Auditory Brainstem Responses in Modern Audiology: Clinical Utility, Advanced Paradigms, and Perspectives as Biomarkers of Cochlear Synaptopathy and Normoacusic Tinnitus

PRODUCT INSIGHTS

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Auditory brainstem responses (ABRs) are short-latency evoked potentials reflecting the synchronous activity of the peripheral auditory nerve and brainstem pathways. Traditionally used for objective threshold estimation and retrocochlear diagnostics, ABRs are experiencing renewed interest due to advanced stimulation paradigms (e.g., paired-click), expansion toward complex stimuli (speech-evoked ABR), and the adoption of automated and artificial intelligence–based waveform analysis. In parallel, a growing body of literature has proposed ABR metrics—particularly wave I amplitude and wave V/I ratio—as indirect markers of cochlear synaptopathy ("hidden hearing loss") and central gain compensation, especially in individuals with tinnitus and normal audiometric thresholds. However, the large inter-individual variability of amplitude measures and the lack of consistent findings across studies require cautious interpretation. In these contexts, ABR should be considered a supportive tool to be integrated with complementary measures such as wideband middle ear muscle reflexes, speech-in-noise testing, otoacoustic emissions, and extended high-frequency audiometry. This review summarizes established clinical applications, methodological considerations, emerging paradigms, and the current evidence for ABR as a potential biomarker beyond threshold estimation.

INTRODUCTION

Celesta is a PC-based evoked potential system for reliable auditory and vestibular diagnostics, including ABR, VEMP, and cortical responses. Fully integrated into the Maestro ecosystem, it features a patient-side bioamplifier, single-cable USB connectivity, and modular licensing for scalable clinical workflows. Celesta streamlines advanced EP testing while ensuring high diagnostic quality, making it ideal for ENT clinics, hospitals, and specialized practices.

ABR is a non-invasive, objective, and highly reproducible neurophysiological technique for assessing auditory pathway integrity up to the brainstem. It remains a cornerstone in newborn hearing screening, objective threshold estimation in difficult-to-test populations, and the identification of retrocochlear dysfunction.

In recent years, the clinical and research focus has shifted toward "beyond-threshold" applications, aiming to detect subclinical neural dysfunction and auditory processing phenotypes not captured by conventional audiometry.

STANDARD RECORDING PARAMETERS

Typical clinical ABR acquisition includes:

- Stimulus: 0.1-ms click, alternating polarity (rarefaction may enhance wave I visibility)
- Intensity: ~90 dB nHL for neurodiagnostic evaluation; descending levels for threshold search
- Rate: ~21/s for morphology (higher for screening)
- Analysis window: 10–15 ms
- Filters: 100–3000 Hz
- Montage: Cz–A1/A2 or Cz–mastoid

Reference to published normative data is essential; however, each laboratory should establish local normative latency values using controlled populations and identical acquisition parameters to ensure clinically valid interpretation.

Based on the clinician's experience, recording parameters may be adjusted to obtain responses that are more specific to the individual patient.

NEUROPHYSIOLOGICAL BASIS AND CORE INTERPRETIVE METRICS

The ABR trace is composed of waves (typically clinically relevant I–V, see Table 1) attributed to generators along the auditory pathway. In clinical practice, absolute latencies (Table 2) and interpeak latencies (I–III, III–V, I–V, Table 3) are considered robust measures of conduction; amplitudes (Table 4) and amplitude ratios (e.g., V/I) add information about peripheral neural output and possible central compensatory mechanisms but exhibit greater variability.

Wave	Main generator
I	Distal auditory nerve
II	Proximal auditory nerve/cochlear nucleus
III	Superior olivary complex
IV	Lateral lemniscus
V	Inferior colliculus

Table 1: Main ABR Waves and Generators

Wave	Mean latency (ms)
I	1.5 ± 0.1
II	2.5 ± 0.1
III	3.5 ± 0.2
IV	4.5 ± 0.2
V	5.5 ± 0.2

Table 2: Typical mean latencies of the five waves

at maximum stimulation intensities.

Interpeak	Mean value
I–III	2.0 ± 0.2 ms
III–V	2.0 ± 0.2 ms
I–V	4.0 ± 0.3 ms

3: Interpeak intervals I–III, III–V, and I–V at maximum stimulation intensities

Wave	Typical amplitude
I	0.1–0.2 μV
III	0.2–0.3 μV
V	0.3–0.6 μV
V/I	> 0.5–1

Table 4: Mean amplitudes of waves I, III, and V

at maximum stimulation intensities.

Correct waveform interpretation requires an integrated evaluation of wave morphology, absolute and interpeak latencies, the latency shift associated with each 10-dB decrease in stimulus intensity, and the intensity–latency functions, all interpreted considering the baseline pure-tone audiogram, which is essential for a physiopathologically coherent reading of the data.

Regarding latency shift, latency increases by approximately 0.3-0.4 ms for every 10-dB reduction in stimulus intensity, a parameter that must always be interpreted with reference to the laboratory's own normative values.

Intensity-latency functions represent a fundamental tool in response analysis, as they allow a dynamic evaluation of the relationship between stimulus level and response timing, improving the ability to differentiate cochlear from retrocochlear patterns. Their construction—based on multiple intensity levels and comparison with laboratory normative data—enables the identification of abnormal slopes, selective delays, or recruitment phenomena, thereby providing a more robust diagnostic framework than latency analysis at a single stimulation level.

ESTABLISHED CLINICAL APPLICATIONS

Objective Threshold Estimation

Click- and tone-burst ABRs remain fundamental for paediatric audiology and non-cooperative patients.

Cochlear, Conductive and Retrocochlear Diagnostics

ABR is a first-line tool for identifying patterns suggestive of neural conduction delay (e.g., prolonged interpeak intervals, interaural wave V differences) and for diagnosing auditory neuropathy spectrum disorder (absent/disorganized ABR with preserved OAEs). Intensity–latency functions of wave V are essential for distinguishing cochlear, conductive, and retrocochlear patterns (Table 5).

Key interpretive points:

- Cochlear loss: latency normalization at high intensities
- Retrocochlear pathology: persistent latency prolongation and abnormal slope
- Conductive loss: parallel rightward shift

Always interpret relative to local normative data and audiometric thresholds.

Monitoring

Applications include ototoxicity surveillance and intraoperative neural monitoring.

Electrically Evoked ABR (EABR)

EABR, elicited via cochlear implant stimulation, is useful for confirming auditory nerve activation, estimating T/C levels in young children, supporting initial mapping, and evaluating non-responsive patients.

EMERGING PARADIGMS

Paired-Click ABR and Synaptic Recovery

Paired-click paradigms probe neural recovery dynamics and synaptic resilience. Recent studies indicate that the response to the second click and derived metrics may vary with age and auditory performance, suggesting their potential role as "synaptopathy-oriented" markers in specific contexts.

Although paired-click paradigms are currently mainly research-oriented and not yet implemented in standard clinical devices, they represent a promising direction for future development of ABR-based assessment tools, especially in the context of synaptic integrity evaluation.

Speech-Evoked ABR

Speech-ABR provides objective measures of temporal and spectral encoding of complex stimuli at the brainstem level, with proposed applications in auditory processing disorders, dyslexia, and language impairment.

While speech-evoked ABR is not yet routinely integrated into conventional clinical ABR platforms, its growing evidence base suggests that future systems may increasingly incorporate complex stimulus paradigms to extend the diagnostic scope beyond threshold estimation.

ABR and Cognitive Function

Associations between ABR timing and cognitive performance suggest that brainstem auditory transmission may reflect broader neurobiological aging processes, raising the possibility of ABR as a non-invasive biomarker for early cognitive decline.

Automation and Artificial Intelligence

Manual peak identification introduces inter-operator variability. Machine learning and deep learning approaches are being developed for automated peak detection, wave V presence classification, and waveform quality assessment.

At present, most AI-based approaches remain primarily research-driven; however, their progressive validation may contribute to improved standardization and reproducibility in high-volume clinical environment

ABR, COCHLEAR SYNAPTOPATHY, AND NORMOACUSIC TINNITUS

Pathophysiological Rationale

Cochlear synaptopathy (loss of inner hair cell–spiral ganglion synapses) may reduce neural output without elevating audiometric thresholds. Central gain mechanisms may compensate, potentially contributing to speech-in-noise deficits and tinnitus.

Reported ABR Patterns

Several studies report:

- Reduced wave I amplitude at high intensities
- Relatively preserved wave V amplitude
- Increased V/I ratio

This pattern has been interpreted as compatible with reduced peripheral output and central gain compensation.

Limitations and Controversies

- High inter-subject variability of wave I amplitude

- Sensitivity to electrode montage, transducer type, and recording parameters
- Need for local normative databases and strict control of confounders
- Limited diagnostic value at the individual level

Thus, ABR should be considered a supportive marker, particularly in research or stratification contexts.

CLINICAL FRAMEWORK: "ABR BEYOND THRESHOLD"

In adults with tinnitus and normal audiograms, ABR may serve to:

1. Exclude clear retrocochlear patterns
2. Describe a "synaptopathy-like" profile (small wave I, elevated V/I ratio, reduced amplitude growth)
3. Guide integration with more sensitive neural function tests (speech-in-noise, MEMR, extended audiometry)

Table 6 reports a brief integrated ABR interpretation checklist.

Interpretation must be multivariate and contextual, avoiding reliance on single metrics.

CONCLUSIONS

ABR remains a cornerstone of audiological diagnostics. Emerging paradigms—including paired-click stimulation, speech-evoked responses, and AI-based analysis—extend its potential toward biomarkers of neural function and auditory processing.

In normoacusic tinnitus and suspected cochlear synaptopathy, amplitude-based metrics are promising but not definitive. The most robust approach is a multimodal, standardized, and cautiously interpreted protocol, integrating ABR with complementary physiological and behavioral measures.

Condition	Latency at high levels	Slope	Curve pattern	Pathophysiological meaning
Normal hearing	Within norms	~0.3 ms/10 dB	Linear	Synchronous conduction
Cochlear loss	Near normal at high levels	Steeper at low levels	Recovery at high intensities	Recruitment, reduced neural threshold
Conductive loss	Prolonged at all levels	Parallel to normal	Right-shifted	Mechanical delay
Retrocochlear lesion	Prolonged even at high levels	Flattened/irregular	Non-parallel, no recovery	Neural desynchrony

Table 5: Wave V Intensity–Latency Patterns

Parameter	What to evaluate	Clinical significance	Operational notes
Wave morphology	Presence, replicability, peak definition	Indicates response quality and neural synchrony	Always verify waveform replicability
Absolute latencies	Latencies of waves I, III, V	Identification of conduction delays	Compare with laboratory normative data
Interpeak latencies	I–III, III–V, I–V	Assessment of brainstem conduction	Useful in suspected retrocochlear pathology
Intensity–latency functions	Latency changes across stimulus levels	Differentiation between cochlear and retrocochlear patterns	Requires acquisition at multiple intensity levels
Latency shifts per ↓10 dB	≈ 0.3–0.4 ms expected	Evaluation of slope integrity	Interpret relative to local normative values
Baseline pure-tone audiometry	Frequency-specific hearing thresholds	Physiopathological contextualization of ABR data	Essential to avoid false positives/negatives

Table 6: Integrated ABR Interpretation Checklist

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