Sensitivity and specificity of auditory steady-state response testing

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INTRODUCTION: The ASSR test is an electrophysiological test that evaluates, among other aspects, neural synchrony, based on the frequency or amplitude modulation of tones.

OBJECTIVE: The aim of this study was to determine the sensitivity and specificity of auditory steady-state response testing in detecting lesions and dysfunctions of the central auditory nervous system.

METHODS: Seventy volunteers were divided into three groups: those with normal hearing; those with mesial temporal sclerosis; and those with central auditory processing disorder. All subjects underwent auditory steady-state response testing of both ears at 500 Hz and 2000 Hz (frequency modulation, 46 Hz). The difference between auditory steady-state response-estimated thresholds and behavioral thresholds (audiometric evaluation) was calculated.

RESULTS: Estimated thresholds were significantly higher in the mesial temporal sclerosis group than in the normal and central auditory processing disorder groups. In addition, the difference between auditory steady-state response-estimated and behavioral thresholds was greatest in the mesial temporal sclerosis group when compared to the normal group than in the central auditory processing disorder group compared to the normal group.

DISCUSSION: Research focusing on central auditory nervous system (CANS) lesions has shown that individuals with CANS lesions present a greater difference between ASSR-estimated thresholds and actual behavioral thresholds; ASSR-estimated thresholds being significantly worse than behavioral thresholds in subjects with CANS insults. This is most likely because the disorder prevents the transmission of the sound stimulus from being in phase with the received stimulus, resulting in asynchronous transmitter release. Another possible cause of the greater difference between the ASSR-estimated thresholds and the behavioral thresholds is impaired temporal resolution.

CONCLUSIONS: The overall sensitivity of auditory steady-state response testing was lower than its overall specificity. Although the overall specificity was high, it was lower in the central auditory processing disorder group than in the mesial temporal sclerosis group. Overall sensitivity was also lower in the central auditory processing disorder group than in the mesial temporal sclerosis group.

KEYWORDS: Auditory evoked potentials; Auditory Perception; Electrophysiology; Temporal lobe epilepsy.

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The ASSR test is most commonly used for estimating behavioral thresholds. It has been used in research to estimate residual hearing in pediatric candidates for cochlear implants, to confirm auditory thresholds,\(^4\),\(^6\) to draw comparisons between click-evoked auditory brain stem responses, ASSRs and behavioral thresholds,\(^7\),\(^8\) and to diagnose neonates who present evidence of auditory neuropathy.\(^9\)

In order to use the ASSR test in clinical practice, it must be borne in mind that the presence of an ASSR threshold (at any frequency) is determined largely by the integrity of the cochlea and the eighth cranial nerve. Therefore, no responses will be observed unless there is neural synchrony. Neuropathology and variations among subjects can influence the responses.\(^10\) Studies of patients with neurologic insults have been conducted in order to determine the influence of cortical lesions on temporal processing, as well as to gauge the sensitivity and specificity of tests in this population.\(^11\),\(^12\)

However, the ASSR test has yet to be used in the investigation of central auditory processing disorders (CAPDs).

Research focusing on central auditory nervous system (CANS) lesions has shown that, compared with normal subjects, individuals with CANS lesions present a greater difference between ASSR-estimated thresholds and actual behavioral thresholds; ASSR-estimated thresholds being significantly worse than behavioral thresholds in subjects with CANS insults. This is most likely because the disorder prevents the transmission of the sound stimulus from being in phase with the received stimulus, resulting in asynchronous transmitter release. As a result of this inappropriate discharge of neurons in the cortical and subcortical areas, ASSR determination has not been considered a valid test.\(^4\),\(^12\),\(^13\)

Another possible cause of the greater difference between the ASSR-estimated thresholds and the behavioral (registered) thresholds is impaired temporal resolution. According to Shinn and Musiek, patients with neurologic insult may be incapable of phase locking to the stimulus.\(^12\)

This affects neural synchrony and, consequently, reduces temporal resolution. Using a cut-off value of 20 dB (the mean difference between the ASSR-estimated threshold and the behavioral threshold plus one standard deviation), the authors found that the sensitivity of the ASSR test was 64% for detecting lesions of the CANS (the brain stem, cortical areas, and subcortical areas). Sensitivity decreased to 45% when a cut-off value of 28 dB (the mean difference plus two standard deviations) was used. The specificity of the test was found to be higher when the cut-off value was 28 dB than when it was 20 dB (91% vs. 81%).

Based on the findings of the studies reviewed, the aim of the present study was to determine the sensitivity and specificity of the ASSR test for the detection of lesions and dysfunctions of the CANS. We focused on CAPDs, since there have been no studies employing the ASSR test in the investigation of such disorders.

MATERIALS AND METHODS

We evaluated 70 volunteers between 16 and 50 years of age, recruited from the School of Medicine, University of São Paulo. The sample was divided into three groups: normal-hearing subjects without auditory complaints or neurologic insults (normal group; n = 30); subjects with mesial temporal sclerosis (MTS), as diagnosed by imaging exams (MTS group; n = 16); and subjects with CAPD, as diagnosed using behavioral tests (CAPD group; n = 24). The mean age for the normal group was 25 years, 39 years for the MTS group and 24 years for the CAPD group.

Procedures were conducted in the Auditory Processing Laboratory of the Speech and Hearing Department of the School of Medicine, University of São Paulo. The study design was approved by the University of São Paulo Research Ethics Committee. All participants gave written informed consent.

Subjects in the MTS group had been diagnosed with temporal lobe insult by a neurologist, based on functional magnetic resonance imaging studies. Subjects having previously undergone neurologic surgery were excluded. The time since insult was not a criterion for inclusion in the MTS group. The diagnosis of auditory processing disorders were made using the following behavioral tests: the staggered spondaic word test; the frequency pattern test; the duration pattern test; the dichotic digits test; the speech-in-noise test and the Gaps-in-Noise (GIN) test. All subjects had to have poor performance at least in two of the six tests applied.

Subjects in the CAPD group were diagnosed using the following behavioral tests: the staggered spondaic word test; the frequency pattern test; the duration pattern test; the dichotic digits test; the speech-in-noise test and the GIN test. Subjects were included in the CAPD group if they performed poorly on at least in two of the six tests applied.

All of the tests had been translated into Portuguese and validated for use in Brazil. Using a battery of six tests rather than a single test allowed us to reduce the chance of error and increase the precision of the diagnosis.

An inclusion criterion for all groups was presenting a hearing threshold of 25 dB HL or lower, in both ears, at all of the frequencies evaluated (250 to 8000 Hz). All participants underwent a basic audiometric evaluation and a case history interview in order to rule out peripheral auditory disorders. For the audiometric testing, we used a GSI-61 audiometer (Grason-Stadler, Madison, WI, USA). The calibrations were made in accordance with American National Standards.\(^14\) Subjects were evaluated in a sound-treated environment using the traditional Hughson-Westlake procedure. To be eligible for ASSR testing, subjects were required to present normal tympanometry results, with a peak between -50 and +50 daPa.

ASSR TESTING

ASSR testing was conducted using the AUDERA™ system (Grason-Stadler). We used the “Awake” protocol, which is designed for use with subjects over 10 years of age and requires participants to remain awake during the testing. The protocol includes a fixed frequency modulation of 46 Hz regardless of the carrier frequency used. The stimuli used in this protocol are sinusoidal in nature. For each frequency tested, the combined amplitude modulation is 100% and the frequency modulation is 10%.

Electroencephalography was performed using a 50-ms window. The trial was terminated if a phase-locked response was identified or after 64 sweeps had been made (in accordance with the equipment protocol). For each carrier frequency, a different signal-to-noise ratio was used (also in accordance with the equipment protocol). Stimuli were calibrated at 0 dB nHL and responses were obtained in a sound-treated environment.
The ASSR test was conducted with the patient seated in a comfortable chair inside a sound-treated room. The skin was prepared for electrode placement by cleaning the electrode site with an abrasive paste. The silver electrodes were placed according to the international 10-20 system of electrode placement: the forehead electrode was attached as high on the forehead as possible; the left and right electrodes were attached to the left and right mastoids; and the common electrode was attached to the lower forehead. Therefore, the inverting lead was ipsilateral to the stimulated ear. The impedance was set to < 5 kΩ for all electrodes. The stimuli were delivered through insert earphones (TIP-50; Grason-Stadler).

The assessment began with a 1000-Hz stimulus, followed by stimuli at 2000 Hz, 4000 Hz, and 500 Hz. Each stimulus was presented to both ears (one ear at a time) and the first ear to be tested was selected at random. For all frequencies tested, the evaluation started at 50 dB HL. Thresholds were determined for each of the carrier frequencies (500, 1000, 2000, and 4000 Hz). However, because of difficulty in identifying thresholds at 4000 Hz, the proximity between 1000 and 2000 Hz, and as a result of the huge amount of data obtained during the study, we opted to analyze only two frequencies (500 and 2000 Hz).

When a phase-locked response was identified, the intensity was decreased in 10-dB steps until the response became random; in other words, the response was not determined to be present statistically. The intensity was then increased in 5-dB steps in order to determine the threshold. The ASSR threshold was defined as the lowest level at which a phase-locked response could be detected. If a noisy response was recorded, the evaluation was repeated in order to determine whether the response was random or phase-locked. After the threshold had been identified, the contralateral ear was tested or another frequency was applied.

At the end of each test, the equipment generated an audiogram with the actual electrophysiological threshold for each of the frequencies evaluated. Using an algorithm, the computer program provided with the equipment employs an algorithm to generate an additional audiogram that indicates the ASSR-estimated thresholds. The difference between the estimated threshold and the behavioral threshold was then calculated for 500 and 2000 Hz. The algorithm used in the “Awake” protocol was that proposed by Cone-Wesson et al. The authors described a different algorithm for each frequency and the thresholds are estimated based on those formulae. Once the behavioral thresholds have been established for a number of frequencies, the software offers the option of generating the audiogram showing the estimated thresholds.

**Statistical Analysis**

The statistical analysis was conducted using descriptive statistics (mean and standard deviation). We also employed analysis of variance with repeated measures, adopting the Bonferroni method. The cut-off values were selected based on the receiver operating characteristic (ROC) curves, which were constructed by combining the results obtained for the normal group with those obtained for the MTS group and with those obtained for the CAPD group.

**RESULTS**

Of the 70 subjects included in the study sample, 30 (42.9%) were normal hearing and neurologically intact individuals, 16 (22.9%) had suffered a neurologic insult, and 24 (34.2%) had CAPD.

Table 1 shows the estimated ASSR and behavioral thresholds at 500 and 2000 Hz, as well as the differences between the two thresholds for the groups assessed. The CAPD group thresholds were closer to those obtained for the normal group in both ears at all of the frequencies assessed, whereas the MTS group thresholds, behavioral and estimated ASSR, as well as the differences between the two thresholds, were much worse than those obtained for the other two groups.

At 500 Hz, there was a statistically significant difference between the two ears, in all groups, in terms of the mean difference between the estimated and behavioral thresholds (p = 0.010), the mean being greater for the left ear than for the right ear. The mean difference was less pronounced in the normal group than in the MTS group (p = 0.027), although the difference between the mean value in the normal group and that obtained for the CAPD group was not significant (p > 0.009). For this same parameter, a marginal difference was detected between the MTS group and the CAPD group (p = 0.090).

At 2000 Hz, there were no significant differences between the left and right ears in terms of the mean difference between the estimated and behavioral thresholds (p = 0.149). The mean difference between the thresholds was less pronounced in the normal group than in the MTS group (p = 0.000), although the difference between the mean value in the normal group and that obtained for the CAPD group was not significant (p > 0.009). The mean difference was

| Group | Age (in years) | ASSR-ET (in dB HL) | Behavioral Thresholds (in dB HL) | Difference | Difference |
|-------|----------------|--------------------|----------------------------------|------------|------------|
|       | 500 Hz         | 2000 Hz            | 500 Hz                           | 2000 Hz    |            |
|       | RE | LE | RE | LE | RE | LE | RE | LE | RE | LE |
| Normal | 25 | 5.67 | 7.67 | 17.0 | 20.0 | 6.33 | 5.67 | 3.17 | 2.5 | -0.67 | 2.0 |
|       | 3.3 | 14.37 | 12.64 | 11.64 | 12.87 | 5.24 | 4.10 | 4.25 | 3.88 | 12.91 | 13.36 |
| MTS    | 39 | 25.28 | 27.47 | 45.13 | 45.25 | 10.31 | 10.00 | 7.19 | 7.30 | 14.97 | 17.47 |
|       | 3.9 | 21.62 | 23.72 | 13.39 | 22.4 | 6.94 | 6.32 | 5.15 | 7.17 | 20.26 | 25.74 |
| CAPD   | 24 | 9.98 | 11.25 | 18.54 | 22.46 | 7.71 | 5.62 | 4.58 | 4.58 | 2.27 | 5.0 |
|       | 6.9 | 20.62 | 15.76 | 15.91 | 22.56 | 5.10 | 5.16 | 6.06 | 5.69 | 18.86 | 15.11 |

**ASSR** = auditory steady-state response test; **ASSR-ET** = ASSR-estimated threshold; **BT** = behavioral threshold; **RE** = right ear; **LE** = left ear; **MTS** = mesial temporal sclerosis; **CAPD** = central auditory processing disorder.
significantly greater in the MTS group than in the CAPD group (p = 0.000).

At 500 Hz, for the MTS group, there were no significant differences between the ear ipsilateral to the lesion and the contralateral ear. The only parameter for which there was a tendency for significant difference between ears was the mean estimated threshold (p = 0.083). However, at 2000 Hz, there were no significant differences between the ipsilateral and contralateral ears in any of the comparisons made (p > 0.1).

We used ROC curves to compare the mean difference between ASSR-estimated and behavioral thresholds, by ear and by group. However, at 500 Hz, there were no significant differences between the normal group and the CAPD group in terms of the mean thresholds in the right or left ears. Therefore, the ROC curves show only the comparisons between the normal group and the MTS group (Figures 1, 2, and 3).

The results obtained from the ROC curves suggested that the cut-off value at 500 Hz should be 5.3 dB for the right ear (Figure 1) and 12.6 dB for the left ear (Figure 2). At 2000 Hz, there was no difference between the normal group and CAPD group or between the left and right ears. Therefore, the cut-off value at 2000 Hz was set at 22.53 dB for the left and right ears (Figure 3).

Tables 2, 3 and 4 show the sensitivity and specificity of the ASSR test at each ROC curve coordinate.

### DISCUSSION

The results obtained with the 46 Hz ASSR test for the estimated threshold as well as for the behavioral threshold show that normal group and the CAPD group were comparable, whereas the MTS group presented discrepant data. This distinction was observed at both of the frequencies studied (500 and 2000 Hz).

Other studies have also demonstrated discrepancies between normal-hearing individuals and those with neurologic insult. Although the aforementioned and present studies utilized different recording parameters with respect

| Sensitivity | Specificity | Cut-off  |
|------------|------------|----------|
| 0.938      | 0.00       | -19.52   |
| 0.938      | 0.27       | -12.45   |
| 0.938      | 0.37       | -7.43    |
| 0.813      | 0.50       | -2.42    |
| 0.688      | 0.67       | 5.29     |
| 0.500      | 0.83       | 12.60    |
| 0.438      | 0.90       | 17.60    |
| 0.375      | 0.97       | 22.61    |
| 0.250      | 0.97       | 27.61    |
| 0.188      | 1.00       | 32.62    |
| 0.063      | 1.00       | 44.44    |

*Bold text indicates the cut-off used in the results*
Table 3 - Sensitivity and specificity of the auditory steady-state response (ASSR) test at 500 Hz for the left ear, according to the receiver operating curve (ROC) coordinates

| Sensitivity | Specificity | Cut-off |
|-------------|-------------|---------|
| 1.000       | 0.13        | -12.50  |
| 0.875       | 0.23        | -7.48   |
| 0.813       | 0.40        | -3.46   |
| 0.563       | 0.60        | 2.56    |
| 0.563       | 0.73        | 7.58    |
| 0.500       | 0.83        | 12.60   |
| 0.438       | 0.90        | 17.62   |
| 0.375       | 0.90        | 22.64   |
| 0.313       | 0.93        | 27.65   |
| 0.125       | 0.97        | 35.06   |
| 0.125       | 1.00        | 50.82   |
| 0.063       | 1.00        | 71.76   |

Bold text indicates the cut-off used in the results

to both the carrier and modulation frequencies (80 Hz), the results demonstrated clear similarities.

Rance et al. observed that subjects with auditory neuropathy presented ASSR-estimated thresholds significantly different from those detected by the auditory brain stem response. Specifically, at high intensities, thresholds were absent from the auditory brain stem response test and present on the ASSR test, showing a weak correlation between the thresholds, mainly at high frequencies. Similarly, Cone-Wesson et al. reported that neurologic lesions affect neurons and can impede the neural synchrony needed to produce responses in phase with the stimulus. This would result in ASSR thresholds being higher than behavioral thresholds in patients with neurologic disorders.

Shinn and Musiek found no correlation between behavioral and ASSR-estimated thresholds in subjects with neurologic insult. The authors suggested that the thresholds presented by such individuals are significantly different from those presented by normal subjects as a result of the impaired CANS sound stimulus transmission in the former. The CANS is unable to phase lock and respond synchronously with the stimulus, which affects the recording of ASSRs. This is an important, positive finding, because it suggests that the ASSR test can be used in making the differential diagnosis in cases of neurologic insult or CAPD.

The ASSR-estimated thresholds found in the present study were similar to those obtained by Van der Reijen et al. and low in comparison with those obtained by Shinn and Musiek. Van der Reijen et al. reported that the estimated thresholds for the normal group were approximately 13 dB HL at 500 Hz and 14 dB HL at 2000 Hz. The mean thresholds found by Shinn and Musiek for the normal group were 9.5 dB HL at 500 Hz and 23.8 dB HL at 2000 Hz. In that study, the mean estimated thresholds found for the neurologic group were 16.8 dB HL at 500 Hz and 34.5 dB HL at 2000 Hz. However, Van der Reijen et al. described characteristics similar to those observed in the present study (estimated thresholds were lower and more reflective of the behavioral thresholds in the normal group, whereas they were higher and more disparate from the behavioral thresholds in the neurologic group). The discrepancy between the present study and that conducted by Shinn and Musiek in terms of the estimated thresholds may be related to the difference in sample sizes, with our sample being larger. A larger number of participants associated with the same pathology (e.g. MTS) could result in a more homogeneous sample. In the present study, only individuals with lesions of the auditory cortex were evaluated, whereas Shinn and Musiek also evaluated individuals with lesions of the brain stem.

In the CAPD group, the mean ASSR-estimated thresholds for the left and right ears, respectively, were 11.25 and 9.98 dB HL at 500 Hz, whereas it was 22.46 and 18.54 dB HL at 2000 Hz. These values were higher than those obtained for the normal group and significantly lower than those obtained for the MTS group. To our knowledge, there have been no previous studies addressing the relationship between ASSRs and CAPD. However, based on studies of neurologic insufficiencies, we hypothesized that the CANS disorders presented by CAPD subjects can result in higher estimated thresholds. Any impairment that leads to weakened transmission of the sound stimulus and an impaired phase response can increase the ASSR (electrophysiological) threshold and, consequently, the estimated threshold.

Previous studies have also discussed the difference between ASSR-estimated thresholds and behavioral thresholds. For the normal-hearing subjects evaluated in the present study, this difference, for the left and right ears, respectively, was 17.50 and 13.83 dB HL at 2000 Hz, whereas it was 2.00 and ~0.67 dB HL at 500 Hz. The difference between ears was statistically significant, with the left ears presenting higher thresholds.

In the present study, the difference between ASSR-estimated thresholds and behavioral thresholds was more pronounced at 2000 Hz than at 500 Hz. The weak correlation between estimated and behavioral thresholds at higher frequencies (2000Hz) was described many studies and could be justified in some ways. The differences between thresholds demonstrated by the neurologic group were, perhaps, a result of the need for more neural substrate than what was available in order to elicit a response. This is only accomplished by increasing the level of the stimulus. That need of more neural...
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Sensitivity and Specificity of the ASSR Test

The best cut-off values, the sensitivity and the specificity (Table 2, 3 and 4) were obtained through the use of ROC curves (Figures 1, 2 and 3). These values were calculated for 500 and 2000 Hz. As there were no significant differences between the normal group and the CAPD group, comparisons were drawn only between the normal group and the MTS group.

To date, there has been only one study assessing the sensitivity and specificity of the ASSR test in individuals with confirmed neurologic insult.\textsuperscript{12} In that study, the authors used a cut-off value of 17.5 dB HL at 2000 Hz, which yielded a sensitivity of 64% and a specificity of 82%. In the present study, the sensitivity of the ASSR test was low at 500 Hz (50% for the left ear using a cut-off value of 5.3 dB HL, and 68% for the right ear using a cut-off value of 12.6 dB HL) but was noticeably higher at 2000 Hz (72% using a cut-off value of 22.5 dB HL). The specificity of the test was higher (from 67 to 83% at 500 Hz; and 83% at 2000 Hz). The low sensitivity found in the present study supports the findings of Shinn and Musiek\textsuperscript{21} and confirms that larger samples can reveal better sensitivity.

In the present study, the specificity was higher than the sensitivity and was similar to the values reported in previous studies. However, the sensitivity was higher at 2000 Hz than at 500 Hz.

It is believed that the ASSR (using a modulation of 46 Hz) is generated by mechanisms similar to those responsible for the MLR.\textsuperscript{20} Therefore, the values obtained in the present study for ASSR sensitivity and specificity can be compared with those obtained in studies evaluating the MLR. One such study, conducted by Japaridze et al., compared ASSRs, MLRs, and cortical potentials in individuals with multiple sclerosis.\textsuperscript{22} The authors found the sensitivity of the ASSR test to be 42%, which is similar to that obtained in the study conducted by Shinn and Musiek,\textsuperscript{21} and to that obtained in the present study. In addition, an MLR study conducted by Schochat et al.\textsuperscript{23} showed the sensitivity of the ASSR test to be 64.7% for identifying CAPD and 55.6% for detecting neurologic insults, values that are also similar to those obtained in the present study.

Although we found the ASSR test to have low sensitivity, we found its specificity to be relatively high compared with that reported in other studies. Larger neurologic and CAPD samples may reveal that this test has greater sensitivity, which could significantly increase its diagnostic value.
The authors do not know whether the results obtained in this study would be the same if the modulation used was 80 Hz. We suggest that further studies should be conducted with different carrier frequencies and frequency modulations in order to investigate the changes in the ASSR and also in CANS functioning.

CONCLUSIONS

The results of the present study show that the ASSR test can be a useful tool for estimating auditory thresholds in normal individuals. In individuals with neurologic insult, this test can yield estimated thresholds higher than those obtained in the behavioral evaluation and, in some cases, can result in a poorer audiologic profile. This is an important characteristic of this potential, assuming that the difference between groups is sufficiently pronounced to differentiate the diagnosis. In addition, the ASSR test showed good specificity and proved to be more sensitive to CANS disorders caused by lesions than to those cause by dysfunctions such as CAPD. Further research involving other pathologies (e.g. multiple sclerosis) or language disorders (e.g. dyslexia) and including larger numbers of neurologic subjects could increase the understanding of the ASSR test and its capacity to assess the temporal processing of such individuals.

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