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ADANO recommendations for the selection of target parameters and measurement processes for the use of auditory evoked potentials, otoacoustic emissions, and impedance audiometry in clinical trials

Prepared by the ERA consortium (AG-ERA)* of ADANO#. Confirmed by the board of ADANO on 18.01.2019

Preamble

In the design of clinical studies, definitions of the target parameters (end points) to be measured are required. These serve as a basis for the selection of suitable statistical methods and thus the calculation of necessary sample sizes. The choice of the target parameters suitable for the respective question is based on relevant previous studies and on any available meta-analyses. The freedom of choice of target parameters is thus constrained by boundary conditions.

We consider the standardization of target parameters as necessary for a number of reasons, notably the comparability of different studies. So far, great heterogeneity has been observed in terms of target parameter choice (e.g., [10]). Dependent on the respective hypothesis, target parameter selection also has a significant impact on sample size planning in clinical trials [13].

As a result of an open process within the German Working Group for Evoked Response Audiometry (AG-ERA) of the Working Group of German-Speaking Audiologists, Neurotologists, and Otologists of the German Society of Oto-Rhino-Laryngology, Head and Neck Surgery (ADANO), uniform minimum standards have been specified.

The use of auditory evoked potentials [11, 12, 15, 16], otoacoustic emissions [4, 6, 7, 9], and impedance audiometry [1, 5, 8, 14] offers a wide range of possible parameters to be measured and also of the configuration of the respective equipment. For this reason, these recommendations also contain information for the measurement process.

These target parameter and process recommendations should also be used for surveys within the framework of quality controls and for possible national and international registers.

These recommendations expressly do not restrict the freedom of choosing target parameters that exceed the minimum requirements described here.

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#*ADANO:* Working Group of German-Speaking Audiologists, Neurotologists, and Otologists of the German Society of Oto-Rhino-Laryngology, Head and Neck Surgery

**AG-ERA:* German Working Group for Evoked Response Audiometry under the umbrella of ADANO, in which audiologists of different professional origin come together for an exchange of experience and scientific projects

Table 1 Target parameter and process recommendations for the different measurement methods

Method	Objective	Target parameter recommendation (end points)	Process recommendation
Impedance audiometry	Determination of the middle ear pressure/eardrum impedance	Ear canal pressure at compliance maximum Tympanogram type according to Jerger (1980)	Probe tone: 226 Hz; children <6 months 1 kHz Indication of residual auditory canal volume
	Absorbance, reflectance	Frequency-dependent absorbance, resonant frequency	Broadband stimulation, 100–6000 Hz
	Proof of the acoustic reflex	Reflex threshold at 500 Hz, 1 kHz, 2 kHz, 4 kHz; if necessary, broadband	Ipsi- and contralateral
Transient-evoked otoacoustic emissions (TEOAE)	Diagnosis of the cochlear amplifier	Sound pressure level of broadband stimulation Corrected emission amplitude in the octave bands 1 kHz, 2 kHz and 4 kHz	Click, 84 dB p.e. SPL Nonlinear Specification of the involved equipment Indication of reproducibility
Distortion product optoacoustic emissions (DPOAE)	Diagnosis of the cochlear amplifier	Corrected emission amplitude in the octave bands 1 kHz, 2 kHz and 4 kHz	f_2/f_1: 1.22 L_{f2} = 65 dB SPL Indication of the measuring device used
Electro-cochleography	Hair cell function	Cochlear microphonics (CM)	Tone pulse 0.5, 1, 2, 4 kHz
	Stimulus response threshold diagnostic	Threshold level of the compound action potential (CAP)	Click-stimulation, alternating polarity Tone pulse (0.5, 1, 2, 4 kHz with alternating polarity)
	Diagnosis of endolymphatic hydrops	SP/CAP ratio	Click, 90 dB nHL, alternating polarity
	Auditory synaptopathy, auditory neuropathy (AS/AN)	CM, SP, and CAP at 90 dB nHL CAP threshold	Click-stimulation, alternating polarity Tone pulse (0.5, 1, 2, 4 kHz) rarefaction and condensation Transtympanally Reference: Fpz or ipsilateral mastoid
Auditory brainstem responses (ABR)	Stimulus response threshold diagnostics	Smallest level with reproducible recordable response (threshold level)	Click or chirp stimulus, alternating polarity, stimulus rate around 20 Hz Cz or Fpz vs. mastoid or earlobe
	Retrocochlear diagnostics	Absolute latencies of waves I, III, and V on both sides	Click stimulus, alternating polarity 80 dB nHL Cz or Fpz vs. mastoid or earlobe
Auditory steady-state responses (ASSR)	Stimulus response threshold diagnostics	Threshold level at 500 Hz, 1 kHz, 2 kHz, and 4 kHz Indication of the signals used	Cz or Fpz vs. mastoid or earlobe No automatic threshold correction nHL calibration
Late or slow auditory evoked potentials (LAEP or SAEP)	Stimulus response threshold diagnostics	Threshold level at 0.5 kHz, 1 kHz, 2 kHz and 4 kHz	Tone burst stimulus 500 ms duration 0.5–1/s stimulus rate Cz or Fpz vs. mastoid

CAP compound action potential, *Cz* electrode positioned at vertex, *Fpz* frontocentral placement of electrode, *nHL* normalized hearing level, *p.e.* peak equivalent,*SP* summation potential

Recommendations

Insofar as objective measurement methods are used for the purposes of these recommendations, at least the target parameters listed in Table 1 shall be measured, determined, and reported. The process recommendations listed therein must, moreover, also be observed.

Definitions

Stimulus response threshold. Lowest stimulus level with (yet) reproducibly identifiable stimulus response, expressed in dB HL or dB nHL (often referred to as threshold level in the text; [3]).

Objective hearing threshold. Estimated hearing threshold derived from the stimulus response threshold, according to defined rules and expressed in dB HL [3].

Corrected emission amplitude TEOAE. From the measured total amplitude of the compound signal (response R, composed of signal S and noise N), the estimated residual noise is subtracted according to the formula:

$$A_{\mathrm{TEOAE}} \equiv \sigma_S = \sqrt{\sigma_R^2 - \sigma_N^2}$$

where $\sigma_R{}^2$ is the variance of the sum and $\sigma_N{}^2$ is the variance of the difference of the subaverages (both divided by 2; [2]). If the corrected emission amplitude A_{TEOAE}

is not available as an explicit quantity, the level of the compound signal and the level of the residual noise should be given.

Corrected emission amplitude DPOAE. The primary measured quantity is the sound pressure amplitude p_R at the frequency f_{DP} composed of residual noise and emission. Using the effective amplitude of the residual noise:

$$p_{\text{Neff}} = \sqrt{\frac{1}{N} \sum_{i=1}^{10} {p_i}^2}$$

the best estimation of the noiseless DP amplitude is given by:

$$A_{DP} = p_R - p_{\text{Neff}}$$

The calculation of p_{Neff} includes ten spectral lines around the frequency f_{DP}. If the corrected emission amplitude A_{DP} is not available as an explicit quantity, the level L_R of the compound signal and the level L_N of the residual noise should be supplied.

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Compliance with ethical guidelines

Conflict of interest T. Rahne, O. Dziemba, A. Lodwig, D. Polterauer, R. Thie, M. Walger, T. Wesarg, and S. Hoth declare that they have no competing interests.

For this article no studies with human participants or animals were performed by any of the authors. All studies performed were in accordance with the ethical standards indicated in each case.

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