicians.

Results of the present study revealed that the mean N1P2 CAEP behavioral threshold difference was –3.5 to 1.7, compared to –1.9 to 8.2 between estimated ASSR audiogram thresholds and behavioral PTA thresholds, depending on the test frequency.

Biagio et al. [34] found that the mean differences between N1P2 CAEP and behavioral thresholds for both a normal hearing group and a group with hearing loss from occupational noise exposure varied between 0 to 6 dB across 0.5, 1, 2, and 4 kHz, with standard deviations of ± 10 dB. The mean difference between ASSR and behavioral thresholds was

larger, varying between 22 to 32 dB with standard deviations of 13–14 dB.

In agreement with our results, Yeung and Wong [23] found that the mean CAEP behavioral threshold difference was –1.8 to 7.9 dB from 500 to 4000 Hz, compared to 4.3 to 13.7 dB between ASSR and behavioral thresholds, depending on the test frequency. Also, Prasher et al. [7] and Tsui et al. [34] found that the mean CAEP behavioral threshold difference was –4.3 to –1.0 dB at 1000 Hz and 2000 Hz.

Yeung and Wong [23] stated that the difference in the degree of deviations between these measures may be attributed to response generation sites. CAEP is generated within the primary and secondary auditory cortex in the superior and lateral surface of the superior temporal gyrus [4]; whereas the generation site of ASSR depends on the modulation frequency between 20 Hz and 200 Hz (ASSR elicited by stimuli presented at rates less than 20 Hz are mainly generated by activity in the primary auditory cortex [35–37]). When ASSRs are elicited by stimuli presented at rates between 20 and 60 Hz, the underlying neural generators are mainly located in the primary auditory cortex, auditory midbrain, and thalamus [35–39]. When ASSRs are elicited by stimuli presented at rates greater than 60 Hz, these responses are generated primarily by contributions from the superior olivary complex, inferior colliculus, and cochlear nucleus [35–37,39–41].

In the present study, ASSR was recorded using narrow-band CE-chirp stimuli at a rate of 40 Hz, so the sites of neural generators were mainly located in the primary auditory cortex, auditory midbrain, and thalamus.

Comparing the different degrees of hearing

In the present study, N1P2 CAEP was equally accurate in all degrees of SNHL at each frequency separately (except at 1 kHz, which only showed statistically significant large differences for the moderately severe and profound hearing losses in the right ear). Correlation between the behavioral PTA threshold and *behavioral PTA minus electrophysiologic N1P2 threshold* showed that *behavioral PTA minus electrophysiologic N1P2 threshold* was greater at milder degrees of hearing loss (Table 7). That is, the less the hearing loss at 1000, 2000, and 4000 Hz, the less the ability of N1P2 CAEP to estimate hearing threshold – thus N1P2 CAEP predicts behavioral thresholds better at more severe degrees of hearing loss.

Lightfoot and Kennedy [2] stated the CAEP threshold gives a slightly more elevated threshold than the PTA. The value of this bias will depend to some extent on the methods used for stimulus calibration, response acquisition and analysis, the presence of any loudness recruitment, and the presence of certain comorbidities. A smaller bias has been observed for greater degrees of hearing loss [2].

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In agreement with our results, Yeung and Wong [23] found that prediction of thresholds using CAEP was more accurate when the hearing loss was greater. Tsui et al. [34] also found that hearing thresholds are more accurately predicted when the degree of hearing loss increases and stated that it was possibly because recruitment had caused ASSR to be recorded at lower sensation levels than when no hearing loss was present [42]. Normal-hearing individuals do not experience loudness recruitment, which would result in less steep N1P2 CAEP growth curves. This in turn might influence cortical assessment of hearing thresholds in normal-hearing individuals [43].

In contrast with our results, Tomlin et al. [1] found the level of the subject's audiogram did not affect the sensation level at which N1P2 CAEP could be recorded. Prasher et al. [7] also reported no relationship between response sensation level and degree of hearing loss.

Tomlin et al. [1] found that ASSR thresholds were obtained at a significantly lower sensation level with increased degree of hearing loss. Yeung and Wong [23] also found that the mean threshold differences across test frequencies were greatest when hearing thresholds were within the normal range, and the smallest when a severe to profound hearing loss was involved.

In the present study, correlation between the behavioral PTA threshold and *behavioral PTA minus estimated ASSR audiogram threshold* showed that the difference of *behavioral PTA minus estimated ASSR audiogram threshold* did not significantly vary with degrees of hearing loss at any frequency. Thus, on studying each frequency separately, ASSR predicts the behavioral thresholds with equal accuracy at all degrees of SNHL. This might be because the estimated ASSR audiogram thresholds were derived by using correction factors implemented in the ASSR device from the electrophysiologic thresholds found by the ASSR test.

Conclusion

The N1P2 CAEP showed advantages over previous frequency-specific evoked potentials like ASSR in hearing threshold estimation in adults – especially at lower frequencies and in normal hearing and milder degrees of hearing loss, where ASSR showed decreased accuracy. Thus, hearing threshold estimation using N1P2 CAEP is a reliable, objective method to estimate the behavioral threshold in normal hearers and patients with various degrees of SNHL. It has equal accuracy at all frequencies and has increased accuracy at more severe degrees of hearing loss.

We therefore recommend using N1P2 CAEP in difficult-to-test adult subjects where accurate behavioral thresholds can not be obtained. We also recommend performing further studies on using N1P2 CAEP to estimate behavioral threshold in late teens.

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