

AUDIOLOGY

Identifying congenital hearing impairment: preliminary results from a comparative study using objective and subjective audiometric protocols

Ipoacusia neurosensoriale congenita: risultati preliminari di uno studio comparativo che ha confrontato protocolli audiometrici oggettivi e soggettivi

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SUMMARY

To compare objective and subjective protocols assessing hearing loss in young children and evaluate frequency-specific hearing impairment through a comparison between auditory steady state responses (ASSR), auditory brainstem responses (ABR), transient otoacoustic emissions and conditioned orientation reflex responses (COR). Thirty-five hearing-impaired children (20 male and 15 female), aged between 14 months and 4 years, participated in the study. Hearing threshold levels and peripheral auditory function were assessed by measurements of ABR, ASSR, otoacoustic emissions and COR. The analysis of the COR and ASSR variables showed significant correlations in the majority of tested frequencies. The data highlight a characteristic of the COR procedure, which is an underestimation of the hearing threshold in comparison to the ASSR estimate. The data show that the COR threshold assessment follows the pattern of the other two established electrophysiological methods (ABR, ASSR). The correlation analyses did not permit evaluation of the precision of these estimates. Considering that the ASSR variables show a better relationship with ABR (higher correlation values) than COR, it might be advantageous to utilize the ASSR to gain frequency-specific information.

KEY WORDS: Sensorineural hearing loss • Otoacoustic emissions (OAE) • Auditory steady state responses (ASSR) • Auditory brain-stem responses (ABR) • Conditioned orientation reflex (COR)

RIASSUNTO

Obiettivo del nostro studio è stato confrontare protocolli di valutazione uditiva oggettivi e soggettivi nei bambini e valutare la perdita uditiva anche in rapporto alle frequenze, mediante il confronto tra i dati ottenuti attraverso l'utilizzo dei potenziali evocati uditivi di stato stazionario (ASSR), i potenziali evocati uditivi del tronco encefalico (ABR), le emissioni otoacustiche (OAE) e l'audiometria a risposte condizionate (COR). Sono stati inclusi in questo studio trentacinque bambini ipoacusici (20 maschi e 15 femmine) di età compresa tra 14 mesi e 4 anni. I valori di soglia uditiva sono stati valutati attraverso l'utilizzo di questi protocolli: ASSR, ABR, OAE e COR. I valori di soglia ottenuti mediante COR e ASSR mostrano una correlazione significativa nella maggior parte delle frequenze testate. Dall'analisi dei dati si è riscontrato che la valutazione della soglia mediante COR segue il modello degli altri due metodi elettrofisiologici (ABR, ASSR). Tuttavia l'analisi di correlazione non permette una valutazione della precisione di queste stime. Considerando che le variabili ASSR mostrano valori di correlazione più alti con l'ABR rispetto al COR, potrebbe essere vantaggioso utilizzare le ASSR per ottenere informazioni di soglia più precise, anche in merito alle diverse frequenze.

PAROLE CHIAVE: Ipoacusia neurosensoriale • Otoemissioni (OAE) • Potenziali evocati uditivi di stato stazionario (ASSR) • Potenziali evocati uditivi (ABR) • Audiometria a risposte condizionate (COR)

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Introduction

The incidence of congenital hearing loss is estimated to be 1-3 cases per 1,000 live births¹⁻⁴. The guidelines for programmes aiming at early hearing detection and intervention (EHDI) suggest that the hearing evaluation of infants presenting congenital hearing loss should be conducted at the earliest possible age. The latter requires the use of test-

ing procedures which can accurately assess and quantify the degree of hearing loss at different frequencies, especially in the range between 0.5 - 4.0 kHz⁵⁻¹². Assessing the infant population is a challenging task because there is no established consensus on the testing protocols that accurately measure hearing threshold. Information on the hearing level of infants presenting hearing deficits is of great

interest when selecting the proper characteristics of hearing aid amplification, which is necessary in order to assist the auditory and language development of these patients¹⁻¹².

In recent years, an increasing number of clinical studies has evaluated the role of auditory steady-state responses (ASSR) in the estimation of hearing threshold. While auditory brainstem responses (ABR) are induced by transient stimuli, ASSRs are evoked by continuous modulated tones which are frequency specific¹³⁻¹⁹. ASSR responses were first reported in the literature decades ago by Galambos et al., and later by Kuwada et al.^{20,21}. The ASSR protocols have advanced considerably, and at present it is possible to assess multiple frequencies (500, 1000, 2000, and 4000 Hz), in both ears simultaneously, even in cases presenting profound hearing loss (up to 120 dB HL).

From the battery of electrophysiological tests assessing hearing status, the ABR, the ASSR, and otoacoustic emissions (OAEs) are considered as the most reliable procedures. However, in some cases (as in early infancy) these procedures are not always able to provide a complete or satisfactory assessment of hearing. To improve the level of information about the hearing status of an infant, subjective procedures such as the conditioned orientation reflex (COR) are often used^{22,23}. The theoretical basis of this technique is the following. During a COR session, an infant is exposed to acoustic stimuli transmitted via loudspeakers. When the infant identifies and localizes the source of the stimulus, he/she responds with a body movement, usually rotation of the head, towards the source of the stimulus. Learning to respond to the appropriate speaker (the stimulus source) may be especially difficult for infants with middle ear disease and unilateral hearing loss^{22,23}. Nevertheless, data obtained by COR may still be useful in diagnosis and follow-up of hearing impaired infants²⁰ as they can contribute to: (i) information about low frequency hearing; (ii) information about the hearing of neurologically immature babies, where there may be doubts about the accuracy of the ABR and ASSR hearing assessment; and (iii) information on uncomfortable loudness levels in hearing aid fitting.

There are no data in the literature on the relationship between the COR procedure and standardized objective procedures such as OAEs, ABR and ASSR. The objective of this study was to shorten this information gap by investigating the relationship of the data obtained with the COR protocol and three clinical procedures in a population of young children. Additionally the performance of the COR procedure in assessing correctly hearing threshold was compared to the ASSR, using hearing level data from the ABR as a reference point.

Materials and methods

Subjects and testing procedures

Thirty-five hearing-impaired children presenting sen-

sorineural hearing losses (thresholds ≥ 40 dB HL according to a click-ABR assessment) participated in the study. The age of the participants varied from 14 to 48 months. These children were identified with a hearing impairment in our EDHI (Early Detection of Hearing and Intervention) screening programme. Each subject was evaluated using three objective protocols (OAEs, ABR and ASSR) and one subjective protocol (COR).

Transient otoacoustic emissions (TEOAEs) were acquired with a Echolab device (Labat, SRL, Italy). TEOAEs were evoked by 80 μ sec click stimuli following a linear protocol (i.e. all clicks in the stimulus train were of the same positive polarity). Details on the protocol and its advantages over other TEOAE protocols are described in previous publications^{24,25}. The stimulus level was set at 72 ± 3 dB SPL. The click rate was 50 per sec and post-stimulus analysis was in the range of 3.5 to 20 msec. A total of 260 sweeps was averaged above the noise rejection level of 47 dB. A TEOAE response was considered valid (i.e. present) when the TEOAE amplitude was > 6 dB above the level of the noise floor and the reproducibility value $> 70\%$. TEOAE protocols were preferred over DPOAE (Distortion Product OAE) procedures to maximize data compatibility with the initial TEOAE measurements during the screening programme.

The ASSR and ABR responses were recorded by the ICS CHAPTER (GN Otometrics, Mercury, Italy). Testing was performed in an acoustically- and electrically-shielded room. Sleep was induced spontaneously without the need for sedation. Electrophysiological activity was recorded ipsilaterally to the stimulated ear using silver chloride cup electrodes, with the active and reference electrodes applied to the vertex and the mastoid, respectively. ABR recording stimuli were given mono-aurally using an earphone and consisted of 0.1 msec clicks with alternating polarity starting from a maximum intensity of 90 dB nHL (approximately 120 dB SPL).

The ASSR responses were recorded using a similar set-up. Steady state potentials were evoked at single frequencies (i.e. 500, 1000, 2000, 4000 Hz), using a frequency modulated tone of 80 Hz. At each frequency an average time of 3 min was required. Additional details on the ABR, ASSR protocols can be found in previous publications^{7,8,26,27}.

The COR evaluation was carried out in a soundproof booth equipped with an audiometer, a speaker and a variety of toys according the age of the tested child. The examination was performed by two experienced audiometrists who worked together to best evaluate the listening behaviour of the child: one audiometrist operated the audiometer, and the other monitored the child's attention and interacted with him/her to avoid any distraction effects. In younger children (age of 6-12 months), it is possible to obtain a conditioned response that is validated by rotation of the head towards the direction of the sound source. Positive reinforcement, such as a lighting toy, was

also employed to counteract any habitual responses that can occur after a number of acoustic stimuli. In children between the ages of 12 and 36 months, a mixed protocol of visual and acoustic stimuli was used to initially attract the child's attention. The intensity of the acoustic signal was progressively reduced to assess the threshold level, frequency by frequency^{10,26}.

Statistical analysis

In the following analyses, more emphasis was placed on the relationship between the ASSR and COR threshold estimates. The strength of association between COR measurements at five frequencies and ASSR, ABR and OAE measurements at four frequencies, and left and right ears, was measured by Pearson's correlation.

The OAE measurements were assigned a value of 1 for 'REFER' and 0 for 'PASS'. The data showed non-normal behaviour, and in particular it seemed that there was an upper boundary on one or both variables. Therefore, p-values for correlations (one-sided tests) were obtained by randomization (100,000 random permutations for each). These p-values were similar to those obtained from large-sample tests except for those obtained for the OAE correlations. The 60 p values were adjusted by the step-down Bonferroni method. For all procedures, the level of significance was considered as $p < 0.05$.

In order to evaluate the probability values from small samples, it is possible to use a randomization procedure, which by definition is the chance assignment of treatments to experimental units (the tested methods in the present case), in order to nullify the effects of unsuspected nuisance factors.

For multiple comparisons, the Bonferroni procedure is the simplest to apply. The Bonferroni method uses the worst case scenario approach to estimate prediction intervals. The Bonferroni intervals are ideal for making a small-number of pre-specified comparisons.

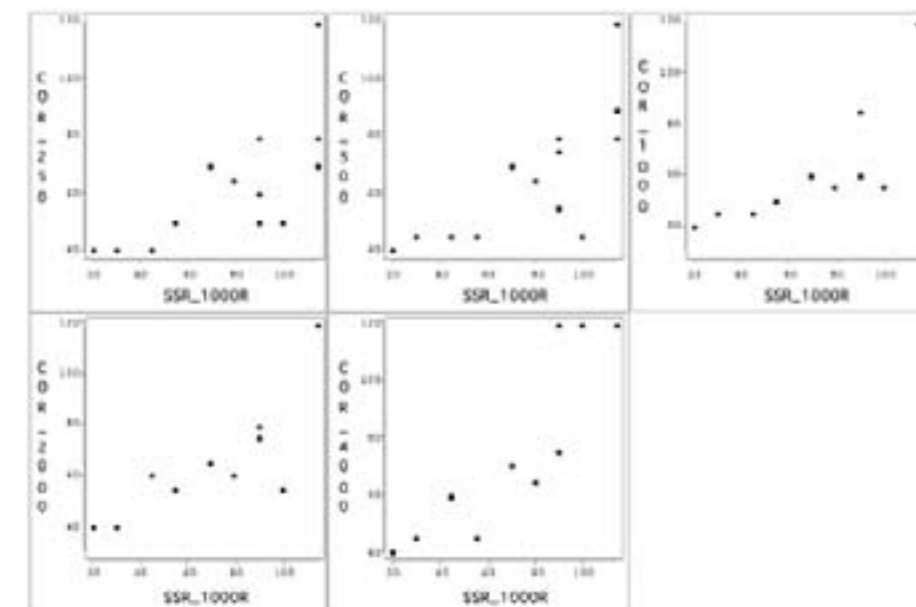


Fig. 1. Distribution of ASSR data (x-axis in all graphs) from right ears at 1000 Hz and all tested COR variables (y-axis in all graphs). The scatter plots show the relationships quantified by the estimated correlations.

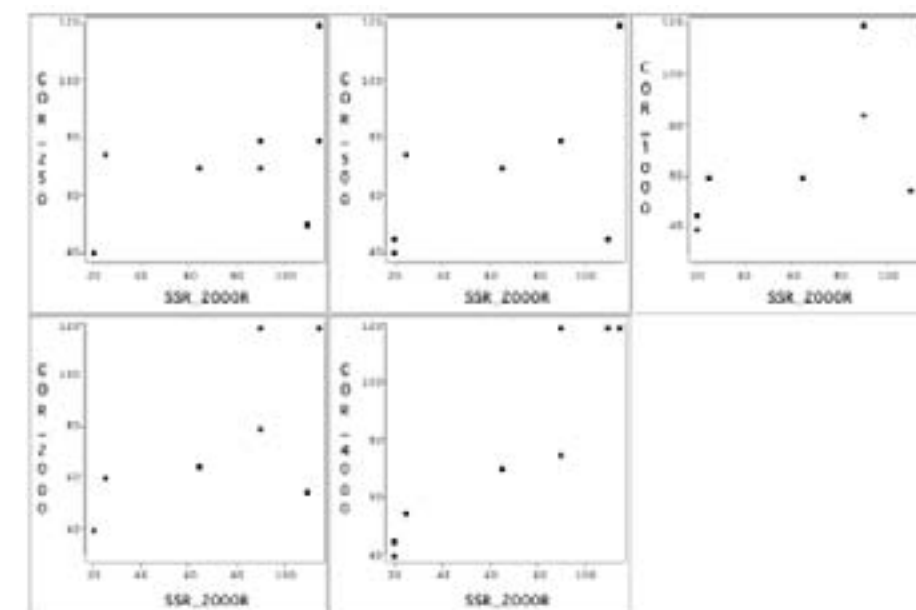


Fig. 2. Distribution of ASSR data (x-axis in all graphs) from right ears at 2000 Hz and all tested COR variables (y-axis in all graphs). The scatter plots show the relationships quantified by the estimated correlations.

Results

ASSR-COR

The distribution of the estimated hearing thresholds via the ASSR and COR protocols presented very different profiles at all tested frequencies. Figures 1 and 2 depict these differences at 1000 and 2000 Hz. For example, in Figure 1 the ASSR distribution is shifted to the left while the COR distribution is shifted to right and extends the threshold range to a value of 120 dB HL. This range-extension pattern was observed at all COR tested frequencies.

The relationship between the two protocols is shown in Tables I (right ear) and II (left ear). From a COR point of view, the correlation pattern with the ASSR frequencies, across the left and right ears, was not the same. For the left ear responses, the 1000 Hz COR values were significantly related to ASSR at 4 frequencies. For the right ear responses, all tested COR frequencies correlated with at least 2 ASSR frequencies.

From the ASSR point of view, the overall pattern was that the ASSR responses at 500 and 1000 Hz were significantly correlated with 5 of 5 COR tested frequencies. The left and right ear responses from the ASSR 2000 Hz data set showed significant correlation only with the COR responses from 4000 Hz. Interestingly, the responses from the ASSR 4000 Hz dataset (right ear) were significantly correlated only with the COR responses from 1000, 2000 and 400 Hz. No significant correlations were observed for the ASSR left ear responses at 4000 Hz and any of the COR variables. This observation may imply a side effect (i.e. left, right) of the data.

ABR-COR

All values but the COR responses at 250 Hz and right ear ABRs were significantly correlated. The highest cor-

relation values (0.675) was observed between the COR response at 4000 Hz and the right-ear ABR response. No effects (i.e. preference) linked to the tested side (right or left) were observed. The data are shown in Table III and Figure 3.

OAE-COR

Only the variables concerning the right ear (except at the 250 Hz frequency) were correlated. There was no significant correlation between the left ear TEOAE values and the COR variables. The data are summarized in Table IV.

ASSR-ABR

This analysis was conducted to create an “indirect metric” or condition useful for the comparison between ASSR and COR threshold estimates. In this context, the ABR assessment was considered the gold standard. The ASSR values were significantly correlated with the ABR threshold estimates at all tested frequencies and the observed correlations were much higher than those observed in the ABR-COR presented in section 2 (see Table III). For both ears, the highest correlation (0.927 right ear, 0.898 left ear) was observed at 2000 Hz. The data are summarized in Table V.

Table I. Strength of association between COR and ASSR measurements. Data from the right ear of the subjects at five COR frequencies (250-4000 Hz) and four ASSR frequencies (500-4000 Hz). The table shows the correlation value and below the corresponding probability.

| | COR 250 | COR 500 | COR 1000 | COR 2000 | COR 4000 |
|-----------|---------|---------|-----------|------------|-----------|
| ASSR 500 | 0.629 | 0.643 | 0.735 | 0.665 | 0.705 |
| p-value | 0.019* | 0.019* | 0.003** | 0.015* | 0.011* |
| ASSR 1000 | 0.728 | 0.764 | 0.847 | 0.861 | 0.891 |
| p-value | 0.011* | 0.005** | < 0.001** | < 0.0001** | < 0.001** |
| ASSR 2000 | 0.600 | 0.644 | 0.750 | 0.756 | 0.936 |
| p-value | 0.198 | 0.198 | 0.130 | 0.130 | < 0.001** |
| ASSR 4000 | 0.784 | 0.919 | 0.908 | 0.943 | 0.941 |
| p-value | 0.130 | 0.056 | < 0.001** | < 0.001** | < 0.001** |

* $P < 0.05$; ** $P < 0.01$

Table II. Strength of association between COR and ASSR measurements. Data from the left ear of the subjects at five COR frequencies (250 – 4000 Hz) and four ASSR frequencies (500 – 4000 Hz). The table shows the correlation value and below the corresponding probability.

| | COR 250 | COR 500 | COR 1000 | COR 2000 | COR 4000 |
|-----------|---------|---------|----------|----------|----------|
| ASSR 500 | 0.597 | 0.643 | 0.660 | 0.624 | 0.660 |
| p-value | 0.011* | 0.003** | 0.003** | 0.008** | 0.007** |
| ASSR 1000 | 0.504 | 0.591 | 0.652 | 0.617 | 0.504 |
| p-value | 0.007** | 0.045* | 0.017* | 0.047* | 0.130 |
| ASSR 2000 | 0.497 | 0.684 | 0.696 | 0.620 | 0.812 |
| p-value | 0.198 | 0.056 | 0.052 | 0.119 | 0.010* |
| ASSR 4000 | 0.404 | 0.502 | 0.549 | 0.465 | 0.688 |
| p-value | 0.198 | 0.198 | 0.198 | 0.198 | 0.119 |

* $P < 0.05$; ** $P < 0.01$

Differences between the correlation values of ASSR-ABR, COR-ABR:

To assess any statistical differences between the estimated correlations in sections 1 and 2, correlation differences (or prediction errors) were estimated between the ASSR-ABR and COR-ABR sets. The raw p-values did not show any significance at the 0.05 level, suggesting that there are no differences in the correlations between ASSR-ABR and COR-ABR.

Discussion and conclusions

Auditory deterioration in infants and children with early hearing loss has been shown to be reduced by auditory intervention within 6 months after birth. As a result, the average age for cochlear implantation is decreasing. Obtaining precise and objective hearing information for a subject in order to guide forthcoming intervention strategies is becoming increasingly important^{1-12 27 28}.

Information on hearing status is commonly obtained by pure tone audiometry; however, for infants and young children it is not always possible to obtain reliable hearing information, as a result of a lack of cooperation and the inability to understand the testing procedure. Alternative approaches to assess hearing threshold in children include the ABR and the ASSR which provide frequency-specific information²⁸⁻³⁵. In addition, visual reinforcement tools may contribute to information regarding low frequency hearing and uncomfortable loudness levels in the case of hearing aid fitting²⁸⁻³².

The present study investigated the relationship between the COR and three standardized procedures in hearing assessment (OAEs, ABR, ASSR). Since a threshold gold standard was not available, the COR and ASSR threshold estimates were evaluated according to their relationship with the ABR threshold values. The analyses highlighted the following:

1. As expected, the data indicate that the threshold estimates obtained with the ASSR and ABR are highly correlated at all tested frequencies. This corroborates with findings in previous reports^{8 9 18 27 28 31}. The data, however, do not offer information on the precision and accuracy of the ASSR measurement.
2. The COR threshold values were correlated with the ABR data, but the observed relationships were not as strong as those observed in the ASSR-ABR dataset. The estimated correlation differences between (ABR-ASSR) and (ABR-COR) were not significant. This finding suggests that although the COR and the ASSR data are associated differently with the ABR threshold values, the observed ASSR threshold estimation errors are not statistically significant from the COR errors.
3. The analysis of the COR-OAE relationship indicated that the COR variables present a “preference” towards the right ear. For left ear measurements, no significant

Table III. Correlation between the COR and ABR (click) variables. The L, R letters in the ABR column indicate left and right ear responses. Starred values indicate statistical significance. The correlation maxima are different between ears. For the right ear, the highest correlation was observed at 4000 Hz, while for the left ear at 1000 Hz.

| COR (Hz) | ABR (Click) | Correlation | p value |
|----------|-------------|-------------|-----------|
| 250 | R | 0.420 | 0.078 |
| 500 | R | 0.506 | 0.017* |
| 1000 | R | 0.629 | 0.001** |
| 2000 | R | 0.604 | 0.003** |
| 4000 | R | 0.675 | < 0.001** |
| 250 | L | 0.526 | 0.010* |
| 500 | L | 0.594 | 0.002** |
| 1000 | L | 0.670 | < 0.001** |
| 2000 | L | 0.575 | 0.005** |
| 4000 | L | 0.629 | 0.002** |

* $P < 0.05$; ** $P < 0.01$

Table IV. Correlation between COR and the presence of a TEOAE response. The r and l letters in the OAE column indicate responses from the right and left ear. Significant correlations are only presented for the right ear OAEs.

| COR (Hz) | OAE | Correlation | p-values |
|----------|-----|-------------|----------|
| 250 | R | 0.390 | 0.056 |
| 500 | R | 0.421 | 0.027* |
| 1000 | R | 0.460 | 0.017* |
| 2000 | R | 0.466 | 0.020* |
| 4000 | R | 0.496 | 0.012* |
| 250 | L | 0.361 | 0.056 |
| 500 | L | 0.344 | 0.095 |
| 1000 | L | 0.342 | 0.130 |
| 2000 | L | 0.347 | 0.130 |
| 4000 | L | 0.360 | 0.130 |

* $P < 0.05$

Table V. Correlation between ASSR and ABR responses. The r and l letters in the ABR column indicate responses from the right and left ear.

| ASSR (Hz) | ABR | Correlation | p-values |
|-----------|-----|-------------|-----------|
| 500 | R | 0.869 | < 0.001** |
| 1000 | R | 0.870 | 0.004* |
| 2000 | R | 0.927 | 0.019* |
| 4000 | R | 0.921 | < 0.001** |
| 500 | L | 0.882 | < 0.001** |
| 1000 | L | 0.825 | 0.001** |
| 2000 | L | 0.898 | 0.001** |
| 4000 | L | 0.868 | 0.016* |

* $P < 0.05$; ** $P < 0.01$

correlations were observed. This observation might be a direct consequence of how the COR technique is executed with the subject turning its head towards the sound stimulus, favouring one ear over the other.

4. The analysis of the COR and ASSR variables showed significant correlations in the majority of frequencies tested. The data presented in Figures 1 and 2 show another characteristic of the COR procedure, which is underestimation of the hearing threshold (in comparison to the ASSR estimate). The latter is shown by the increase in the hearing threshold range from 90 (max estimate of the ASSR assessment) to 120 dB HL. The latter could have been influenced by a number of factors such as (i) the presentation of the stimulus (i.e. intensity of sound arriving at the ear); (ii) the age of the infant/child and its adaptive response to sound; and (iii) the evaluation of response by the operator. These factors are cumulative and can affect the COR assessment in multiple ways, but the mechanics and interactions of these factors were not evaluated in the present study.

The data show that the COR threshold assessment follows the pattern of the other two established electrophysiological methods (ABR, ASSR). The correlation analyses did not permit an evaluation of the precision of these estimates. Considering that the ASSR assessment shows a better relationship with ABR (higher correlation values) than COR, it might be advantageous to utilize such an approach to gain frequency-specific information.

To fine-tune these findings, it is necessary to use a larger sample to eliminate the variability induced by the various techniques in the assessment of hearing threshold.

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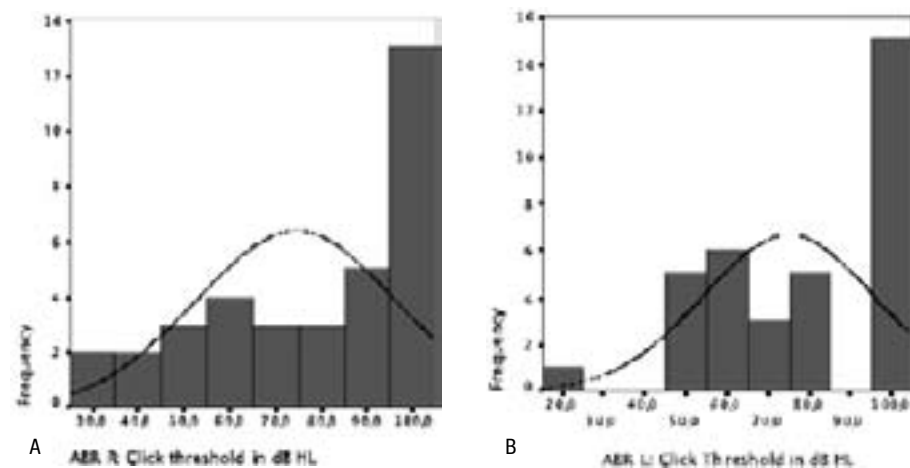


Fig. 3. Distribution of click-evoked ABR thresholds from the right and left ears. Both distributions show asymmetries to the right.

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