

ORIGINAL ARTICLE

## Evaluation of residual hearing in cochlear implants candidates using auditory steady-state response

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### Abstract

**Conclusion:** The correlations between behavioral and auditory steady-state response (ASSR) thresholds were significant at 500, 1000, 2000, and 4000 Hz. ASSR presented high sensitivity and specificity in the detection of residual hearing in cochlear implant candidates when compared with warble-tone audiometry. **Objectives:** To assess residual hearing in cochlear implant candidates by comparing the electrophysiological thresholds obtained in dichotic single-frequency ASSR with behavioral thresholds at 500, 1000, 2000, and 4000 Hz. **Methods:** This was a comparative study between ASSR and warble-tone audiometry thresholds in 40 cochlear implant candidates (80 ears) before cochlear implantation with bilateral severe-to-profound sensorineural hearing loss. **Results:** Thresholds were obtained in 62.5% of all frequencies evaluated in warble-tone audiometry and in 63.1% in the ASSR. ASSR sensitivity was 96% and specificity was 91.6%. Mean differences between behavioral and ASSR thresholds did not reach significance at any frequencies. Strong correlations between behavioral and ASSR thresholds were observed in 500, 1000, and 2000 Hz and moderate in 4000 Hz, with correlation coefficients varying from 0.65 to 0.81. On 90% of occasions, ASSR thresholds were acquired within 10 dB of behavioral thresholds.

**Keywords:** Auditory evoked potentials, auditory thresholds, sensorineural hearing loss, residual hearing, cochlear implantation

### Introduction

Identification and preservation of residual hearing in cochlear implantation are becoming more important as increasing numbers of patients with significant residual hearing are implanted, the minimum age of implantation falls, and more patients undergo bilateral implantation [1]. Residual hearing also allows combination of electrical and acoustic stimulation in the same ear [2], additional benefit from contralateral acoustic stimulation [3], and application of future technologies.

Behavioral audiometry is the gold standard method for determining and quantifying hearing loss in subjects able to respond and cooperate. Alternative

methods are essential in the characterization of hearing ability when behavioral responses are unreliable or incomplete across critical areas of frequency or intensity. Difficult-to-test individuals require the use of objective measures for hearing evaluation [4]. The most widely used electrophysiological procedure to estimate hearing thresholds is the click or tone burst auditory brainstem response (ABR). Due to the transient nature of the stimuli employed to evoke ABR, maximum presentation level is 90 dB HL, precluding investigation of residual hearing at profound levels [5]. The absence of an ABR is consistent with significant hearing impairment; however, it cannot differentiate between severe and profound hearing losses [6].

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Auditory steady-state response (ASSR) is elicited by continuous modulated tones with frequency selectivity and allows stimulation at increased intensity levels [7]. Thus, ASSR may provide frequency-specific information regarding the auditory thresholds at maximum intensity levels of 120 dB HL [5], providing more accurate and reliable investigation of residual hearing. However, high intensity air-conduction stimuli can produce artifactual ASSR [8–10], especially at 500 and 1000 Hz [9]. ASSR was investigated in several studies comprising adults and children with varying degrees of hearing loss [7,11–13]. Nevertheless, few studies evaluated its use in severe to profound sensorineural hearing loss [5,14–18], especially after the assumption of false-positive responses to high intensity stimuli [8–10]. Because of its characteristics, the ASSR is a unique tool in the assessment of residual hearing in cochlear implant candidates. However, the lack of adequate clinical data and standardization limit its applicability in determining auditory sensitivity. The exact relationship between behavioral and electrophysiological thresholds at high intensities is not clear and requires cautious investigation.

The objective of the present study was to assess residual hearing in cochlear implant candidates with severe to profound sensorineural hearing loss before cochlear implantation by comparing the electrophysiological thresholds obtained in dichotic single-frequency ASSR with behavioral warble-tone thresholds at 500, 1000, 2000, and 4000 Hz.

## Material and methods

### Participants

Forty cochlear implant candidates (80 ears), aged between 15 and 63 years (mean =  $38 \pm 15$ ), 25 females and 15 males, were enrolled in the study before cochlear implantation. All subjects participated voluntarily and provided signed informed consent in accordance with the Declaration of Helsinki. This research was approved by the ethical committee of the Clinics Hospital of the University of São Paulo School of Medicine (protocol no. 0164/2010).

Inclusion criteria were: (a) normal micro-otoscopic findings; (b) normal middle ear function, confirmed by type A 226 Hz tympanogram; (c) absent product distortion otoacoustic emissions; (d) absent click ABR. Subjects with inner ear and cochlear nerve abnormalities identified on computed tomography (CT) and/or magnetic resonance imaging (MRI) that could interfere in the measurement of residual hearing were excluded, such as inner ear aplasia, cochlear nerve aplasia or hypoplasia, or transverse fracture of the temporal bone.

### Warble-tone audiometry

Audiometry was performed in double-walled, sound attenuating room with a Madsen Midimate 622 clinical audiometer (GN Otometrics, Taastrup, Denmark), calibrated according to ANSI S3.6-1996 standard. Behavioral air-conduction thresholds were carried out with warble-tone at 500, 1000, 2000, and 4000 Hz presented in each ear through TDH-39 headphones (Telephonics, Farmingdale, NY, USA). The upper limit of stimulation was 120 dB HL. Threshold seeking was conducted using a 10 dB down, 5 dB up technique, in each frequency.

### ASSR stimulus

The Multiple Auditory Steady-State Response (MASTER) software (version 2.04.i00) running on the Bio-Logic Navigator Pro System (Natus Medical Incorporated, San Carlos, CA, USA) was used for the ASSR measurements.

The stimuli used to evoke air-conduction ASSR were continuous sinusoidal tones modulated 100% in exponential amplitude and 20% in frequency. These sinusoidal tones were presented through ER-3A insert earphones (Etymotic Research, Elk Grove Village, IL, USA) by means of dichotic single-frequency stimulation. The carrier frequencies of interest were 500, 1000, 2000, and 4000 Hz, modulated at 66.797 Hz in the left ear and 69.141 in the right according to the default specifications of the system [16]. Maximum presentation levels were 117, 120, 119, and 118 dB HL for the frequencies 500, 1000, 2000, and 4000 Hz, respectively.

Air-conduction stimuli were calibrated in dB HL, according to the ANSI S3.6-1996 standard, using a Quest Electronics model 1700 sound level meter (Quest Technologies, Oconomowoc, WI, USA) with Brüel & Kjær DB0138 2 cm<sup>3</sup> coupler (Brüel & Kjær Sound & Vibration Measurement A/S, Nærum, Denmark).

### ASSR recordings

Recordings were carried out in a darkened, sound-attenuated, electrically shielded room with the subjects remaining relaxed in supine position. No sedative agents were administered. All examinations were performed by the same examiner, without prior knowledge of the behavioral thresholds.

Surface electrodes were positioned with Ten20 conductive paste (Weaver and Company, Aurora, CO, USA) and adhesive tape as non-inverting on the high forehead (Fz), inverting on the nape (Oz), and ground on the right shoulder (Pz). The skin beneath the electrodes was abraded with Nuprep

abrasive skin prepping gel (Weaver and Company). All electrode impedances were less than 3 kOhm.

Electroencephalographic activity was filtered using a bandpass of 30–300 Hz and amplified by a gain of 10 000. Data were collected and digitized with an analog-to-digital conversion rate of 1200 Hz, with a 16-bit precision. The data were recorded in epochs lasting 0.8533 s. Sixteen data epochs were collected and linked together to form one sweep with an overall duration of 13.653 s. An individual data epoch containing excessive myogenic noise was eliminated when amplitudes exceeded an artifact rejection level of  $\pm 60 \mu\text{V}$ . The next acceptable epoch was then used to construct the sweep. Epochs that contained electrophysiological activity exceeding 90 nV were rejected [13]. If noise levels were below 30 nV, measurement was continued, and if the noise was higher than 30 nV, the subject was repositioned until better noise levels were achieved. The maximum amount of sweeps was determined according to the preset specifications of the equipment: 10 sweeps in intensities above 100 dB HL, 12 sweeps between 90 and 99 dB HL, and 18 sweeps between 80 and 89 dB HL.

Once completed, each sweep was averaged in the time domain and subsequently submitted to a fast Fourier transform. The resulting amplitude spectrum enabled steady-state responses to be analyzed in the frequency domain. The frequency spectrum was analyzed automatically by the software, determining whether the response amplitude at the modulation frequency was significantly different from the mean amplitude of the electroencephalographic background noise in adjacent frequencies. The significance of the signal-to-noise ratio was assessed by F-ratio with a confidence interval of 95% for each sweep collected. A response was considered to be 'present' when the F-ratio was significant at a level of  $p < 0.05$ , for at least four consecutive sweeps [19]. Consequently, a 'no response' result was considered when the signal-to-noise ratio did not reach significance ( $p < 0.05$ ) after the maximum number of sweeps.

#### *ASSR threshold evaluation*

The ASSR measurement procedure started at an intensity of 110 dB HL at the carrier frequency of 1000, followed by 500, 2000, and 4000 Hz. Thresholds were determined using a 10 dB down and 5 dB up technique, until no responses could be collected. If a significant response was not obtained at 110 dB HL, the intensity was increased to the upper limits of the equipment for each frequency. All thresholds obtained were confirmed with retest. Absence of responses was also confirmed with retest. The ASSR threshold was defined as the lowest intensity at which a significant

response was detected, and a no response was found 5 dB below this level.

#### *Data analysis*

The statistical evaluation of data was carried out with SPSS 17.0 software (IBM, Armonk, NY, USA).

The relationship between presence or absence of behavioral responses and ASSR was examined at 500, 1000, 2000, and 4000 Hz in each evaluated ear.

Sensitivity, specificity, positive predictive value, and negative predictive value were calculated to determine the accuracy of ASSR in the identification of residual hearing.

The relationship between behavioral and ASSR thresholds for each frequency was assessed using descriptive statistics and Pearson product-moment coefficient. Paired samples *t* test was applied to compare mean differences in behavioral and ASSR thresholds. Significance was set at  $p < 0.05$ .

## **Results**

#### *Percentage of behavioral and ASSR responses*

Behavioral thresholds were obtained at 62.5% (200/320) of all frequencies evaluated for all subjects. The largest percentage of responses was obtained at 500 Hz, decreasing along the frequencies. Detectable ASSR thresholds were acquired on 63.1% (202/320) of occasions. The distribution of the responses was similar to that found in the warble-tone audiometry. No significant difference was observed between right and left ears, in both warble-tone audiometry and ASSR.

Figure 1 shows that the presence of responses in both tests decreased progressively across evaluated frequencies. Absence of responses at maximum levels in both warble-tone audiometry and ASSR was greater at 4000 Hz.

#### *Sensitivity, specificity, and predictive values of ASSR*

The sensitivity, specificity, positive predictive value, and negative predictive value were calculated considering the behavioral responses as the gold standard for detection of residual hearing (Table I).

#### *Behavioral and ASSR thresholds*

Means and standard deviations of behavioral hearing level and ASSR thresholds in ears with measurable responses are summarized in Table II. The mean differences between behavioral and ASSR thresholds were similar for each frequency, varying from  $-1.9$  dB

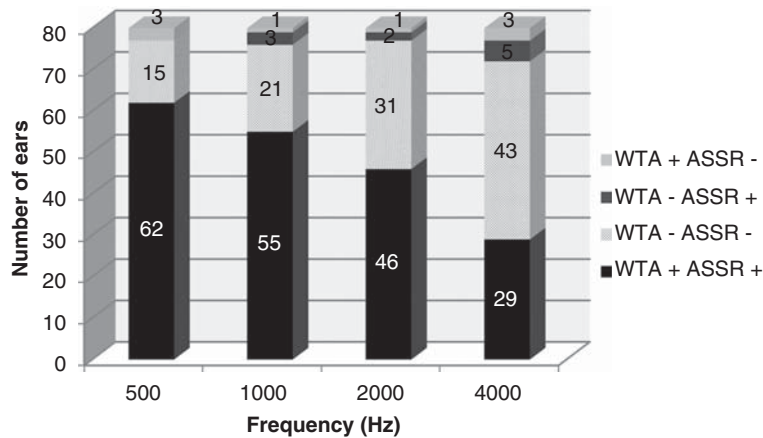


Figure 1. Relationship between presence (+) and absence (-) of responses in warble-tone audiometry (WTA) and auditory steady-state response (ASSR) for the carrier frequencies of 500, 1000, 2000, and 4000 Hz.

to 1.7 dB. Statistical significance was not reached at any frequencies.

In all, 63% of behavioral thresholds were recorded between 100 and 120 dB HL and 25% were obtained at levels equal to or lower than 90 dB HL, especially at 500 Hz. The majority (63%) of ASSR recorded thresholds were concentrated at intensities equal to or higher than 100 dB HL. Also, 19% of the ASSR thresholds obtained for ears with residual hearing were at levels equal to or lower than 90 dB HL, predominantly at 500 Hz.

In ears that showed no behavioral responses at maximum presentation levels of 120 dB HL, all ASSR thresholds were in the profound hearing loss range. Among these values, about 90% were equal to or higher than 110 dB HL.

#### *Relationship between behavioral and ASSR thresholds*

Overall, 192 comparisons of behavioral and ASSR thresholds were obtained from the 40 subjects (80 ears); 62 were at 500 Hz, 55 at 1000 Hz, 46 at

2000 Hz, and 29 at 4000 Hz. These findings represent the occasions on which both behavioral and ASSR thresholds were established. Instances in which either behavioral response or ASSR were absent at maximum stimulation levels were not included in the correlation analysis.

The relationship between warble-tone audiometry and ASSR thresholds was assessed by calculating the Pearson product-moment correlation. The data showed a strong and significant correlation ( $p < 0.01$ ) at 500, 1000, and 2000 Hz, with correlation coefficients of 0.79, 0.81, and 0.71, respectively. The correlation at 4000 Hz was moderate ( $r = 0.65$ ) and significant ( $p < 0.01$ ) (Figure 2).

ASSR thresholds typically were obtained at close proximity to the behavioral hearing levels. The differences in auditory thresholds determined by warble-tone audiometry and ASSR were equal to or less than 10 dB in 87%, 98%, 87%, and 86% of recordings for the carrier frequencies of 500, 1000, 2000, and 4000 Hz, respectively. There were no instances where the ASSR threshold was more than 25 dB from the behavioral threshold.

Table I. Sensitivity, specificity, positive predictive value, and negative predictive value for the ASSR at 500, 1000, 2000, and 4000, and overall.

Frequency (Hz)	Sensitivity	Specificity	PPV	NPV
500	95.4%	100%	100%	83.3%
1000	98.2%	87.5%	94.8%	95.4%
2000	97.9%	93.9%	95.8%	96.9%
4000	90.6%	89.6%	85.3%	93.5%
Overall	96.0%	91.6%	95.0%	93.2%

ASSR, auditory steady-state response; NPV, negative predictive value; PPV, positive predictive value.

## Discussion

An ideal auditory evoked potential should obtain electrophysiological thresholds comprising as many frequencies as possible, without the need for a behavioral response from the patient. The electrophysiological thresholds must accurately estimate the behavioral hearing levels, maintaining frequency specificity of the responses. The continuous nature of the stimuli used to elicit ASSR limits its spectral distortion, therefore the stimuli exhibit high frequency selectivity. This



Table II. Mean behavioral thresholds and auditory steady-state response (ASSR) estimates and mean differences between behavioral and ASSR thresholds.

Frequency (Hz)	Behavioral		ASSR		Mean difference ± SE
	Mean ± SD (dB HL)	<i>n</i>	Mean ± SD (dB HL)	<i>n</i>	
500	93.77 ± 12.87	65	94.87 ± 9.52	62	-1.9 ± 1 ( <i>p</i> = 0.06)
1000	100.98 ± 10.02	56	99.91 ± 9.10	58	1.3 ± 0.8 ( <i>p</i> = 0.11)
2000	106.81 ± 11.10	47	105.31 ± 8.87	48	1.7 ± 1.2 ( <i>p</i> = 0.15)
4000	109.68 ± 10.54	32	110.26 ± 7.75	34	0.6 ± 1.6 ( <i>p</i> = 0.76)

*n*, number of thresholds; SD, standard deviation, SE, standard error.

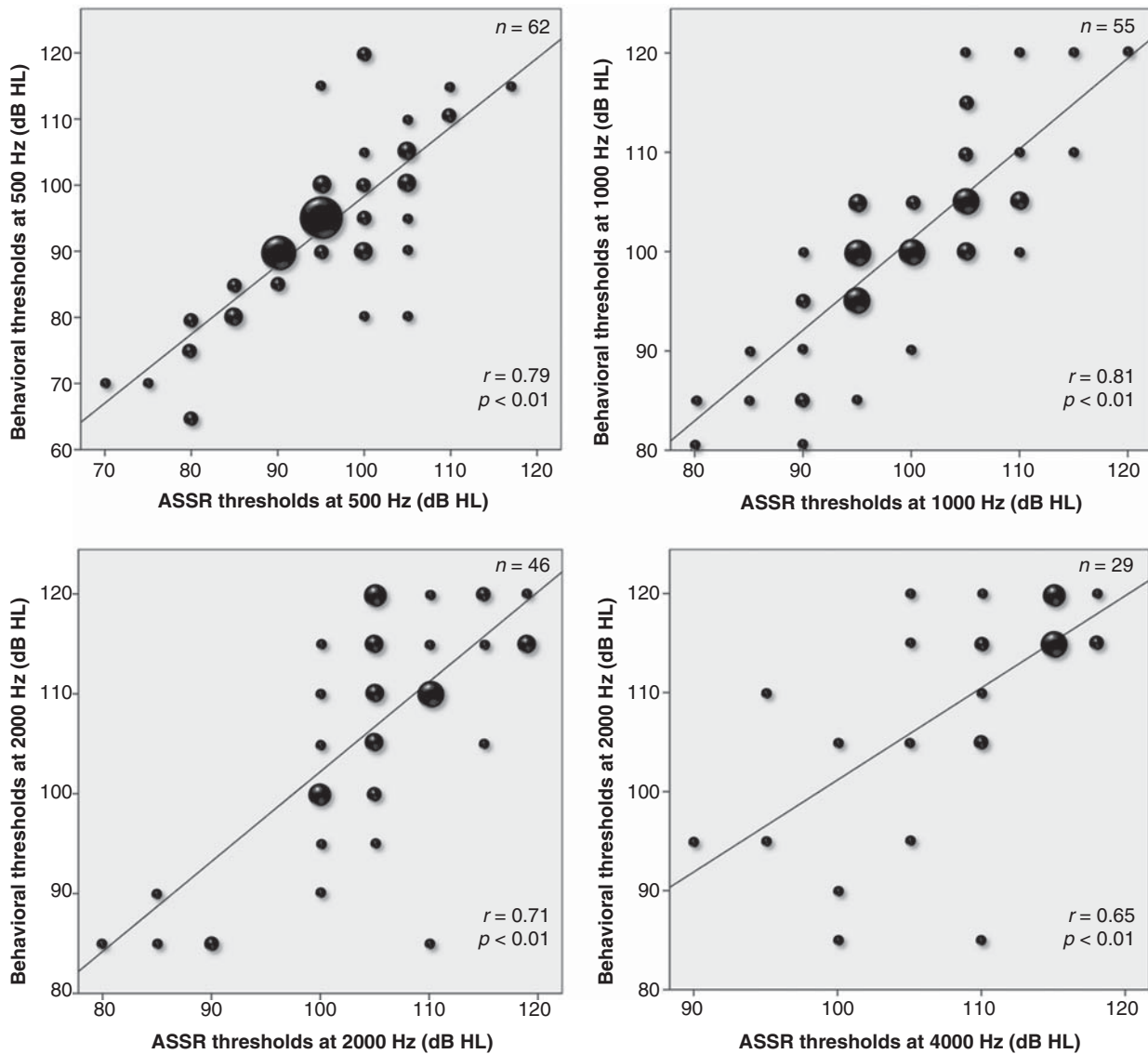


Figure 2. Scatterplots of the relationship between behavioral and auditory steady-state response (ASSR) thresholds at 500 (A), 1000 (B), 2000 (C), and 4000 Hz (D). The size of the points varies with the number of overlapping points.

same property of the stimuli also allows increased stimulation intensity up to 120 dB HL [7]. Strong correlations were reported on behavioral and ASSR thresholds, particularly for subjects with sensorineural hearing loss [7,12,13]. Furthermore, a number of studies have shown that the difference between behavioral and ASSR thresholds decreases as the severity of hearing loss increases [7,12].

To confirm that the absence of click ABR does not preclude the possibility of residual hearing, only subjects with no response on click ABR in both ears were included in this study [5,17,18]. Moreover, individuals who showed presence of product distortion otoacoustic emissions were excluded due to the possibility of auditory neuropathy spectrum disorder.

According to Rance et al. [5], the absence of ASSR at maximum stimulation levels is a reliable indicator of profound or total hearing loss. The authors found that in 82.5% of the occasions in which no ASSRs were obtained, behavioral thresholds were consistent with total hearing loss. Furthermore, behavioral thresholds were found within 15 dB of the maximum presentation level of ASSR. Rance and Briggs [14] reported that in the absence of ASSR, behavioral responses were equal to or greater than 115 dB HL in 93.4%. In the present study, on 93.2% of the occasions with no detectable ASSR no behavioral response was found. In the few cases in which behavioral thresholds were obtained in conjunction with absent ASSR, the thresholds differed by 15 dB or less from the maximum stimulation of ASSR in 87.5% of circumstances, and were equal to or greater than 115 dB HL on 75% of occasions.

Most evaluated ears showed measurable ASSR thresholds in at least one frequency. Thus, 63% of the frequencies tested showed responses in the ASSR, similar to the values-described by Rance et al. [5] (66%) and Attias et al. [13] (64%), and higher than the results of Swanepoel and Ebrahim [4] (24%), and Beck et al. [17,18] (40% and 25%, respectively).

Swanepoel and Hugo [15] found the largest number of responses at 2000 Hz, followed by 1000, 4000, and 500 Hz, attributing this distribution to the difference of maximum stimulation intensity across frequencies. Attias et al. [13] also observed a higher rate of no response on ASSR at 500 Hz. Problems in estimating 500 Hz ASSR thresholds can be explained by poor neural synchronization at low frequencies [11]. The percentage of thresholds obtained in ASSR in this study was higher at 500 Hz, decreasing gradually across evaluated frequencies. The values attained apparently do not depend on the maximum intensity level, since the upper limit of stimulation of the device was 120, 119, 118, and 117 dB HL at 1000, 2000, 4000, and 500 Hz, respectively. Unlike

previous studies, 77.5% of the ears showed response at 500 Hz, possibly related to the exponential modulation envelope of the stimuli. This attribute increases response amplitude for lower frequencies [20], resulting in better detection of the response.

For most evaluated frequencies, ASSR thresholds were close to those reported by Swanepoel and Hugo [15], Swanepoel et al. [16], Swanepoel and Ebrahim [4], and Beck et al. [17]. However, some differences between these studies must be considered. The ASSR recording can be performed while the subjects are awake, in natural sleep, under sedation or under general anesthesia. Swanepoel and Hugo [15], Swanepoel and Ebrahim [4], and Beck et al. [17] investigated children up to 65 months under sedation or general anesthesia. In the present study, individuals were awake and relaxed during the acquisition of ASSR. The majority of the aforementioned studies used small sample sizes, ranging from 20 to 30 ears. As mean threshold is composed only by ears with presence of ASSR, the mean may reflect a lower number of ears. Larger sample sizes yield more precise estimates of the population parameters. In the present study 80 ears were assessed.

Among the behavioral thresholds obtained for each frequency in ears with residual hearing, 25% were equal to or lower than 90 dB HL. Theoretically, these thresholds could be detected by the ABR, whereas its maximum stimulation level is 90 dB HL. Data from the present study support the observation by Rance et al. [5] that the lack of response on click ABR does not preclude the possibility of residual hearing in severe and profound levels. The majority (80.7%) of ASSR thresholds was acquired at intensities above the maximum stimulation level of ABR, as exposed by Swanepoel and Hugo [15]. Given this fact, it is assumed that the ASSR can provide additional information about the residual hearing in individuals with absence of ABR.

The correlations between behavioral and ASSR thresholds were significant at all frequencies tested, being strong at 500, 1000, and 2000 Hz and moderate at 4000 Hz. The worst correlation coefficient obtained at 4000 Hz may result from the smaller number of comparisons between behavioral and ASSR thresholds for this frequency, because of absent responses at upper limits of stimulation in either warble-tone audiometry and/or ASSR. Pearson correlation coefficients in this study were superior to those acquired by Swanepoel et al. [16] at 500, 1000, and 2000 Hz. Attias et al. [13], in turn, found higher correlation only at 2000 Hz and the relationship did not reach significance at 4000 Hz. Several studies involving varying degrees of hearing loss reported poor correlation between pure-tone

audiometry and ASSR thresholds at 500 Hz [13,16]. However, this finding was not observed in the present study. One possible explanation would be the application of exponential modulation.

Mean differences between behavioral and ASSR thresholds were smaller than those reported in other studies that investigated severe and profound hearing loss [13,14,16]. However, the accuracy of threshold estimation depends on the variability of estimation rather than on any mean difference between behavioral and electrophysiological thresholds. This study has shown that in 90% of the comparisons, the ASSR thresholds were seen within 10 dB of the behavioral level. Rance et al. [5,7] observed this fact on 82% and 94% of occasions, respectively, and Swanepoel et al. [16] on 69%. The close relationship between warble-tone audiometry and ASSR was consistent throughout the frequency range evaluated.

The agreement between both methods – i.e. presence of ASSR associated with presence of behavioral responses and absence of ASSR associated with absence of behavioral responses – is similar at 500 (96.25%), 1000 (95%), 2000 Hz (96.25%) and slightly inferior at 4000 Hz (90%). There were few occasions where the residual hearing was found in the warble-tone audiometry in the absence of the ASSR, varying from 1.25% to 3.75% at the frequency range of 500–4000 Hz. Rance et al. [5] attained higher rates: 12% at 500 Hz, 21% at 1000 Hz, 18% at 2000 Hz, and 8% at 4000 Hz. The presence of ASSR in the absence of any behavioral response was also uncommon, seen in 3.1% of the frequencies tested. Since automatic and objective response analysis is associated with type I error, ASSR detection using a significance level of  $p \leq 0.05$  implies that incorrectly identifying electroencephalographic noise as response occurs in 5% of recordings by chance [19]. The number of ASSRs obtained in the absence of behavioral responses was not greater than expected by chance.

Gorga et al. [8], Small and Stapells [9], and Picton and John [10] reported the presence of ASSR at high intensities of stimulation in individuals who were not able to hear the continuous modulated tones used to elicit ASSR, due to total hearing loss or no placement of insert earphones in the ear canal. They suggested that such responses were electroencephalographic artifacts caused by aliasing, mistakenly defined as auditory responses. Gorga et al. [8] observed artifactual ASSRs in all subjects at all frequencies, with 72% of thresholds equal to or lower than 100 dB HL.

Small and Stapells [9] and Picton and John [10] recommended using high analog-digital conversion rates and selecting rates for which the carrier frequency of the stimulus is not an integer multiple,

to minimize the likelihood of artifactual ASSR. In contrast to the studies of Gorga et al. [8], Small and Stapells [9], and Picton and John [10], in the present study the ASSR was recorded at analog-digital conversion rates of 1200 Hz that theoretically would avoid spurious responses due to aliasing. The few ASSRs collected in the absence of behavioral responses were equal to or greater than 110 dB HL in 90% of cases. Beck et al. [18] did not find spurious responses at any frequency, at maximum presentation level of 110 dB HL.

Because of the small proportion of false-negative and false-positive results, the ASSR demonstrated high sensitivity (96%) and specificity (91.6%) in the identification of residual hearing in cochlear implant candidates. Thus, the ASSR can be used in clinical practice to provide reliable estimations of hearing thresholds in adults with severe to profound sensorineural hearing loss. However, the results of this study cannot be applied to children. More studies are necessary comparing ASSR thresholds with behavioral responses in this population.

## Conclusions

The correlations between behavioral and ASSR thresholds were significant at 500, 1000, 2000, and 4000 Hz. ASSR presented high sensitivity and specificity in the detection of residual hearing in cochlear implant candidates, compared with warble-tone audiometry.

**Declaration of interest:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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