Steady State Auditory Evoked Potentials in Normal Hearing Subjects: Evaluation of Threshold and Testing Time

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Key Words

Steady state response · Auditory brainstem response · Behavioral threshold

Abstract

Background: Steady state responses (SSRs), between 75 and 110 Hz, evoked by auditory amplitude modulated single or multiple tone stimuli, may be used to estimate objective hearing threshold. **Methods:** The aim of this study was to compare SSRs and click-evoked auditory brainstem responses (ABRs) in both ears of 20 adults (10 males and 10 females, aged between 24 and 36 years) with normal hearing threshold. **Results:** Mean ABR threshold was found at 21.25 (± 5.9) dB nHL. Mean SSR threshold was found at 15.6 (± 9.6) dB nHL after a single frequency stimulus (1 kHz); at 10.5 (± 18.2) dB nHL and at 7.1 (± 12.4) dB nHL after bifrequency stimulation (0.5 and 2 kHz). SSR thresholds after multifrequency stimulation (0.5, 1, 2 and 4 kHz) were found, respectively, at 12.1 (± 12.9) dB nHL, 12.2 (± 12.8) dB nHL, 12.3 (± 8.3) dB nHL and 18.9 (± 17.2) dB nHL. Mean duration of the recording session was 6 min in the case of ABRs, while it was 25 min in the single frequency condition and 29 min in the multifrequency condition in the case of SSRs. **Conclusion:** SSRs can be used for frequency-specific objective audiometry. The multifrequency stimulation greatly reduces the whole testing time.

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Introduction

A steady state evoked potential can be defined as a response 'whose constituent discrete frequency components remain constant in amplitude and time over an infinitely prolonged time period' [1]. During repetitive stimulation, if one increases the repetition rate responses to individual stimuli can superimpose to responses to preceding stimuli.

The generation of human steady state responses (SSRs) is determined by the complex interaction of several mechanisms [2, 3]. However, the most quoted hypothesis states that SSRs are generated by linear addition of responses to individual stimuli under favorable phase relationship between components of the responses, to create a large periodic response [4]. The most widely known auditory SSR is the 40-Hz evoked potential described by Galambos et al. [5] in 1981. Rickards and Clark [6] have found that SSRs can be evoked by tonal amplitude modulated single stimuli, within a large frequency range. A recent work by Bohórquez and Özdamar [7] demonstrated that 40-Hz SSRs are composite responses generated by the superposition of the major waves of the auditory brain responses (ABR) and the MLR, and dramatic amplitude increase of the auditory SSR at 40 Hz is primarily due to the superposition of the resonating Pb component to the Pa wave. Picton et al. [8] demonstrated that SSRs can be obtained using a combination of both amplitude and frequency modulation and the optimal modulation frequency is near 40 Hz. Cohen et al.

[9] reported that simultaneous modulation in both amplitude and frequency evoked larger responses than amplitude modulation alone. SSRs elicited by continuous, single or multiple, tones modulated in amplitude at rates between 75 and 110 Hz, have been proposed as a technique to estimate objective audiometric threshold [10–14]. Using a multifrequency stimulus, a simultaneous activation of different cochlear regions can be obtained. For instance, using a stimulus including frequencies of 0.5, 1, 2 and 4 kHz, each one with a different modulation frequency, an objective threshold for these frequencies can be evaluated. The generation site of SSRs is still debated. It can be attributed to several neural regions of the auditory brainstem system [4, 15]. To date, the modality and the regions where the elaboration of the amplitude and frequencies modulation occur are still unknown. Similar to the ABR, SSRs are not affected by sleep or sedation.

Clinical evaluation of SSRs can be simplified by means of an automatic detection of the responses. In particular, the presence of a response is represented by distinct spectral peaks in the frequency domain, which are detectable with a statistical indicator and easily automated [10, 11, 13, 16, 17]. SSRs have been employed in determining hearing thresholds in adults and children [11–14, 18–21]. Many studies have been carried out to define the clinical applications of SSRs and their correlation with other objective and subjective techniques, such as ABRs and behavioral tests.

Our work is aimed to: (1) evaluate SSR threshold after single 1-kHz stimulation (SFS), bifrequency (0.5 and 2 kHz) stimulation (BFS) and multifrequency (0.5, 1, 2 and 4 kHz) stimulation (MFS) in adult normal-hearing subjects; (2) compare the SSR threshold with the behavioral threshold for the same modulated tones and compare the SSR 2- to 4-kHz threshold with the click-evoked ABR threshold; (3) evaluate the time needed for electrophysiological recordings (ABR and SSR), and (4) compare our results with the data from the literature.

Materials and Methods

This study was approved by the local Ethics Committee and written consent was obtained from each subject. Twenty volunteers (10 males and 10 females), aged between 24 and 36 years, with normal hearing and without history of otological pathology were studied.

For our system calibration, we used the responses obtained from another population of normal hearing people (50 subjects for pure tones' calibration, 30 subjects for clicks' calibration and 30 subjects for modulated tones' calibration); therefore, our results are expressed in dB nHL, where 'n' stands for 'normalized' with reference to the above-mentioned normal hearing group.

Each subject underwent an audiometric evaluation and their pure-tone threshold was better than 15 dB nHL for frequencies between 0.25 and 8 kHz in both ears.

Subjects underwent: (1) evaluation of individual behavioral thresholds for the modulated tones used for the SSR recording, and (2) recording of ABR and SSRs. ABR and SSR recordings were obtained by means of a commercially available instrument (Audix Neuronic® system, Neuronic S.A., Havana, Cuba). Normal hearing subjects were tested during spontaneous sleep, resting on a bed and in muscular relaxation. Surface electrodes were placed at the vertex (+), ipsilateral mastoid (–) and contralateral mastoid (ground). Impedance values were always kept below 5 k Ω .

Individual behavioral thresholds for the modulated tones used for the SSR recording was obtained monaurally using the psychoacoustic procedure of ascending and descending limits (20 dB nHL down and 10 dB nHL up).

With regard to ABR recording, EEG signal was amplified (100 K) and filtered with a bandpass between 10 and 3,000 Hz. The stimulus was an alternating polarity click of 0.1 ms duration, presented monaurally through earphones (Telephonics TDh4). The total number of stimuli was between 500 and 2,000. The starting stimulation level for the ABR was 80 dB nHL and the lowest level was 20 dB nHL. Threshold was evaluated monaurally and the procedure was that of ascending and descending limits (20 dB nHL down and 10 dB nHL up). We recorded two replications of the responses for each intensity level. The presence of the response was determined by visual inspection and was based on the identification and replicability of the V wave.

For the SSR recording, we used the response detection algorithm described by Savio et al. [10]. The signal was amplified (100 K) and filtered with a bandpass between 10 and 300 Hz. Recordings were not maintained for a defined number of averages and they were closed when a specific response was present and stable, as the automated algorithm implemented in the AUDIX software showed by the statistical indicator [10–11]. Each stimulus consisted of a carrier tone at 1, 2 or 4 audible frequencies (0.5, 1, 2 or 4 kHz) modulated in amplitude at a rate between 75 and 110 kHz. Preliminarily, we carried out a careful calibration of stimulus intensity, so as to be sure that the strength used in the calibration phase for the SSR was exactly the same used in the determination of threshold in SFS, BFS and MFS conditions. Three types of stimuli were used to record SSRs: (1) single carrier frequency at 1 kHz modulated at 89 Hz; (2) combination of two carrier frequencies at 0.5 and 2 kHz modulated at 81 and 97 Hz, and (3) combination of four carrier frequencies at 0.5, 1, 2 and 4 kHz modulated at 81, 89, 97 and 105 Hz, respectively. Stimuli were presented monaurally through earphones. Threshold was determined monaurally using the technique of ascending and descending limits (20 dB down and 10 dB up). The first stimulation level was 80 dB nHL. The signal/noise ratio was considered adequate when RNL (residual noise level) was ≤ 0.01 μ V. Response was considered present when the statistical indicator (expressed by the significant values on the polar plot) remained stable for three blocks of 100 averages. It was considered absent when this condition was not respected or when there was no response after 30 blocks. In order to increase reliability in threshold detection and minimize possible mistakes due to the automatic response indicator, a trained operator always evaluated each recording not only waiting for the persistence of the response's statistical indicator but also for the presence of the reliable peaks in the frequency domain.

Table 1. Mean value ($\pm$ SD) of SSR threshold after SFS, bifrequency stimulus (BFS) and MFS

Condition	Frequency, kHz	dB nHL
SFS	1	15.6 ($\pm$ 9.6)
BSF	0.5	10.5 ($\pm$ 18.2)
	2	7.1 ($\pm$ 12.4)
MFS	0.5	12.1 ($\pm$ 12.9)
	1	12.2 ($\pm$ 12.8)
	2	12.3 ($\pm$ 8.3)
	4	18.9 ($\pm$ 17.2)

Table 2. Testing time for SSR recording after SFS (for each intensity level), SSR after MFS and ABR

SSR SFS	25/2 ($\pm$ 6/45)
80 dB HL	2/0 ($\pm$ 0/43)
70 dB HL	2/8 ($\pm$ 0/37)
60 dB HL	3/12 ($\pm$ 1/56)
50 dB HL	4/36 ($\pm$ 1/51)
40 dB HL	5/2 ($\pm$ 2/43)
30 dB HL	8/0 ($\pm$ 4/3)
20 dB HL	4/51 ($\pm$ 6/0)
SSR MFS	29/32 ($\pm$ 5/58)
ABR	5/56 ($\pm$ 1/17)

Mean values ($\pm$ SD) are expressed in minutes and seconds, separated by a slash.

Finally, the effective duration of each test was determined as the time from the beginning to the end of electrophysiological recording. The time needed for instructions and to prepare subjects was not considered. The total duration of recordings for threshold evaluation was determined for ABRs. With regard to the SSRs, the total duration of the test was evaluated for the SFS and for the MFS condition. For the SSR, the duration of the test for each level of intensity of SFS was also considered. When needed, values are expressed as mean $\pm$ SD. In the statistical analysis the paired Student's *t* test was used.

Results

Pure tone audiometry hearing threshold was 10 dB nHL for all frequencies in each subject by definition. The behavioral thresholds for the single carrier frequency modulated tones were: 21.5 ($\pm$ 5.5) dB nHL at 0.5 kHz; 25 ($\pm$ 3.5) dB nHL at 1 kHz, 19.5 ($\pm$ 1.5) dB nHL at 2 kHz, 12 ($\pm$ 2.4) dB nHL at 4 kHz; the behavioral threshold for the

two carrier frequencies modulated tones (0.5–2 kHz) was 24.5 ($\pm$ 5.0) dB nHL, while in multifrequency condition (0.5–1 to 2–4 kHz) the behavioral threshold for modulated tones was 21.5 ($\pm$ 6.5) dB nHL. The electrophysiological threshold was 21.25 ($\pm$ 5.9) dB nHL in the case of click-evoked ABR. The mean values of SSR thresholds are depicted in table 1: thresholds after bifrequency stimulus were 10.5 ($\pm$ 18.2) and 7.1 ($\pm$ 12.4) at 0.5 and 2 kHz, respectively; thresholds after multifrequency stimulus were 12.1 ($\pm$ 12.9), 12.2 ($\pm$ 12.8), 12.3 ($\pm$ 8.3) and 18.9 ($\pm$ 17.2) at 0.5, 1, 2 and 4 kHz, respectively. The lowest threshold was at 2 kHz (7.1 dB nHL in BFS) and the highest one at 4 kHz (18.9 dB nHL in MFS).

When considering the same carrier frequency in different stimulation conditions differences in threshold values were found. The greatest difference was 5.2 dB. However, differences never attained statistical significance ($p > 0.01$). It is worth mentioning that during SSR recording, we frequently found in several subjects that responses were automatically detected at high level of stimulation, not detected at intermediate level and again present at minimal level, as previously found by Perez-Abalo et al. [11]. Comparing threshold values obtained with the two techniques, we observed differences with better values always given by ABR and differences varied from 14.4 dB (at 2 kHz, BFS) to 2.6 dB (4 kHz, MFS). Difference attained significant level only for 2 kHz, after BFS and MFS ($p < 0.01$).

Testing time for ABRs and SSRs recording are reported in table 2. The mean time needed to record ABR was 5 min 56 s ($\pm$ 1/17). As regards SSR after MFS, time recording was higher. Indeed, total duration of recording was 25 min for SSR after SFS and 29 min in MFS condition. Table 2 shows mean recording times for single intensity levels (from 80 to 20 dB nHL) for SSR under MFS. Recording times show a tendency to increase with decreasing intensity and they approximate 8 min near threshold.

Discussion

Our findings provide evidence that in normal hearing subjects, mean SSR threshold for modulated amplitude tones is 10 dB nHL, and lowest and highest values are respectively 7.1 and 18.9 dB nHL. Moreover, our data indicate that there is not statistically significant difference among SSR after SFS, BFS and MFS. This result confirms that MFS may be advantageous as they allow minimizing SSR testing time while maintaining a good diagnostic reliability in the evaluation of hearing threshold.

Our results are consistent with previous findings in the literature [16–18, 21]. Perez-Abalo et al. [11], with the same recording system, found the SSR threshold to be 5–13 dB worse than the behavioral threshold in sensorineural hearing impaired children. Despite differences regarding age and audiological conditions of the enrolled subjects, these results are consistent with our findings. Similar results have also been obtained by Swanepoel et al. [20] in adult patients with moderate sensorineural hearing loss, confirming that the SSR can reliably estimate behavioral thresholds of 60 dB HL and higher. Nevertheless, the authors recommend caution when estimating thresholds of less than 60 dB, due to increased variability. Kariya et al. [22] observed that in patients with sensorineural hearing loss, pure-tone audiometry thresholds and auditory steady-state response thresholds did not differ significantly at any frequencies and were significantly correlated. Moreover, according to Schmulian et al. [23], multifrequency SSRs are highly sensitive to variations in degree of hearing loss while they are not affected by the configuration of hearing loss. On the other hand, Canale et al. [13], using the same Audix equipment, obtained different results and found that multifrequency SSR thresholds had a mean difference of 28 dB from behavioral thresholds. This result is consistent with the observation of Rance et al. [14], who found differences of about 10 dB in the case of moderate and severe hearing loss and about 20 dB in the case of normal hearing or mild hearing loss.

In a recent paper, the same authors claimed that the tone burst-ABR technique, when applied to normal babies, offer a more reliable basis for prediction of hearing levels than SSRs assessment, probably because the response is less affected by maturational development [24]. In the present work, we also found high variability of SSR threshold values. Standard deviation values are about 10 dB nHL at all frequencies, with a maximum observed at 0.5 kHz (18.2 dB nHL after BFS). Similar findings have been found by Swanepoel et al. [21] and Kei et al. [18], who showed standard deviations varying from 8 to 12 dB [21] and from 9 to 11.5 dB [18], respectively. In the literature, many authors agree that there is a strong positive relationship between tone-evoked ABR and SSRs thresholds, both in hearing impaired adults [25] and children [26].

With regard to the comparison between the ABR and SSR thresholds, we observed nonsignificant differences, except when ABR was compared to SSR after BFS and MFS at 2 kHz with better values observed for the SSR. In contrast with our data, previous studies in normal adult subjects [27] and children [28] showed better values for the ABR, with a difference of about 10 dB. This difference

was found when the ABR threshold was determined by visual inspection but not when it was detected automatically [27]. Roberson et al. [29] showed a sensitivity equal to that of ABR for individuals with hearing levels from 0 to 90 dB HL, while in patients with hearing impairment greater than 90 dB, SSR showed a distinct advantage over ABR testing. Finally, Martinez et al. [30] observed better threshold values with SSR than in ABR recordings. Interpretation of these discrepancies is difficult but we should take into account differences in the procedure used in threshold determination (descending versus ascending, steps of 10 versus 5 dB), systems for recordings ABR and SSR (one or two different types of equipment were used) and, especially, procedure employed to determine the stimulus level. We used a psychoacoustical calibration procedure in dB nHL both for ABR and SSR.

As far as the testing time is concerned, our results indicate a remarkable advantage of the ABR. Mean values in recording times for SSR are 4 or 5 times longer than ABR for SFS and MFS, respectively. Mean total time to determine SSR threshold after MFS is 29 min and 32 s. Savio et al. [10] and Perez-Abalo et al. [11] reported 21 min for determination of threshold after binaural stimulation, while 42 min are reported in the study of Luts et al. [12]. Comparison of these data should be made with caution due to differences in the procedure of threshold evaluation. In our study, a starting level at 80 dB nHL was chosen as more suitable for diagnostic application. In addition, we used restrictive criteria for the SSR identification at the threshold level. As previously stated by Luts et al. [12] and Vander Werff et al. [28], the adoption of restricted criteria in response identification strongly influences the recording time, since it requires to increase the signal-to-noise ratio to a longer recording time. Finally, a further increase in our recording time could be due to the careful evaluation of each response which was aimed to optimize the reliability and efficacy of threshold detection.

Taking into account our and previously reported data, we can conclude that SSR should be considered an additional and useful procedure in objective audiometry to estimate frequency specific threshold. In particular, we believe that SSR recording could integrate other electrophysiological techniques as an effective method to evaluate low frequency hearing threshold.

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References

- 1 Regan D: Human Brain Electrophysiology: Evoked Potentials and Evoked Magnetic Fields in Science and Medicine. New York, Elsevier, 1989.
- 2 Azzena GB, Conti G, Santarelli R, Ottaviani F, Paludetti G, Maurizi M: Generation of auditory steady-state responses (SSRs). I. Stimulus-rate effects. *Hear Res* 1995;83:1–8.
- 3 Santarelli R, Maurizi M, Conti G, Ottaviani F, Paludetti G, Pettorossi VE: Generation of auditory steady-state responses (SSRs). II. Addition of responses to individual stimuli. *Hear Res* 1995;83:9–18.
- 4 Picton TW, Dimitrijevic A, John AS: Multiple auditory steady state responses. *Ann Otol Rhinol Laryngol* 2002;111:16–21.
- 5 Galambos R, Makeig S, Talmachoff PJ: A 40-Hz auditory potential recorded from the human scalp. *Proc Natl Acad Sci USA* 1981;78:2643–2647.
- 6 Rickards FW, Clark GM: Steady-state evoked potentials to amplitude-modulated tones; in Npodar RH, Barber C (eds): *Evoked Potentials*, ed 2. Boston, Butterworth, 1984, pp 163–168.
- 7 Bohórquez J, Özdamar Ö: Generation of the 40-Hz auditory steady-state response (ASSR) explained using convolution. *Clin Neurophysiol* 2008;119:2598–2607.
- 8 Picton TW, Skinner CR, Champagne SC, Kellet AJ, Maiste AC: Potentials evoked by the sinusoidal modulation of the amplitude or frequency of a tone. *J Acoust Soc Am* 1987;82:165–178.
- 9 Cohen LT, Rickards FW, Clark GM: A comparison of steady state evoked potentials to modulated tones in awake and sleeping humans. *J Acoust Soc Am* 1991;90:2467–2479.
- 10 Savio G, Cardenas J, Perez Abalo M, Gonzales A, Valdes J: The low and high frequency auditory steady state responses mature at different rates. *Audiol Neuro-Otol* 2001;6:279–287.
- 11 Perez-Abalo MC, Savio G, Torres A, Martin V, Rodriguez E, Galan L: Steady state responses to multiple amplitude-modulated tone: an optimized method to test frequency-specific threshold in hearing impaired children and normal hearing subjects. *Ear Hear* 2001;22:200–211.
- 12 Luts H, Desloovere C, Kumarc A, Vandermeersch E, Wouters J: Objective assessment of frequency-specific hearing thresholds in babies. *Int J Pediatr Otorhinolaryngol* 2004;68:915–926.
- 13 Canale A, Vacilla M, Cavalot AL, Albera R: Auditory steady-state responses and clinical applications. *Eur Arch Otorhinolaryngol* 2006;263:499–503.
- 14 Han D, Mo L, Liu H, Chen J, Huang L: Threshold estimation in children using auditory steady state responses to multiple simultaneous stimuli. *ORL* 2006;68:64–68.
- 15 Presacco A, Bohórquez J, Yavuz E, Özdamar O: Auditory steady state responses to 40-Hz click trains: relationship to middle latency, gamma band and beta band responses studied with deconvolution. *Clin Neurophysiol* 2010;121:1540–1550.
- 16 Rance G, Rickards FW, Cohen LT, De Vidi S, Clark GM: Automated prediction of hearing threshold in sleeping subjects using auditory steady-state evoked potentials. *Ear Hear* 1995;16:499–507.
- 17 Lins O, Picton W, Boucher B, Duriex-Smith A, Champagne S, Moran L, Perez-Abalo MC, Martin V, Savio G: Frequency-specific audiometry using steady state responses. *Ear Hear* 1996;17:81–96.
- 18 Kei J, Smith D, Joseph S, Stopa J, Kang K, Darnell R: Effects of ambient acoustic noise on the auditory steady state response thresholds in normally hearing adults. *Audiol Neurotol* 2008;13:13–18.
- 19 Ahn JH, Lee HS, Kim YJ, Yoon TH, Chung JW: Comparing pure-tone audiometry and auditory steady state response for the measurement of hearing loss. *Otolaryngol Head Neck Surg* 2007;136:966–971.
- 20 Swanepoel D, Erasmus H: Auditory steady-state responses for estimating moderate hearing loss. *Eur Arch Otorhinolaryngol* 2007;264:755–759.
- 21 Swanepoel D, Hugo R, Roode R: Auditory steady-state responses for children with severe to profound hearing loss. *Arch Otolaryngol Head Neck Surg* 2004;130:531–535.
- 22 Kariya S, Fukushima K, Kawasaki A, Katoaka J, Nishizaki K: Auditory steady-state responses to multiple simultaneous stimuli in children with functional or sensorineural hearing loss. *Eur Arch Otorhinolaryngol* 2008;265:769–773.
- 23 Schmulian D, Swanepoel D, Hugo R: Predicting pure-tone thresholds with dichotic multiple frequency auditory steady state responses. *J Am Acad Audiol* 2005;16:5–17.
- 24 Rance G, Tomlin D, Rickards FW: Comparison of auditory steady-state responses and tone-burst auditory brainstem responses in normal babies. *Ear Hear* 2006;27:751–762.
- 25 Lin YH, Ho HC, Wu HP: Comparison of auditory steady-state responses and auditory brainstem responses in audiometric assessment of adults with sensorineural hearing loss. *Auris Nasus Larynx* 2009;36:140–145.
- 26 Rodrigues GRI, Lewis DR: Threshold prediction in children with sensorineural hearing loss using the auditory steady-state responses and tone-evoked auditory brain stem response. *Int J Pediatr Otorhinolaryngol* 2010;74:540–546.
- 27 Cone Wesson B, Dowell RC, Tomlin D, Rance G, Ming WJ: The auditory steady-state response: comparison with the auditory brainstem response. *J Am Acad Audiol* 2002;13:173–187.
- 28 Vander Werff KR, Brown CJ, Gienapp BA, Schmidt Clay KM: Comparison of auditory steady-state response and auditory brainstem response thresholds in children. *J Am Acad Audiol* 2002;13:227–235.
- 29 Roberson JB, O'Rourke C, Stidham KR: Auditory steady-state response testing in children: evaluation of a new technology. *Otolaryngol Head Neck Surg* 2003;129:107–113.
- 30 Miranda León MT, Sainz Quevedo M: Comparative study between auditory steady-state responses, auditory brain-stem responses and liminar tonal audiometry. *Acta Otorrinolaringol Esp* 2007;58:290–295.