Hearing threshold prediction with Auditory Steady State Responses and estimation of correction functions to compensate for differences with behavioral data, in adult subjects.

Part 1: Audera and CHARTR EP devices

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Summary

Background: The objective of the study was the evaluation and comparison of hearing threshold values extrapolated from Auditory Steady State Responses, using 2 commercial systems and the estimation of correction factors applicable to the ASSR data.

Material/Methods: One hundred ten subjects participated in the study. All subjects were initially examined with otoscopy, pure-tone audiometry, and admittance. Data were acquired by 2 clinical systems: the Audera (Viasys) and the CHARTR EP (ICS), using identical protocols. The acoustic stimuli consisted of single carrier frequencies at 1000, 2000, and 4000 Hz modulated at 40 Hz.

Results: The data show that the threshold estimates from both devices differ significantly from the measured behavioral thresholds. The ICS device presented significantly larger mean-ASSR estimated hearing level values at the tested frequencies, implying an underestimation of the hearing threshold. Both sets of prediction errors overestimated hearing levels for the normal group. The prediction errors were in all cases greater for the Audera than for the ICS.

Conclusions: The errors encountered in the estimates of the 2 widely-used commercial devices suggest that the current ASSR protocols are not ready for a wide-range use and that significant developments in the area of threshold prediction/precision are necessary. If, on the other-hand, the ASSR predicted threshold is used on a purely consulting basis, as in hearing-aid fitting, then such errors might be acceptable in a clinical setting.

key words: ASSR • Steady State • modulation • hearing threshold estimation • normal • hearing impairment

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BACKGROUND

The last decade auditory steady state responses (ASSRs) have been proposed as a clinical tool for use in gaining more information about the hearing threshold, especially at the low frequencies threshold [1,2]. The ASSRs are recorded in response to pure tones, which are modulated in amplitude or frequency, and are frequency-specific. It is assumed that the electrical sources of the ASSR arise from multiple sources, partly in the cortex, partly in the brainstem, with different contributions depending on the temporal pattern of the stimuli [3–5].

Recent studies have demonstrated that the ASSR responses can be recorded at each frequency, with stimuli at levels close to the behavioral threshold [1,2,6,7]. This represents an important development in pediatric audiology, given the possibility that this technique could evaluate hearing in the low-middle frequency range. Indeed, as the most popular evoked responses (auditory brainstem response) are elicited by acoustic transients, they may precisely estimate the hearing at 2–4 kHz only. ASSR has multiple applications with regard to hearing screenings and diagnostic audiometry. ASSR facilitates a rapid and statistically valid estimate of hearing thresholds, and can add significant threshold information while evaluating patients unable or unwilling to participate in behavioral tests [2].

The relationship between hearing threshold and ASSR is quite complicated and depends on numerous parameters such as the hearing level, the audiometric frequency, the ASSR modulation frequency, and the ASSR detection algorithm, which is the algorithm that provides the threshold values from ASSR values. Data from the literature suggest that ASSR protocols can predict hearing levels from subjects with hearing deficits in the frequencies 2000 and 4000 Hz, while threshold prediction in normal hearing adults presents significant errors [8–11].

In a previous paper [12], we suggested that the difference between ASSR and behavioral threshold significantly decreases with the amount of hearing loss. The relationship followed a linear form of the type y=ax+30, where y is the ASSR threshold and x the behavioral threshold. Our data showed that for a10 dB increment of the PTA behavioral threshold, the ASSR threshold increased by 7 dB. This means that the difference between the 2 measurements (30 dB as predicted by the intercept) tends to cancel-out when the hearing loss reaches 95–100 dB (severe-to-profound hearing loss cases). In this context it is advantageous to examine the clinical performance of ASSR threshold estimation in cases presenting normal hearing levels, or mild-to-moderate hearing losses.

The objective of the study was two-fold. First, the hearing threshold was assessed with 2 widely-used clinical ASSR devices and inter-subject and inter-group differences were calculated. Second, to improve the clinical applicability of the ASSR estimated hearing levels, correction functions were computed from the available behavioral data and applied to the ASSR values.

MATERIAL AND METHODS

Subjects

One hundred ten subjects – 37 males and 73 females – participated to the study. All subjects were initially examined with otoscopy, pure-tone audiometry and admittance. Eighty-five subjects presented normal hearing thresholds (ie, <20 dB HL) at the frequencies 125 to 8000 Hz and 25 presented steeply sloping, high-frequency, sensorineural hearing losses (>25 dB HL) at 4000 and 8000 Hz. The behavioral hearing thresholds were obtained with the TDH 49 earphone transducer.

ASSR recordings

All subjects were tested in a supine position within a sound-treated and electrically shielded room. The only instructions were to relax and to avoid excessive movements.

Data were acquired by 2 clinical systems – the Audera (Viasys) and the CHARTR EP (ICS), using identical protocols. Additional details on the Audera protocol can be found in a previous publication [12]. The steady state potentials were collected by means of surface electrodes, with a vertex-mastoid montage, ipsilateral to the stimulated ear. The electrode impedance prior to the recordings was less than 5 kΩ. The acoustic stimuli consisted of single carrier frequencies at 1000, 2000, and 4000 Hz modulated at 40 Hz. The stimulus intensity was initially set to 30–40 dB above the behavioral threshold, and then changed by descending and ascending steps of 5 and 10 dB, respectively, until the minimal intensity corresponding to a significant ASSR was determined.

Statistical analyses

Since left and right ears showed ASSR responses with very high positive correlations (>0.9 in most cases), it was decided to average the L-R values and weight observations for all subjects equally. For each tested frequency, the pairwise differences for each subject were taken and 95% and 99% confidence intervals for the mean difference were computed. Three sets of difference data were generated: (i) Audera – PTA; (ii) ICS-PTA; and (iii) Audera-ICS.

For the correction of the obtained ASSR data, a statistical 3-stage approach was devised and the full details are reported in the Appendix.

RESULTS

Audera and PTA measurements

Pearson correlation estimates and stepdown-Bonferroni-adjusted p-values were obtained for the ASSR and PTA measurements, for both normal and hearing impaired subjects. For the normal group, significant and very significant correlations were observed at 1 and 2 kHz (0.4611 p=0.0234, 0.6961, p<0.0001), while at 4 kHz the correlation was not significant (0.3632, p=0.1064). For the hearing impaired group all correlations were very significant (0.8418, p<0.0001; 0.9139, p<0.0001; 0.9158, p<0.0001), with the highest value at 4 kHz.

For each tested frequency, the pairwise differences between the pure tone audiometry hearing thresholds and the Audera-derived hearing levels for each subject were taken, and level 95% and 99% confidence intervals for the mean difference were computed. All intervals showed a higher
mean Audera value compared with mean PTA. The data are summarized in Table 1A.

**ICS and PTA measurements**

Pearson correlation estimates and stepdown- Bonferroni-adjusted p-values were obtained for the ASSR and PTA measurements, for both normal and hearing impaired subjects. For the normal group, no significant correlation values were observed at 1 and 4 kHz (–0.2947 p=0.0801, –0.0398 p=0.7648), while very significant values were observed at 2 kHz (–0.3773 p=0.0080). For the hearing impaired group, all correlations were very significant (0.8191, p<0.0001; 0.9123, p<0.0001; 0.8868, p<0.0001), with the highest value at 2 kHz.

As in the previous section, significant and very significant mean pairwise differences were observed between the pure tone audiometry hearing thresholds and the ICS derived hearing levels, at all tested frequencies. All intervals show a higher mean ICS value compared with mean PTA. The data are summarized in Table 1B.

**Audera and ICS measurements**

The mean pairwise differences in hearing thresholds from the 2 devices were found to be statistically different in all 3 tested frequencies. All intervals showed a higher mean ICS value compared with mean AUDERA. The data are summarized in Table 1C.

**Correction functions and the Audera, ICS-derived hearing thresholds**

The Appendix describes the 3-stage procedure used to obtain correction functions for the Audera and ICS-derived hearing thresholds. The problem can be thought of as a prediction problem: how can one best predict the PTA threshold from an “Audera or ICS” measurement? The reason for the chosen procedure can perhaps be explained by looking at Figures 1–6, which show the PTA versus Audera and ICS thresholds. The black plusses show values for the subjects with normal hearing, the gray circles for the hearing impaired. A simple regression function (linear or non-linear) of the PTA on the Audera values would provide a prediction that would be highly dependent on the relative numbers of normal and impaired subjects in the study. To avoid this problem, the likelihood of an impaired subject being given the Audera or ICS, the threshold was first estimated. This quantity would be less dependent on the normal/impaired mix in the sample. Prediction functions for each group (normal and impaired) were computed by simple linear regression, and the final prediction was an average of these weighted by the likelihood of a subject being impaired or normal. The grey curves in Figures 1–3 show the resulting prediction functions, which serve as correction functions for the device at various frequency combinations. Table 2 summarizes these data. The first column of Table 2 shows the ASSR-predicted hearing level, while the other columns show the correction of this value per frequency and per device. For example, for a predicted hearing level value of 50 dB HL, the corrected values for Audera are: 29.67, 24.23 and 21.05 dB HL for 1.0, 2.0 and 4.0 kHz, respectively. For ICS the corrected values are 13.81, 9.86, 9.13 dB HL for 1.0, 2.0 and 4.0 kHz, respectively. The data show that the adjustments were more severe for ICS than for Audera.

**Discussion**

The objective of the study was the evaluation of ASSR-estimated hearing levels at 1, 2 and 4 kHz, obtained with 2 commercial devices. The data show that the threshold estimates from both devices differ significantly from the measured behavioral thresholds. This fact suggests that the ASSR threshold values cannot be as useful as intended in the evaluation of hearing impairment in children and adults.

### Table 1. Comparison of hearing levels between the ASSR devices and behavioral values: (A) Comparison between Audera and behavioral values (PTA). The second column reports the tested frequencies. The other two columns report the confidence intervals of the mean differences at 95% and 99% accuracy. Starred values indicate statistically significant differences. (B) Comparison between the ICS and behavioral values. The format follows that of (A). (C) Comparison between the Audera and the ICS estimated hearing levels. The format follows that of (A).

| Frequency | 95% Interval | 99% Interval |
|-----------|--------------|--------------|
| Audera vs. PTA: A | | |
| 1 kHz | –7.57 to –3.14* | –8.31 to –2.41** |
| 2 kHz | –9.45 to –3.68* | –10.40 to –2.72** |
| 4 kHz | –37.23 to –28.93* | –38.58 to –27.58** |
| ICS vs. PTA: B | | |
| 1 kHz | 23.06 to 28.75* | 22.13 to 29.68** |
| 2 kHz | 23.84 to 30.56* | 22.74 to 31.66** |
| 4 kHz | 28.93 to 37.23* | 27.58 to 38.58** |
| Audera vs. ICS: C | | |
| 1 kHz | –7.57 to –3.14* | –8.31 to –2.41** |
| 2 kHz | –9.45 to –3.68* | –10.40 to –2.72** |
| 4 kHz | –37.23 to –28.93* | –38.58 to –27.58** |
One way to address the high-variance threshold estimates from the various ASSR devices is to introduce a correction procedure. Similar procedures are already incorporated in the majority of ASSR equipment, and the details of these procedures are not available to the public. It is assumed that the correction function is based on a regression-fit approach, which is very popular in the estimation of the hearing threshold as well. This approach presents a strong bias related to the data used to obtain the regression estimates. In this context, samples that well represent the properties of both groups (probably large in size) are required to calibrate the recorded ASSR potentials and extrapolate the hearing threshold values. Regarding sample sizes, large representative samples are preferable to small representative samples and to unrepresentative samples of any size, but small representative samples are preferable to unrepresentative samples of any size.

In this study we addressed the issue of the large sample size requirements and its “population representativeness” with a 3-step procedure. Nevertheless, the accuracy of the calculated correction functions depends on the features of the ASSR responses. A key feature of the proposed procedure is the estimation of the likelihood of a subject presenting sensorineural deficits, given the Audera or ICS threshold measurement. Such a subject might have normal behavioral hearing levels at the low frequencies (ie, ≤1 kHz) and pronounced deficits in the midrange to high frequencies. The ASSR profile of such a case contains normative and hearing loss data. Summing up the profiles of all included cases, one can observe an overlap of frequency features in the low frequencies, which cause a bias in the estimated correction function. For example, Table 2 shows that for the observed Audera ASSR values at 1 kHz from 15 to 35 dB HL, the corrected values are ≤10 dB. To assess the quality of prediction, in-sample and cross-validated (leave
Table 2. Observed and corrected ASSR estimated hearing levels, per frequency and device.

| Observed ASSR threshold | Audera | Corrected ASSR Threshold | ICS Chartr EP |
|-------------------------|--------|--------------------------|---------------|
|                         | 1 kHz  | 2 kHz        | 4 kHz  | 1 kHz  | 2 kHz  | 4 kHz  |
| 10                      | 10.02  | 10.23        | 9.07   | 7.14   | 7.17   | 4.76   |
| 15                      | 7.79   | 8.07         | 8.35   | 6.10   | 6.22   | 4.71   |
| 20                      | 5.88   | 6.23         | 7.76   | 5.18   | 5.40   | 4.70   |
| 25                      | 4.94   | 5.07         | 7.44   | 4.51   | 4.79   | 4.77   |
| 30                      | 6.00   | 5.15         | 7.60   | 4.28   | 4.51   | 4.96   |
| 35                      | 9.84   | 7.06         | 8.61   | 4.78   | 4.69   | 5.35   |
| 40                      | 15.99  | 11.11        | 10.94  | 6.34   | 5.51   | 6.06   |
| 45                      | 22.98  | 17.09        | 15.03  | 9.30   | 7.18   | 7.25   |
| 50                      | 29.67  | 24.23        | 21.05  | 13.81  | 9.86   | 9.13   |
| 55                      | 35.73  | 31.71        | 28.61  | 19.72  | 13.65  | 11.95  |
| 60                      | 41.25  | 38.95        | 36.93  | 26.61  | 18.58  | 15.96  |
| 65                      | 46.42  | 45.74        | 45.16  | 33.94  | 24.49  | 21.29  |
| 70                      | 51.38  | 52.07        | 52.78  | 41.24  | 31.17  | 27.91  |
| 75                      | 56.23  | 58.00        | 59.62  | 48.22  | 38.32  | 35.55  |
| 80                      | 61.01  | 63.65        | 65.77  | 54.77  | 45.64  | 43.78  |
| 85                      | 65.77  | 69.11        | 71.36  | 60.90  | 52.90  | 52.13  |
| 90                      | 70.50  | 74.43        | 76.57  | 66.68  | 59.96  | 60.22  |
| 95                      | 75.23  | 79.67        | 81.52  | 72.17  | 66.72  | 67.82  |
| 100                     | 79.96  | 84.85        | 86.29  | 77.45  | 73.17  | 74.83  |
| 105                     | 84.68  | 90.00        | 90.95  | 82.57  | 79.31  | 81.29  |
| 110                     | 89.40  | 95.12        | 95.54  | 87.59  | 85.18  | 87.27  |

1 out) prediction errors of the form (y-E(y|x)) were computed for all the prediction functions (see Appendix). As expected, both sets of prediction errors display little bias for the combined data, but overestimate hearing levels for the normal group. The observed over-and under-estimates are more severe when the 2 groups overlap substantially in
The errors encountered in the estimates of the 2 widely-used commercial devices suggest that the current ASSR protocols are not ready for wide-range use and that significant developments in the area of threshold prediction/precision are necessary. If, on the other-hand, the ASSR predicted threshold is used on a purely consulting basis, as in hearing-aid fitting, then such errors might be acceptable in a clinical setting.

**Appendix**

Three Stage Prediction using Ordinary Least Squares (OLS)

In order to use the AUDERA and ICS measurements in the prediction of the behavioral hearing level and overcome the fact that the data did not represent a truly random sample, the following three-stage approach was devised.

In what follows, \( y \) represents the response being predicted (here the behavioral value), and \( x \) the predictor (here either the AUDERA or ICS measurement). The conditional expectation \( E(y|x) \) is used as the predictor. One might try to do the prediction by fitting a linear regression model to the data. However, the result can be severely biased if the data are not a random sample. To circumvent this problem, the prediction was done in three stages.

**First stage**

Estimate the probability a subject is impaired given the observed value of \( x \). Logistic regression was chosen as the most common method for estimating:

\[
p(x) = \frac{\beta_0 + \beta_1 x}{1 + \beta_0 + \beta_1 x}
\]

where \( \beta_0 \) and \( \beta_1 \) are estimated from the data.

**Second stage**

Simple linear regression was used to predict \( y \) for each group separately. For the normal group, the predictor was \( E(y|x, \text{normal}) = \delta_0 + \delta_1 x \). For the impaired group, the predictor was \( E(y|x, \text{impaired}) = \gamma_0 + \gamma_1 x \), where \( \delta_0, \delta_1, \gamma_0, \gamma_1 \) are estimated from the data.

**Third stage**

The data from Stage two were combined to obtain:

\[
E(y|x) = E(y|x, \text{normal}) p(x) + E(y|x, \text{impaired}) (1 - p(x))
\]

where \( p(x) = \frac{\beta_0 + \beta_1 x}{1 + \beta_0 + \beta_1 x} \).

The various parameter estimates from the data are reported in Table 3. To assess the quality of prediction, in-sample prediction errors of the form \( (y-E(y|x)) \) were computed for the prediction functions. Table 4 shows their means and standard deviations for the combined data and for each group separately. Cross-validated (leave one out) prediction errors were also obtained. Their means and standard deviations are shown in Table 5.
### Table 3. Model estimated-parameters.

| Fit       | Overall | Normal group | Impaired group |
|-----------|---------|--------------|----------------|
| p1/a1     | 0.0000 (9.407) | −1.597 (7.835) | 3.372 (11.616) |
| p2/a2     | 0.0000 (11.117) | −2.986 (10.100) | 6.303 (10.764) |
| p4/a4     | 0.0000 (12.584) | −4.471 (9.115) | 9.438 (13.875) |
| p1/i1     | 0.0000 (10.118) | −2.610 (7.585) | 9.424 (13.770) |
| p2/i2     | 0.0000 (11.779) | −3.446 (8.563) | 12.444 (13.559) |
| p4/i4     | 0.0000 (16.136) | −5.713 (11.141) | 21.843 (13.492) |

### Table 4. In-sample prediction errors: means (std. deviation).

| Fit       | Overall | Normal group | Impaired group |
|-----------|---------|--------------|----------------|
| p1/a1     | 0.069 (10.182) | −1.743 (8.339) | 3.896 (12.697) |
| p2/a2     | −0.059 (11.132) | −3.236 (10.847) | 6.647 (11.590) |
| p4/a4     | 0.053 (13.399) | −4.729 (9.638) | 10.147 (14.821) |
| p1/i1     | 0.064 (10.746) | −2.707 (7.851) | 10.070 (13.770) |
| p2/i2     | 0.027 (12.398) | −3.573 (8.873) | 13.027 (14.716) |
| p4/i4     | −0.031 (16.780) | −5.928 (11.627) | 22.5193 (14.251) |

### Table 5. Cross-validated prediction errors: means (std. deviation).

| Fit       | Overall | Normal group | Impaired group |
|-----------|---------|--------------|----------------|
| p1/a1     | 0.069 (10.182) | −1.743 (8.339) | 3.896 (12.697) |
| p2/a2     | −0.059 (11.132) | −3.236 (10.847) | 6.647 (11.590) |
| p4/a4     | 0.053 (13.399) | −4.729 (9.638) | 10.147 (14.821) |
| p1/i1     | 0.064 (10.746) | −2.707 (7.851) | 10.070 (13.770) |
| p2/i2     | 0.027 (12.398) | −3.573 (8.873) | 13.027 (14.716) |
| p4/i4     | −0.031 (16.780) | −5.928 (11.627) | 22.5193 (14.251) |

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