

EABR on cochlear implant – measurements from clinical routine compared to reference values

Abstract

Measurements of electrically evoked potentials of the auditory system (EAEP) are important cornerstones of objective diagnostics in cochlear implant care. For differential diagnosis, the combined evaluation of electrically evoked compound action potentials (ECAP) and electrically evoked brainstem responses (EABR) can be used. The aim of this case series is to compare measurements from difficult cases to previously published reference values of ECAP and EABR.

The reference values for ECAP and EABR were determined using a broadband stimulus on 20 CI patients with normal speech recognition scores. Five cases of EAEP measurements from clinical routine will be presented and discussed in comparison to the reference values.

For both ECAP and EABR, reference values of amplitude growth functions, absolute latencies and latency differences were obtained. The following cases are shown in comparison to the reference values:

1. Normal findings;
2. EABR at initial CI fitting;
3. Extended latencies;
4. Objective evaluation before re-implantation;
5. Unexpected insufficient speech perception.

Based on the reference values, a comprehensive differential diagnosis of the peripheral auditory system is possible.

Keywords: EABR, electrically evoked brainstem responses, reference values, clinical routine, cochlear implant

1. Introduction

Cochlear implantation is an established therapy of severe to complete hearing loss. However, there is a large variability in the outcomes of cochlear implantation across subjects. Previous work has shown that speech perception following implantation can be attributed partially to certain preoperative factors such as etiology and duration of hearing loss respectively deafness [4], [16] and advantageous individual conditions such as age and preoperative residual hearing [18].

Besides the aforementioned factors [4], [16], [18], [17] an objective assessment of the peripheral and central auditory nervous system may provide deeper insights [20], [27]. Those objective measurements may contribute to the preoperative evaluation of CI candidacy [2], the assessment of longitudinal development [12], the support of cochlear implant (CI) fitting [13], and diagnostic assessment in difficult CI cases [21], [26]. Also, cochlea implantation in subjects with rather disadvantageous medical conditions [1], [24] can be supported via objective assessments.

Amongst the test battery of objective measurements, the acoustically evoked auditory brainstem responses (ABR) are well established in clinical routine. In analogy to its

acoustic counterpart the electrically evoked auditory brainstem responses (EABR) can be used to identify possible disorders topographically by comparative analysis of individual EABR observation in relation to normal findings [19]. For this purpose, a broadband click-stimulus can be applied for the acoustically evoked response. In order to achieve the same effect for electrically evoked responses, a dedicated stimulus was developed and verified for its broadband characteristics via measurements of electrically evoked compound action potentials (ECAP) in CI recipients [8], [9]. The acceptance in awake recipients was optimized by the use of broader pulse widths triggered by findings in ECAP-recordings with decreased loudness perception [3].

This case series demonstrates the importance of clearly defined and reference based broadband stimuli for the rehabilitative course and differential diagnosis of CI-recipients. To this purpose we used previously published reference values for CI-recipients without known co-morbidities that achieve open speech perception, a monosyllabic score larger than 50% [8].

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2. Materials and methods

All of the presented cases, respectively EABR measurement were recorded during the guideline-compliant treatment and rehabilitation process [5], [6] at our department. For all patients of this case series there was a need to objectively determine hearing function with CI [5]. All measurements were made between 2012 and 2019.

2.1 EABR setting

For EABR measurements, two devices are available in our clinic. These systems are GSI Audera™ (Grason-Stadler, Eden Prairie, MN, USA) and Eclipse (Interacoustics, Middelfart, Denmark). Both recording systems meet all recommended technical requirements for measuring evoked auditory potentials by ADANO [25] and all standard requirements according to DIN EN 60645-7:2010 [7].

For stimulation via the CI the clinical software Custom Sound® EP in version 3 or higher (Cochlear™ Ltd. Macquarie, Australia) was used. The stimulation mode for a broadband excitation of the hearing nerve was directly derived from recent findings [8], [9]. They applied electrode 11 as active and electrode 18 as indifferent electrode with a pulse width of 100 µs. The resulting bipolar, alternating, and intracochlear stimulation mode provides a sufficient broadband excitation of the spiral ganglion and is suitable for the recording of electrically evoked auditory potentials. It can be used for objective electrophysiological diagnostics via an inserted CI and can be applied for intraoperative and postoperative measurements.

Synchronization between the CI system and the EABR device was done via a TTL-compatible trigger signal. This was sent via a commercially available cable (3.5 mm jack) from the programming interface of the CI system to the EABR recording system.

There is a technical difference between the two EABR recording systems with respect to the time scale namely the onset of the stimulus (identical to trigger timepoint) and recording $t=0$ ms. The stimulus onset is clearly visible in all EABR recordings. This corresponds to $t=0$ ms. For the GSI Audera a correction needs to be applied to all recordings since the stimulus onset does not correspond to $t=0$ ms. The Eclipse does not need any correction since the stimulus onset (identical to trigger timepoint) corresponds to $t=0$ ms.

2.2 Measuring procedure

All measurement series were performed according to the following procedure during which the patient was observed by the examiner permanently.

1. Determination of the individual ECAP threshold in bipolar mode (ECAP_{11/18}) by using the above described EABR stimulus.

2. Estimation of the expected supra-threshold dynamic based on the ECAP_{11/18} threshold and the appropriate stimulation intensity (comp. Table 1).

Table 1: Reference group (n=20). Mean stimulation intensity at the ECAP_{11/18} threshold and at maximum tolerated loudness (LAPL) of the EABR stimulus; the median difference of stimulus intensities at ECAP_{11/18} threshold and LAPL was 35 CL.

	Stimulus intensity	Stimulus current
ECAP _{11/18} threshold	142.7 CL	230.3 µA
Max. accepted loudness	178.2 CL	437.2 µA

The stimulation current is calculated according to the equation: $I[\mu A] = 17.5 \cdot 100 \left(\frac{CL}{255}\right)$

3. Start of the EABR measurement with a stimulation intensity near the ECAP threshold. In case where ECAP_{11/18} measurement was not possible (for older implant generation Nucleus 22), the maximum tolerated stimulation intensity can be used but not exceeded.
4. Successive variation in stimulation intensity with small increments without exceedance of the maximum tolerated stimulation intensity.
5. Completion of the EABR measurement if the differential diagnostic question can be answered satisfactorily or the maximal accepted stimulation level of the patient is reached.

2.3 Reference values

Reference values are important in evaluating individual EABR measurement for differential diagnosis. For that reason, it is indispensable to collect reference values by using the same stimulation and measuring modes one would use in patients [8].

The reference values which were used in this case report were determined in a pilot study including 20 EABR measurements of postlingually deaf adults. The mean age was 56.2 years (26 to 81 years). The mean CI hearing experience was 21.4 months (2 to 62 months). The implant types were CI24RE, CI422 and CI512 (Cochlear™ Ltd. Macquarie, Australia). The CI recipients of the reference group were recruited during their individual rehabilitation process. The inclusion criterion was defined as a speech perception score in quiet equal or larger than 50% at 65 dB_{SPL} for Freiburg monosyllabic words. The reference values of the stimulation dynamic between ECAP_{11/18} threshold and maximum accepted loudness of the special stimulation mode are listed in Table 1. The latency and inter-peak-latency of the evoked potentials including standard deviation of all measured potentials are listed in Table 2. None of the patients described in this case series was used for the reference group.

In addition, comparative values from the literature were used for the evaluation [12], [15]. Previous work of Gordon et al. [12] specifically reported the developmental

Table 2: Reference group (n=20). Mean (μ) and standard deviation (σ) of latency (ipsilateral) in order to the suprathreshold stimulation level

		eJ5*		eJ3*		eJ1 (ECAP)*		eJ3-eJ1*		eJ5-eJ3*		eJ5-eJ1*	
		μ	σ	μ	σ	μ	σ	μ	σ	μ	σ	μ	σ
Stimulation level above ECAP _{11/18} threshold	40	3.48	0.23	2.02	0.18					1.46	0.23		
	35	3.58	0.27	2.03	0.15	0.40	0.04	1.76	0.04	1.53	0.25	3.28	0.31
	30	3.60	0.27	2.04	0.17	0.39	0.04	1.78	0.08	1.54	0.22	3.34	0.27
	25	3.68	0.25	2.06	0.17	0.39	0.03	1.74	0.15	1.61	0.16	3.38	0.24
	20	3.72	0.27	2.07	0.18	0.41	0.03	1.68	0.19	1.64	0.18	3.34	0.28
	15	3.73	0.28	2.06	0.18	0.41	0.03	1.64	0.18	1.64	0.17	3.31	0.29
	10	3.74	0.25	2.06	0.19	0.42	0.03	1.64	0.19	1.71	0.12	3.32	0.26
	5	3.81	0.28	2.10	0.20	0.45	0.03	1.65	0.19	1.74	0.16	3.36	0.27
	0	3.79	0.28	2.11	0.20	0.47	0.02	1.64	0.20	1.66	0.13	3.32	0.28

*ms

time course of electrically evoked potentials in children using cochlear implants. Their results were consulted in order to interpret EABR recordings in patients younger than our reference group.

3. Results

3.1 Case 1 – normal

ECAP and EABR measurements were performed in a 3-year old female patient under general anesthesia after cochlear implantation at two years on the right side due to congenital deafness. The implant CI422 was intra- and postoperatively checked according to Wesarg et al. [28]. Impedance telemetry showed a perfect function of the implant. During the rehabilitation process the patient displayed defensive behavior against all audiological and therapeutic steps. Consequently, a regular rehabilitation was not possible. The mother also reported the child not reacting in everyday life. Figure 1 shows the ECAP_{11/18} and EABR measurement. The latencies and inter-peak-latencies of all measured electrically evoked potentials are listed in Table 3.

The absolute latencies are increased. However, the measurements must be interpreted under respect of the developmental time course of the auditory pathway [12]. They found latency shift in dependence of age of up to 0,5 ms. Therefore, this result can be assumed to be within normal range.

The absence of adequate reactions of a child to acoustic stimuli or speech repeatedly represents difficulties to the disciplines involved in CI care. The measurement of monopolar ECAP is usually sufficient for threshold estimation. However, a further diagnostic of the auditory pathway is indicated. Based on the measurement, a change or even increase of the CI stimulation level was abandoned.

3.2 Case 2 – EABR at initial CI fitting

In this case of a male 11 month old patient ECAP and EABR measurement took place within the initial fitting appointment in spontaneous sleep, four weeks postoperatively.

The medical and audiological examinations showed bilateral congenital deafness with a radiologically confirmed Mondini dysplasia in both sides. The intraoperative audiological measurements were done according to Wesarg et al. [28]. The impedance telemetry showed a perfect function of the implant. The ECAP threshold measurement yielded a complete ECAP threshold profile with very high thresholds. The regular insertion of the electrode carrier was confirmed via imaging.

The electrode specific ECAP measurements in spontaneous sleep during initial fitting yielded no reliable results, so an ECAP_{11/18} and EABR measurement using the aforementioned standardized stimulation mode was indicated. The results of both measurements are shown in Figure 2 and Table 4. As with ECAP in monopolar mode, the ECAP_{11/18} revealed no reliable typical potentials. Taking into account maturing processes of the auditory pathway described by Gordon et al. [12], the latency of the EABR might be considered as within normal and age-typical ranges.

Table 3: Latencies and inter-peak-latencies of the measured EABR of case 1 and measures prior to EABR recordings

Stimulation level*	Stimulation level above ECAP _{11/18} threshold*	eJ5**	eJ3**	eJ1**	eJ3-eJ1**	eJ5-eJ3**	eJ5-eJ1**
175	35	4.33	2.18				
170	30	4.21	2.13	0.38	1.75	2.08	3.83
165	25	4.25	2.17	0.38	1.79	2.08	3.87
160	20	4.42	2.17	0.38	1.79	2.25	4.04
155	15	4.38	2.30	0.38	1.92	2.08	4.00
150	10	4.46	2.18	0.38	1.80	2.28	4.08

Indication for EABR recording: Parents complain about missing response	
Measure	Results
Speech perception	Not available (child/not German native speaker)
Impedance telemetry	In specification
Electrode specific ECAP threshold	Within expected range [5], [22]
Integrity check by manufacturer	Not indicated
Electrode position	Correct

*CL

**ms

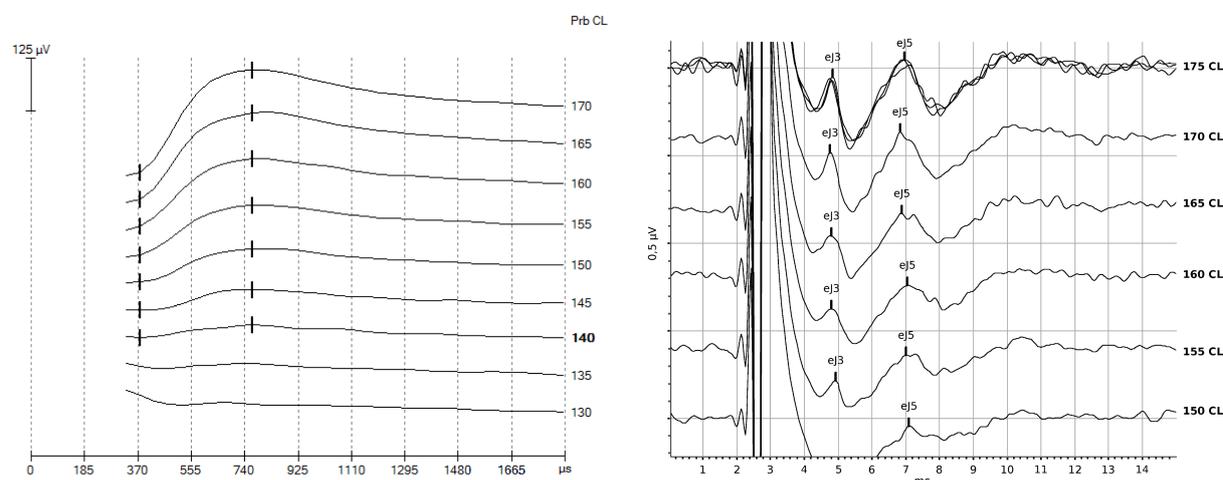


Figure 1: Case 1 – ECAP_{11/18} (left side) and EABR (right side) measurement of a regular functioning CI measured under general anesthesia

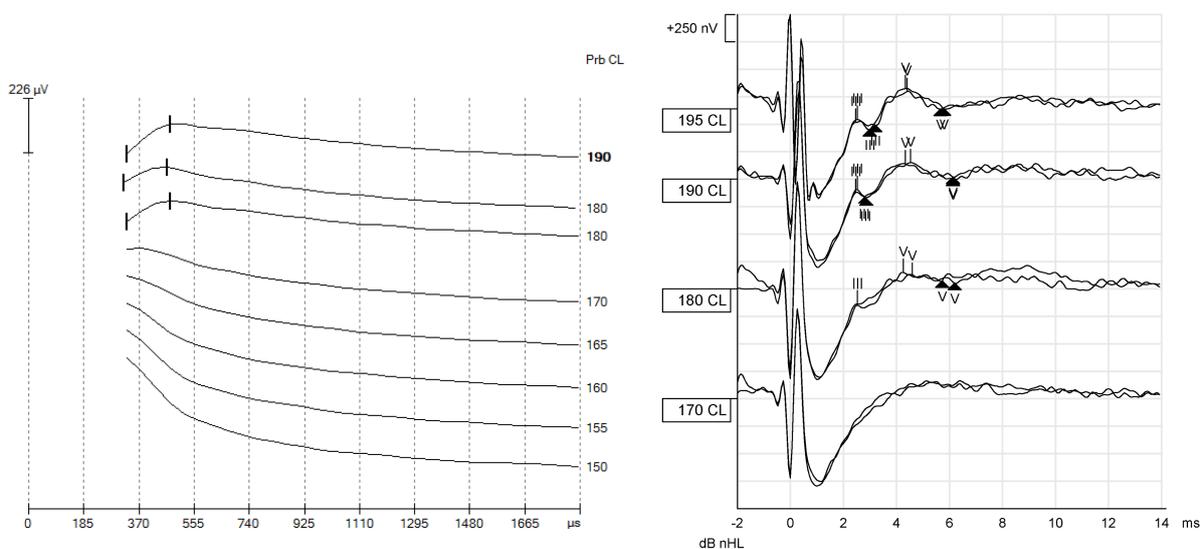


Figure 2: Case 2 – ECAP_{11/18} (left side) and EABR (right side) measurements during initial fitting of a male child (11 months); both measurements were done while spontaneous sleep; stimulation level above 195 CL were out of compliance of the CI.

Table 4: Latencies and inter-peak-latencies of the measured EABR of case 2 and measures prior to EABR recordings

Stimulation level*	Stimulation level above ECAP _{11/18} threshold*	eJ5**	eJ3**	eJ5-eJ3**
195	15	4.37	2.50	1.87
190	10	4.43	2.50	1.94
180	0	4.44	2.53	1.90
Indication for EABR recording: missing ECAP at initial activation				
Measure	Results			
Speech perception	Not available at initial activation			
Impedance telemetry	In specification			
Electrode specific ECAP threshold	Intraoperatively with high thresholds, Postoperatively not measurable in spontaneous sleep			
Integrity check by manufacturer	Not indicated			
Electrode position	Correct with respect to anatomy (imaging)			

*CL

**ms

3.3 Case 3 – extended latency

A seven-year-old male child was presented for objective implant check and measurements of the peripheral auditory pathway function. This was indicated by subjectively perceived poor outcomes resulting in a denial of system usage. Bilateral deafness caused by intrauterine infection with cytomegalovirus led to CI implantation (CI24RE CA) on the right side at 11 months.

An integrity test of the CI system and EABR measurements were done under general anesthesia. The mean monopolar ECAP thresholds were within the normal range according to Berger et al. [3] and Müller et al. [22]. The EABR_{11/18} measurement showed considerably increased latencies (see Figure 3 and Table 5) and a mean latency increase of 1.15 ms for eJ5 and a mean increase of the inter-peak-latency $\Delta t_{eJ5 eJ3} = 0.45$ ms.

Table 5: Latencies inter-peak-latencies of the measured EABR of case 3 and measures prior to EABR recordings and measures prior to EABR recordings

Stimulation level*	eJ5**	eJ3**	eJ5-eJ3**
170	4.69	2.63	2.06
162	4.75		
160	4.94		
158	4.92		
Indication for EABR recording: poor outcome and denial of system usage			
Measure	Results		
Speech perception	Not available (mental retardation)		
Impedance telemetry	In specification		
Electrode specific ECAP threshold	Within expected range [5], [22]		
Integrity check by manufacturer	Adverse reaction B ₂ [1]		
Electrode position	Correct		

*CL

**ms

3.4 Case 4 – re-implantation

This 73-year-old female patient underwent sequential bilateral CI implantation at the age of 55 years on the left side (Nucleus® 22) and at 71 years on the right side (CI512). 18 years after the left implantation a gradual deterioration in speech understanding without any stroke or intracranial masses became unsolvable by corrections of the CI fitting. Integrity tests by the manufacturer revealed a technically functional device, however, the observed performance decrement led to a B₂ classification [11].

A standardized EABR measurement at maximal tolerated stimulation intensity was performed to contribute to an estimation of a success ratio of a possible re-implantation of the left CI. This measurement was repeated three times. The results are shown in Figure 4 and Table 6. Due to the lack of ECAP recording functionality of this CI system, a relation to reference values cannot be established via ECAP thresholds. Therefore, only the second reference, namely via loudness scaling, could be used. Nevertheless, since the latency shift in EABR is far below the observed latencies of acoustically evoked ABR a reliable classification of the recordings is justifiable in this case. We found absolute and interpeak latencies clearly to be within normal range.

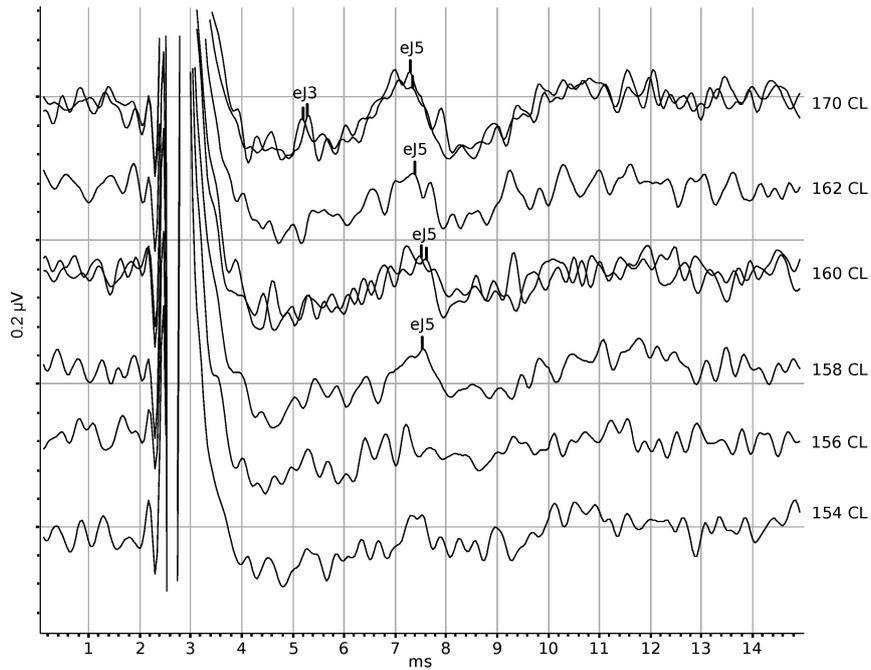


Figure 3: Case 3 – Prolonged latencies of EABR wave III and V 6 years after implantation and without any clear audiological findings

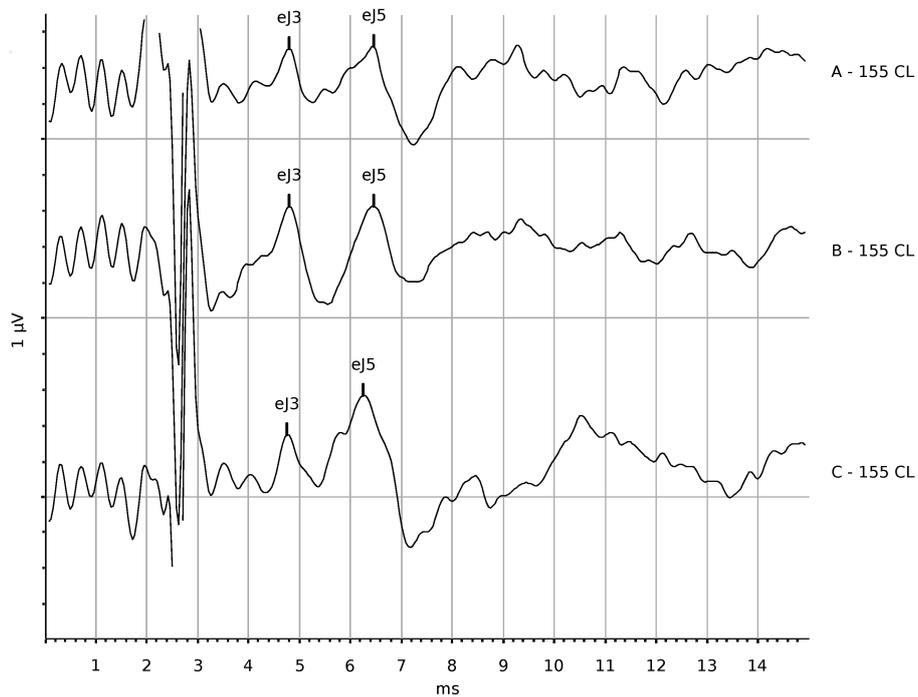


Figure 4: Case 4 – EABR measurement at maximum tolerated simulation intensity at Nucleus® 22 implant; to reproduction, the measurement was performed triplicate.

Table 6: Latencies and inter-peak-latencies of the measured EABR of case 4; the lowest line lists the mean of each row and measures prior to EABR recordings.

Stimulation level*	eJ5**	eJ3**	eJ5-eJ3**
A – 155	3.83	2.17	1.67
B – 155	3.83	2.17	1.67
C – 155	3.63	2.13	1.50
mean	3.76	2.16	1.61
Indication for EABR recording: decreased speech perception, suspected retrocochlear hearing impairment			
Measure	Results		
Speech perception	Gradual decrement		
Impedance telemetry	Not available (N22)		
Electrode specific ECAP threshold	Not available (N22)		
Integrity check by manufacturer	Performance decrement B ₂ [1]		
Electrode position	Correct		

*CL

**ms

3.5 Case 5 – unexpected insufficient speech perception

The expected onset of speech perception in an 81 year-old female patient was not reached, even though all pre-, peri-, and postoperative audiological measurements indicate a regular rehabilitation course. The unilateral CI patient (CI632, right side) showed preoperative residual speech perception of 100% Freiburg polysyllabic numerals at 100 dB_{SPL} and a maximum word recognition score of 5% Freiburg monosyllabic words at 110 dB_{SPL}. All mandatory preoperative medical, audiological, and imaging examinations were inconspicuous. The intraoperative measured ECAP showed regular thresholds [22] and regular electrode positioning [10], [14], [23], which was confirmed by intraoperative imaging as well. During the initial fitting sessions, a slightly lowered, complete, and stable ECAP profile was measured. According to our clinical experience and recent results on predictive modeling [17] this CI recipient did not match our expectations with respect to speech perception. A differential diagnosis of the peripheral auditory system was indicated.

The results of the ECAP_{11/18} and EABR measurements are summarized in Figure 5 and Table 7. Both, the absolute and the interpeak-latencies were increased.

The assessment of speech perception yielded six months scores as follows: Speech reception threshold for Freiburg polysyllabic numerals of 53 dB_{SPL}, Freiburg polysyllabic numerals 80% at 65 dB_{SPL}, Freiburg monosyllabic words 25% at 65 dB_{SPL}.

4. Discussion

The recording of EABR may support differential diagnostics in cases with poor, unexpected low, or unclear benefit from the CI-system. The root causes within the described cases series were identified as being related to physiological, behavioral, or technical issues.

The cases 1 and 2 highlight the additional diagnostic value of EABR recordings for the counselling of involved hearing professionals and parents. The ECAP provide information about the most peripheral auditory pathway only. The EABR recordings complemented this information in case 1 or confirmed regular electrophysiological function of both, device and auditory periphery. Nevertheless, more centrally located hearing impairments remain undetected with the presented method. In such cases, further standardized diagnostics can be advantageous [5], [6], [19]. In all pediatric cases the maturation-dependent shift in the identification of normal or pathological findings must be taken into account [12]. The assessment of reference values in a pediatric population presents an ambitious goal for future examinations.

Such considerations indicated the EABR recording in case 3. However, in this case the result has a larger impact on the recipient, its parents, and involved professionals. The abnormal findings suggest a very strong focus should be made as well on other communication strategies than hearing for this child. The denial of system use by this child is not due to high stimulation, this was extensively checked beforehand during the initially regular habilitation approach. In case 4, a technical defect of the implant was not clearly identified as the root cause of the gradually deteriorating CI outcome. The suspicion of a possible peripheral neuronal hearing impairment made the success of a CI reimplantation especially uncertain. EABR measurements did not confirm this concern, as the mean absolute latencies and latency differences of potentials eJ3 and eJ5 were within the standard deviation of the reference values. To summarize, the normal EABR recordings triggered the re-implantation in this case 4 which resulted in a restored hearing performance. Especially in B₂ cases [11], normal device function with performance decrement, the results of EABR recording may contribute to an appropriate decision with regards to further treatment. Such considerations played a role also for case 5. For this recipient with unexpected insufficient speech perception right from the beginning an early intervention was indicated. However, different to case 4, the abnormal findings somehow made a technical root cause unlikely. Consequently, the recipients and relatives can be counseled about an expected slower progress and the long-term rehabilitation program can be planned accordingly.

To summarize, EABR may complete the diagnostics after cochlear implantation. In some cases, a differentiation between technical and patient intrinsic causes of poor performance can be facilitated. Supportive information for the planning of the further treatment can be derived. Being able to objectify postoperative findings is an essen-

Table 7: Latencies and inter-peak-latencies of the measured ECAP and EABR of case 5 and measures prior to EABR recordings and measures prior to EABR recordings

Stimulation level*	Stimulation level above ECAP11/18 threshold*	eJ5**	eJ3**	eJ1**	eJ3-eJ1**	eJ5-eJ3**	eJ5-eJ1**
160	+15	4.17	2.37	0.43	1.94	1.80	3.74
155	+10	4.37	2.37	0.43	1.94	2.00	3.94
150	+5	4.20	2.43	0.48	1.95	1.77	3.72
145	0	4.23	2.57	0.48	2.09	1.67	3.75
140	-5	4.27	2.37			1.90	
135	-10	4.50					
130	-15						
Indication for EABR recording: Unexpected insufficient speech perception							
Measure		Results					
Speech perception		Inconstant audiometric findings, 4 months postoperatively: <ul style="list-style-type: none"> • loudness scaling within expected range, • 10% Freiburg monosyllabic score at 65 dB_{SPL}, Speech recognition threshold for Freiburg numbers 50 dB_{SPL} 					
Impedance telemetry		In specification					
Electrode specific ECAP threshold		Within expected range [5], [22]					
Integrity check by manufacturer		Not indicated					
Electrode position		Correct					

*CL

**ms

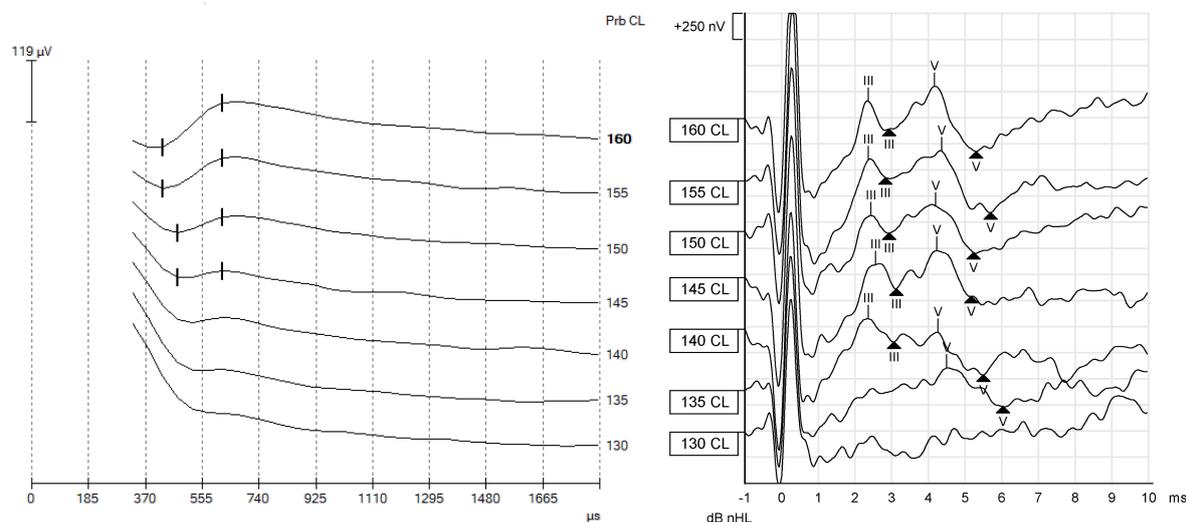


Figure 5: Case 5 – ECAP_{11/18} (left side) and EABR (right side) measurement in a patient with unexpectedly insufficient speech intelligibility results

tial part of rehabilitation after cochlear implantation. For this, electrically evoked auditory potentials (EAEP) methods can assist in the reliability and quality of cochlear implant provision [19].

Advantages and limits of the EABR paradigm: The applied stimulus paradigm enables suprathreshold measurements also in awake patients. The broadband stimulus potentially enables the transfer of criteria qualitatively derived from findings in the acoustically evoked ABR via

broadband click excitation. The application of cut-off criteria for absolute and interpeak latencies for adults is based on previous studies [8]. However, absolute latencies might depend on the used EABR system. Therefore, system specific correction values might be required. The application on findings in children with CI remains difficult up to a certain degree. The references [12] used for indirect comparison were provided with monopolar stimulation on single electrodes. The estimation of supra-

threshold dynamic (maximum tolerated loudness) in cases of missing ECAP represent a sufficient approach in order to compare individual EABR latencies. Additionally, we avoid too loud stimulation intensity during the measurements in children and nonresponsive patients (e.g. intraoperative).

The applied paradigm inherits a robustness of the stimulation which will facilitate systematic measures of intracochlear evoked EABR [26]. However, frequency specific information about neural processing, as it is not possible as well with acoustic broadband clicks, cannot be derived. On the other hand, a considerable portion of the established clinical routine with acoustically evoked ABR for retrocochlear diagnostics is based on broadband excitation. A transfer of the established clinical knowledge to the postoperative care of CI recipients would be most desirable. This would support the efficient handling of clinical resources in managing difficult cases, especially as there is no established objective test battery yet [20].

5. Conclusions

EABR recording potentially provides supportive information for effective management of difficult cases. The application of a broadband stimulus may enable the transfer of already established clinical experience from acoustically evoked to electrically evoked ABR evaluation.

Notes

Competing interests

The authors declare that they have no competing interests.

Author Hocke T is an employee of Cochlear Deutschland GmbH & Co. KG.

Ethical statement

The retrospective evaluation of data from the clinical routine of hearing implanted patients was approved by the local Ethics Committee (BB 049/17).

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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Please cite as

Dziemba OC, Hocke T, Müller A. EABR on cochlear implant – measurements from clinical routine compared to reference values. *GMS Z Audiol (Audiol Acoust)*. 2022;4:Doc05. DOI: 10.3205/zaud000023, URN: urn:nbn:de:0183-zaud0000238

This article is freely available from

<https://doi.org/10.3205/zaud000023>

Published: 2022-08-26

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