Electrophysiological exploration of hearing

D. Bakhos, M. Marx, A. Villeneuve, E. Lescanne, S. Kim, A. Robier

ENT department, université François-Rabelais de Tours, CHRU de Tours, 2, boulevard Tonnellé, 37044 Tours, France
Eqipe 1, CNRS ERI 3106, UMRs imagerie et cerveau, Inserm U930, université François-Rabelais de Tours, CHRU de Tours, 2, boulevard Tonnellé, 37044 Tours, France
Service d’otologie-otoneurologie, CHU de Toulouse, hôpital Purpan, place du Docteur-Baylac, 31059 Toulouse, France
Laboratoire CerCo, université Paul-Sabatier, 31059 Toulouse, France

Article Info

Keywords:
Electrophysiology
Hearing
Otoacoustic emissions
Auditory brainstem response
Auditory steady-state response
Electrocochleography

Abstract

Electrophysiological hearing tests have been developed since the 1960s to determine hearing thresholds objectively. They are now implemented in newborn hearing screening. While they determine thresholds, interpretation requires subjective pure-tone and speech audiometry to determine the type of hearing loss. Each examination tests a different anatomic region, enabling the auditory system to be explored from the organ of Corti to the auditory cortex. Thus, the various objective audiometric examinations are complementary.

2. Electrophysiological auditory exploration techniques

2.1. Otoacoustic emissions (OAEs)

2.1.1. Principle

OAEs were first described by Kemp in the late 1970s [1]. They are induced by outer hair-cell (OHC) contraction in response to acoustic stimulation [2], based on OHC electromotility. Acoustic stimulation induces an acoustic emission in the OHCs, which spreads out from the organ of Corti in all directions, and notably in a retrograde direction to the tympanic membrane. OAEs can then be recorded by a miniaturized electrode in the external auditory canal. Transient-evoked OAEs (TEOAE) can be differentiated from background noise, as they are reproducible and differentiated from the acoustic stimulus, being recorded at a post-stimulus interval of 20 ms.

Various acoustic stimuli can be used. Clicks consist of a mixture of sounds of differing frequencies presented with short duration; TEOAEs are thereby recorded. Two pure tones that are close in frequency (referred to as f1 and f2) can be presented to analyze the amplitude of the 2f1–f2 response, known as the distortion product OAE (DPOAE); the probe comprises two transmitters each delivering a pure tone, and a microphone to record the response.

Recording uses a miniaturized probe comprising a transmitter delivering a 2.5 ms acoustic stimulus, and a microphone receiver recording the response (OAE) at a 20 ms interval. The probe is introduced along the axis of the external auditory canal, reaching the tympanic membrane as closely as possible. Tightness between the probe and the canal walls should be ensured. Total
recording time is short: < 1 min. Testing does not require any special premises.

2.2. Indications

2.2.1. Transient evoked otoacoustic emissions (TEOAEs)

TEOAEs (Fig. 1) are mainly indicated in neonatal hearing screening [3,4]. The response is binary: presence or absence of TEOAE. Presence indicates a threshold better than 30 dB (above which responses saturate). Another technique used in neonatal hearing screening is the automated auditory brainstem response (AABR), which has the advantages of being quick (< 1 min), reproducible, non-invasive, automated, and able to detect pseudo-hypacusis [5,6].

2.2.2. Distortion-product otoacoustic emissions (DPOAEs)

DPOAEs enable objective audiometry between 1000 and 6000 Hz, assessing OHC functional status. In some centers, they are part of the audiologic work-up for ototoxic hearing loss (notably secondary to administration of molecules such as cisplatin, liable to damage the OHCs or stria vascularis), acoustic trauma and intracochlear pressure variation [7–9]. They are also used by some teams for intraoperative monitoring of cochlear function during vestibular schwannoma surgery [10].

2.3. Limitations

Response may be affected by parasitic noise (swallowing, sucking, nasal or ambient noise) or by obstacles in the external auditory canal or retro-tympanic effusion. Thus, for neonatal hearing screening, TEOAE recording requires good-quality sleep. As the response originates in the OHCs, OAEs explore only the inner ear and not the auditory cortex or auditory pathways (false negatives). False positives also occur, at a rate of 1–19% [11], usually due to retro-tympanic mucosal secretion, necessitating re-testing before, notably, a congenital inner ear lesion can be diagnosed.

3. Electrocochleography (ECoGh)

3.1. Principle

ECoGh records responses from the cochlea and cochlear nerve. It was developed in the late 1960s [12], and laid the foundations of modern auditory electrophysiology techniques. Widespread at first, it has come to be replaced by ABR.

Recording the electrophysiological response requires a reference electrode, and an active electrode either on the promontory or, in latest generation models, placed extratympanically, making it easier to implement. Three responses with different origins are recorded. Firstly, the presynaptic cochlear microphonic (CM) corresponds to micromechanical OHC movements in the cochlear OHCs; then, summation potentials (SP) comprise the envelope of stimulation generated in the OHCs of the organ of Corti; finally, the postsynaptic responses comprise the cochlear nerve auditory potential (AP) and ABR wave I. The SP/AP ratio generally lies between 0.5 and 0.75.
Table 1
Main brainstem auditory-evoked response generators and wave latencies.

<table>
<thead>
<tr>
<th>Wave</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latency (ms)</td>
<td>1–2</td>
<td>Cochlear nerve (distal)</td>
<td>Cochlear nucleus</td>
<td>Superior olivary complex</td>
<td>5–6</td>
</tr>
<tr>
<td>Main generator</td>
<td>Cochlear nerve (proximal)</td>
<td>3–4</td>
<td>4–5</td>
<td>Inferior colliculus</td>
<td></td>
</tr>
</tbody>
</table>

3.2. Indications

Two main indications are reported in the literature. Firstly, in children, hearing thresholds are determined by analysis of wave I latency and amplitude, with an accuracy of about 10 dB. In case of suspected auditory neuropathy, ECochG indicates neural dysfunction, CM and SP (generated by the cochlea) being conserved while AP (corresponding to cochlear nerve fiber response) is desynchronized [13]. Secondly, diagnosis of endolymphatic hydrops in Menière’s disease is currently under assessment: elevated SP/AP ratio may indicate hydrops [14,15]. Finally, ECochG has been used to monitor hearing during vestibular schwannoma resection, providing almost simultaneous intraoperative functional information on the cochlea and on the distal part of the cochlear nerve [16]. Application in cochlear implantation is currently a focus of research [17].

3.3. Limitations

The main limitations of the technique are, firstly, the need for general anesthesia or sedation in child patients. Secondly, sensitivity for diagnosis of hydrops in Menière’s disease is poor, at 60% [15], due either to the technique as such or to patient selection in reported studies.

4. Auditory brainstem response (ABR)

4.1. Principle

ABRs record auditory nerve activity from the cochlear nerve to the brainstem. The test was developed in the early 1970s [18,19]; it is painless, and now routine in audiology. External electrodes record electrical responses to click stimuli. The acoustic stimulator is connected up to headphones and to an averager to synchronize the stimuli, which consist in 2000 Hz clicks. Response amplitude is very weak, so that background noise has to be eliminated by amplification, filtering and averaging.

Testing requires a soundproof chamber and faradic current. The patient has to be relaxed, lying down in calm surroundings; for children, the test is run either after a meal, to favor sleep, or under sedation. Four electrodes are placed on the scalp, with the positive electrode on the vertex (Cz) or forehead (Fz), negative electrodes on the mastoids (left and right), and the reference electrode on the forehead, recording the difference in potential between the positive and negative electrodes, in a bipolar set-up. Clicks are delivered via headphones or inserts.

The recorded response consists of 5 waves, numbered I to V, corresponding to electrical activity in 5 distinct relays of the auditory pathway:

- wave I: distal part of the cochlear nerve;
- wave II: proximal part of the cochlear nerve;
- wave III: cochlear nucleus;
- wave IV: contralateral superior olivary complex;
- wave V: inferior colliculus.

Wave VI (medial geniculate body) may also be recorded. The waves are recorded within the 10 ms following stimulation, and represent the early-latency components of the brainstem auditory-evoked response. Table 1 shows the respective generators and peak latencies. As well as latency study, the intervals between the waves help determine the lesion site. The most frequently used intervals are:

- I–V (normal value: 4 ms), reflecting auditory processing from cochlea to the contralateral inferior colliculus;
- I–III (normal value: 2.2 ms), reflecting auditory processing in the cochlear nerve;
- III–V (normal value: 1.8 ms), reflecting brainstem auditory processing.

Interaural differences > 0.35 ms are considered pathological. Thus, in screening vestibular schwannoma without brainstem involvement, cochlear nerve conduction shows I–III interval lengthening with normal III–V interval. The various latencies and intervals are compared against normal values and against contralateral responses.

4.2. Indications

One indication for ABR is to determine the hearing threshold by detecting wave V. This is mainly implemented for suspected childhood hearing deficit, especially when OAEs are absent, but also in non-cooperative or malingered adults. Stimuli are delivered at decreasing intensity; high intensities detect all 5 waves, and are decreased by 10 dB steps to determine the wave V detection threshold: at low intensities, only wave V remains (Fig. 2). It has to be borne in mind that peak latencies for the 5 waves vary according to the child’s age: central auditory pathways are immature at birth, and elevated latencies before the age of 1 year can, to a certain extent, be considered physiological. In case of asymmetric sensorineural hearing loss, unilateral tinnitus, acoustic distortion or discrepancy between pure-tone and speech audiometric thresholds (Fig. 3), ABRs screen for retrolabyrinthine pathology. Interaural difference (notably in wave V latency), I–V and I–III interval lengthening (Fig. 2B) or curve desynchronization suggest retrolabyrinthine pathology, and MRI centered on the internal auditory canals and cerebellopontine angle is prescribed to screen for vestibular schwannoma. Contralateral responses should also be analyzed, not only to compare interaural latencies but also to check for contralateral impact on the brainstem, especially in case of large vestibular schwannoma. In a meta-analysis by Koors et al. [20], the sensitivity of ABR in detecting vestibular schwannoma ranged between 74 and 100%. One study showed that combining all audio-vestibular examinations achieved sensitivity of 99–100% [21], demonstrating the need to associate objective and subjective measures. Derived potentials have been developed to enhance detection of intracanal tumor [22]. In follow-up for intracanal vestibular schwannoma, ABR confirms normal auditory information processing in the ascending pathways when the various wave latencies lie within normal limits, so that any hearing loss can be managed by means of a hearing aid.

The third indication is intraoperative monitoring, used by some teams in vestibular schwannoma surgery, vestibular neurotomy, endolymphatic sac decompression and trigeminal decompression. Wave I is known to reflect cochlear vascularization, I–III interval cochlear nerve integrity, and III–V interval the integrity of the

central auditory pathway from the cochlear nucleus to the contralateral inferior colliculus.

4.3. Limitations

Examination time is relatively long (30–40 minutes), and the patient has to remain immobile. For children, it is performed after a meal, to induce sleep, or after sedation (e.g., phenobarbital or melatonin); exceptionally, it may be performed under general anesthesia. The acoustic stimulus is high-frequency (2000 or 4000 Hz), as sensitivity is much poorer at low frequencies, and low-frequency hearing-loss may go undetected. Sensitivity is poor in case of threshold <70 dB. The false-positive rate is 10%.

4.4. Automated auditory brainstem response (AABR)

The principle is the same as for ABR. AABR uses clicks at a rate of 35–37 per second; the frequency range is wide, and intensity is 35 dB HL. Examination time is 4–8 minutes. AABR is used in neonatal hearing screening. The advantage over OAEs is a sensitivity of 90–100% and specificity of 96%. The drawbacks are higher cost than OAE, and longer examination time [23, 24].

5. Auditory steady-state response (ASSR)

5.1. Principle

ASSR and multiple ASSR are among the objective electrophysiological hearing exploration examinations, developed in the early 1980s [25]. They determine perception thresholds at various frequencies (500, 1000, 2000 and 4000 Hz) without requiring the subject’s active participation. Correlation studies with pure-tone audiometry have confirmed validity in neonatal, pediatric and young adult normal-hearing or impaired populations [26–30].

The acoustic stimuli are continuous sinusoidal periodic pure tones, frequency- and amplitude-modulated for each carrier frequency inducing synchronization of auditory neurons (CE-Chirp®). The idea of the CE-Chirp is to compensate for the stimulation delay, which differs according to frequency for clicks, in each part of the basilar membrane so as to stimulate the 4 areas of interest simultaneously. The carrier frequencies studied are limited to conversational levels: 500–4000 Hz. Patient positioning is the same as for ABR: 1 electrode on either mastoid and 2 on the forehead, with impedance ideally <3 kΩ. Headphones or, preferably, inserts [31] deliver the stimuli. Responses in auditory neurons of the brainstem and primary auditory cortex that follow the acoustic envelope and the rhythm of the frequency modulation are isolated on the electroencephalogram [32]. The signal is isolated from the background noise (notably EEG activity, eye movement and muscle activity) by various means: artifact rejection by a low pass-band filter with a threshold generally of 40 μV, averaging, frequency and amplitude modulation of each carrier frequency (which vary with age and wakefulness), thereby allowing enhanced amplitude, summation with EEG data, and phase modulation to minimize noise. Thresholds are determined on 10 dB steps, each threshold being confirmed by stagnating the curve for 6 minutes. The examination results in an audiogram estimated in dB eHL (Fig. 4), after applying a correction table to the determined physiological thresholds; correction ranges from −0 to −25 dB HL depending on the threshold that is found, the
5.2. Indications

ASSRs are indicated for objective determination of hearing thresholds [33], usefully complementing audiometry in children showing poor cooperation, in autistic subjects and malingerers. Studies are ongoing to assess their application in bone conduction in conductive and mixed hearing loss in the same populations, in which subjective audiometry is vitiated. They can also be implemented in free field for patients with hearing aids or cochlear implants [34].

5.3. Limitations

The main drawback of ASSRs is examination time (30–40 minutes); some authors have reported examination lasting around 20 minutes [35], although this was with prior pure-tone audiometry with ASSR recording beginning around the audiometric thresholds. ASSR is influenced by wakefulness; but this can be palliated by adapting stimulus frequency modulation to age (child or adult) and vigilance (awake or sleeping).

ASSR is unreliable in case of auditory neuropathy: thresholds may approximate 100 dB in moderate hearing loss, while the pure-tone audiometric threshold is 35 dB [36]. Such a discrepancy is considered by some [36] as further evidence of auditory neuropathy in patients with sensorineural hearing loss showing OAEs but desynchronized ABRs.

**Fig. 3.** Patient presenting with asymmetric predominantly left sensorineural hearing loss. Right: speech and pure-tone audiometry agree. No impairment of speech perception. ABRs show normal wave I to V latencies. Left: Speech audiometry shows impaired left-ear speech perception compared to pure-tone audiometry. Delayed onset of wave V and increased I–III interval compared to normal and to contralateral values.

6. Conclusion

The electrophysiology of hearing enables testing of various anatomic areas of the auditory system, from cochlea to auditory cortex, depending on the examination. The techniques are attractive, allowing objective assessment without the subject’s active participation. It is, however, important to be aware of the origins of the respective responses (Table 2) and the limitations specific to each technique. The techniques can be complementary, depending on the question the clinician seeks to answer, and are indissociable from pure-tone and speech audiometry. Further developments should allow routine use of speech-ABR and also of medium-latency and cortical ABR in coming years. In the future, they will improve diagnosis in pathologies such as Ménière’s disease and auditory neuropathy.

Disclosure of interest

The authors declare that they have no competing interest.

References


Table 2

Objective audiometry examinations, regions explored, responses, and indications.

<table>
<thead>
<tr>
<th>Audiometry examination</th>
<th>Anatomic region</th>
<th>Responses</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>OAE</td>
<td>OHC</td>
<td>Binary: present/absent</td>
<td>Neonatal screening</td>
</tr>
<tr>
<td>Electrocochleography</td>
<td>CC-cochlear nucleus</td>
<td>Cochlear microphonic</td>
<td>Endolymphatic hydrops</td>
</tr>
<tr>
<td>ABR</td>
<td>Central auditory pathways</td>
<td>5 waves: 1 to V</td>
<td>Retrocochlear injury</td>
</tr>
<tr>
<td>ASSR</td>
<td>Inferior colliculus</td>
<td>EEG</td>
<td>Hearing threshold</td>
</tr>
</tbody>
</table>