



## Review Paper

# Gap in Noise Auditory Brainstem Responses: A Systematic Review



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## ABSTRACT

**Background and Objectives:** The gap in noise auditory brainstem responses (GIN-ABR) is a valuable assessment tool for auditory temporal processing, offering non-invasive and objective measurements encompassing the entire auditory system from the cochlea to the brainstem. This method has been utilized in investigating various factors, including age-related effects, hearing loss, and tinnitus. This systematic review was conducted to present a thorough examination of (GIN-ABR), encompassing its methodology, applications, and inherent limitations.

**Methods:** This study was conducted based on preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. Cochrane, PubMed, and Ovid databases were used to extract English articles from 1990 to June 2023. The search terms used were “gap in noise auditory brainstem response”, “ABR gap detection”, “ABR gap duration”, “ABR gap threshold”, and “ABR temporal processing”. Articles were included if gap-evoked ABR was used, investigating the effect of any factor on the responses, and using any gapped stimulus type. Articles whose evoked potentials did not include ABR waves were excluded. The outcome of interest was gap-evoked ABR in different participant groups.

**Results:** A total of 10 studies were deemed suitable for inclusion in the review. The articles were reviewed that including the study population, the methods, and the results. Despite the variability in the results of the studies, in the aged group, longer latency shifts and decreased peak amplitude were reported compared to the young group. Correspondence of behavioral thresholds with GIN-ABR has also been mentioned in studies.

**Conclusion:** The GIN-ABR method has been extensively utilized in investigating various factors, including age-related effects, hearing loss, and tinnitus. Notably, GIN-ABR has several clinical advantages, such as cost-effectiveness, shorter test duration, independence from alertness levels, attention, sleep depth fluctuations, or medication. Additionally, it has shown its compatibility with psychophysical tests. Further research is warranted to explore the impact of various factors on different components of GIN-ABR. Consequently, with its promising findings and growing body of research, the gap in noise test has the potential to be gradually integrated into the set of audiological clinical evaluations.

**Keywords:** Auditory brainstem responses, Noise, Gap detection, Electrophysiology, Review



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↑ *What is “already known” in this topic:*

*One form of auditory brainstem response (ABR) testing is the gap in noise ABR (GIN-ABR), which evaluates the ability to detect gaps in a continuous noise signal. This non-invasive and objective method serves as a measure of auditory temporal processing. By analyzing multiple waveform components of the ABR, this test provides insights into the ability of both the auditory periphery and brainstem to process temporal gaps within ongoing sound. In previous studies, this method has been utilized in investigating various factors, including age-related effects, hearing loss, and tinnitus using ABR wave components, such as latency and amplitudes, and gap detection thresholds.*

→ *What this article adds:*

*In this study, an attempt has been made to analyze and classify the investigated features, such as the amplitude and latency of the waves in the form of a systematic review. Each of the previous studies used a separate methodology, and this review study helps the subsequent studies in this field to use a more consistent methodology in the design and construction of the stimulus and ABR wave recording features.*

## Introduction

The auditory brainstem response (ABR) is a test designed to assess the functioning of the auditory brainstem in response to auditory stimuli [1]. It is a simple, objective, and noninvasive procedure to evaluate the brainstem's cochlear nerve and auditory circuits [2]. The ABR test is used to evaluate suspected neurologic disorders of the eighth cranial nerve and its related auditory pathways, as well as to objectively estimate hearing sensitivity for persons who are unable to offer correct behavioral hearing evaluation information [3].

The gap in noise (GIN) test is a commonly utilized clinical procedure that belongs to the behavioral methods category in the field of clinical psychoacoustic evaluation [4]. However, it is essential to note certain limitations associated with these behavioral approaches and psychoacoustic evaluations. These methods heavily rely on patients' subjective judgments, which may be influenced by instructions given before and during the testing process. Furthermore, the results obtained may be affected by factors, such as the frequency of test administration. Additionally, individual performance in these tests can be influenced by various factors, including attention, concentration, and motivation [5-7].

The GIN-ABR is a type of auditory brainstem response testing that focuses on detecting gaps in continuous noise signals. This method serves as an objective and non-invasive measure of auditory temporal processing, providing valuable information about the functionality of the auditory system spanning from the cochlea to the brainstem. By analyzing various waveform components

of the ABR, GIN-ABR offers insights into both peripheral and brainstem auditory processing abilities when detecting temporal gaps in ongoing sounds [8].

GIN-ABR offers several notable advantages compared to alternative approaches to evaluate auditory temporal processing. These include its non-invasive nature, objective measurement of auditory temporal processing, and comprehensive assessment of the auditory system. This method is valuable to investigate a range of conditions including age-related hearing loss, auditory processing disorders, and tinnitus [4, 8-13]. Furthermore, studies have explored the correlation between gap detection thresholds obtained through ABR testing and behavioral thresholds [10, 11, 14].

GIN-ABR uses a broadband noise stimulus with a silent gap embedded in the noise. To determine the minimal detectable gap duration, researchers manipulated the duration of the gap in stimuli and observed participants' responses. The GIN-ABR waveform consists of a series of peaks and troughs that correspond to different neural generators in the auditory pathway. The ABR waveform is analyzed to determine the latency and amplitude of each peak and trough, which can be utilized as a means to evaluate the integrity of the auditory processing system [4, 5].

ABR shows a remarkable synchronization with the onset of a stimulus, demonstrating precise alignment both in terms of time and phase. Figure 1 shows this synchronicity, where the presence of a gap in the stimulus gives rise to two distinct points of origin, one preceding the gap (referred to as pre-gap) and another succeeding it (known as post-gap). As a result, due to its close re-

semblance to the shape and physical characteristics of the stimulus, ABR enables the recording of two separate responses- corresponding to the pre-gap segment and another representing the post-gap segment [13, 14].

This review was conducted to present a thorough examination of the gap in noise auditory brainstem responses, encompassing its methodology, diverse applications, and inherent limitations. Additionally, we address the current state of research on GIN-ABR, focusing particularly on its utilization in exploring the impacts of auditory processing disorders, hearing loss, tinnitus, and age-related factors. Furthermore, we explore potential future avenues for research about GIN-ABR testing and discuss its prospective clinical applications.

## Materials and Methods

This study adhered to the guidelines outlined by the preferred reporting items for systematic reviews and meta-analyses (PRISMA) framework. PubMed, Cochrane, and Ovid databases were used to extract data from 1990 up to June 2023. In addition, a manual search was also performed through Google Scholar to find studies that were not identified in the above databases for any reason. The search terms used were “gap in noise auditory brainstem response”, “ABR gap detection”, “ABR gap duration”, “ABR gap threshold”, and “ABR temporal processing”. The keywords used alone or in combination (“and”) and mesh (medical subject headings) terms were searched when available. The search was not limited to human studies and also included animal studies. Letters to the editor, review articles and case reports were not included in the search. The main focus of the research was to investigate gap-evoked auditory brainstem responses in various groups of participants. Gaps, which refer to silent intervals in a stimulus sound, were precisely defined for this purpose and ABR were recorded by pre or post-gap stimulus sections. Articles were included if there was the use of gap-evoked ABR, investigating the effect of any factor on the responses, and using any gapped stimulus type. Articles whose evoked potentials did not include ABR waves were excluded. To ensure the reliability and quality of the included content, non-peer-reviewed sources, such as magazines, conference proceedings, editorials, manuals, and articles in languages other than English were excluded from this study.

The initial phase of the review process entailed screening the titles and abstracts of studies to assess their eligibility based on predetermined inclusion criteria. Subsequently, all selected articles were reviewed in full-text form to further refine the selection and eliminate any

studies that did not align with the research objectives. This meticulous evaluation ensured that only relevant and suitable research was included in the final analysis. The chosen studies were then carefully analyzed for their content and organized into a table based on features, such as authors, year of publication, journal and indexing, individual characteristics (e.g. sample size, age, gender, hearing status, species studied), ABR gap in noise stimulus details (noise bandwidth, rise/fall time, duration, filters, gap duration), methods used (e.g. examining onset or offset of gaps, manipulating gap features, employing different gap durations, using various stimulus frequencies), dependent variables measured and major results.

## Results

The initial search yielded a total of 1 198 studies using the specified keywords. After removing duplicates, 903 unique studies remained for further evaluation based on the inclusion and exclusion criteria, primarily through assessing their titles and abstracts. Articles were excluded from consideration due to factors, such as the use of electrophysiological tests other than ABR, the use of gapless stimuli, limited availability of full-text access in English, or conference proceedings. Following this screening process, 58 studies met the eligibility criteria and underwent a thorough examination of their full texts. Eventually, after careful analysis, 10 studies were deemed suitable for inclusion in the review. [Figure 2](#) shows the selection process using the preferred reporting items for systematic reviews and meta-analyses (PRISMA) flowchart methodology. [Table 1](#) presents the summarized information extracted from the final included studies.

### Population

Of the 10 articles that were finally reviewed, 7 articles were about people with normal hearing, 3 articles about people with sensory-neural, age-related, or salicylate-induced hearing loss, and 1 article about people with tinnitus. Humans were investigated in 7 studies, and in other studies, the investigation was conducted on animals (1 on Mongolian gerbils and 2 on CBA Carter mice.).

The number of participants in all human studies was 121, of which 44% were men and 56% were women. This number for animal studies was 48 animals. In the human studies, young individuals ranged in age from 18 to 30 years, while the age groups included individuals aged between 58 and 72 years. In animal studies, the reported age range was between 2-4 months in Lowe et al.'s study [10], young (4-8 m) and aged (33-37 m) in

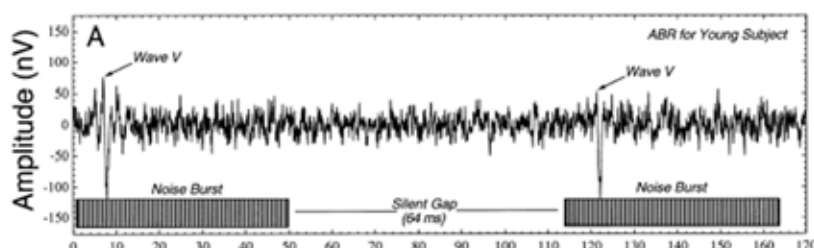


Figure 1. Example of a gap in noise auditory brainstem responses (GIN-ABR)

Wave V is observed in response to the onset of the pre and post-gap noise stimulus. from Poth et al. [4]

Boettcher et al.'s study [12], young adults (3-4 m) and middle age (15-18 m) in Williamson et al.'s study [9].

In human studies, the hearing assessment involves measuring pure tone thresholds. Normal hearing was defined as pure tone thresholds equal to or below 25 dBHL according to Poth et al. and Aluossaini et al. [4, 15], equal to or less than 20 dBHL in Grose et al.'s study [16] and equal to or lower than 15 dBHL in Duda-Milloy et al.'s study at each clinical octave in the range of 250 to 8000 Hz [5]. Also in Fan et al.'s study, the thresholds equal to or lower than 25 dBHL in 250-8000 Hz were considered normal hearing [17]. In Werner et al.'s study, normal hearing status was verified through screening audiometry at octave frequencies from 500 to 8000 Hz, with thresholds set at 15 dBHL. Additionally, click-evoked ABR testing was performed at a level of 20 dB nHL to further confirm the participants' normal auditory function [11]. In a study, normal hearing was reported, without specifying exact thresholds [14]. Hearing thresholds exceeding 8 kHz were not reported in any human studies. In an animal study conducted by Williamson et al., the functionality of the outer hair cell system was assessed using distortion product otoacoustic emissions (DPOAEs) [9]. The study conducted by Lowe et al. described hearing changes as an increment in the average ABR thresholds [10]. Boettcher et al did not mention hearing status measurement protocol [12].

## Methods

The human studies investigated the auditory brainstem wave V features, such as absolute peak latency and amplitudes, latency, and amplitudes shift, latency and amplitude ratios. Wave V was recorded in response to pre and post-gap stimulus onsets. The animal studies focused on examining the characteristics of auditory brainstem waves 1 to 4. Most of these studies utilized wideband noises with gaps inserted, employing various filters (n=5). Alternatively, narrowband noises within different frequency bands were used in the remaining studies (n=4), covering frequencies ranging from 750 Hz to

36000 Hz. It is worth noting that human data was only reported up to 4000 Hz. Fan et al used a harmonic complex [17].

In terms of stimulus presentation levels, they typically ranged from 60 to 85 dB sound pressure level (SPL) in three studies, but in two studies, the level varied between 10 to 50 dB SPL (n=1) or was fixed at 100 dB peSPL (n=1). The length of pre and post-gap stimuli was different in studies. Signals with a length of 12 ms (n=1), 15 ms (n=2), 25 ms (n=1), 50 ms (n=4), 100 ms (n=1), and 150 ms (n=1) were used in the studies. In Allhussaini et al. and experiment 2 of Fan et al., gaps of constant length were inserted between two signals, with the gap duration set at 12 ms and 5 ms, respectively [15, 17]. Similarly, in Mori et al.'s study, the gap length was determined individually for each listener based on their gap thresholds. The gap duration used in this study was either identical to the measured threshold or 0.5, 1, or 1.5 times longer than the individual's gap threshold duration for each frequency combination [14]. Most of the remaining studies used gaps with lengths of 0 to 64 ms in different combinations. Werner et al used 0 to 125 ms gap durations in their study [11].

Seven studies used the gap in noise stimuli in within-channel conditions, meaning that the frequency content of pre and post-gap noise did not differ from each other. However, three studies used between-channel mode. Grose et al. used frequency-asymmetric markers [16] containing a single primary tone with a two-tone trailing marker (2285 Hz, 4000 Hz). In the study conducted by Mori et al., various combinations of center frequencies were used in 800/1600 Hz, 800/3200 Hz, 1600/800 Hz, 3200/800 Hz (between channel), and 800/800 Hz (within channel) [14]. Fan et al stimuli contained two signals. The first signal consisted of ten 200 to 2 kHz harmonics at frequency intervals of 200 Hz. The second signal, referred to as the target signal, was a tone with a frequency of 1000 Hz combined with the fifth harmonic of the first signal [17].

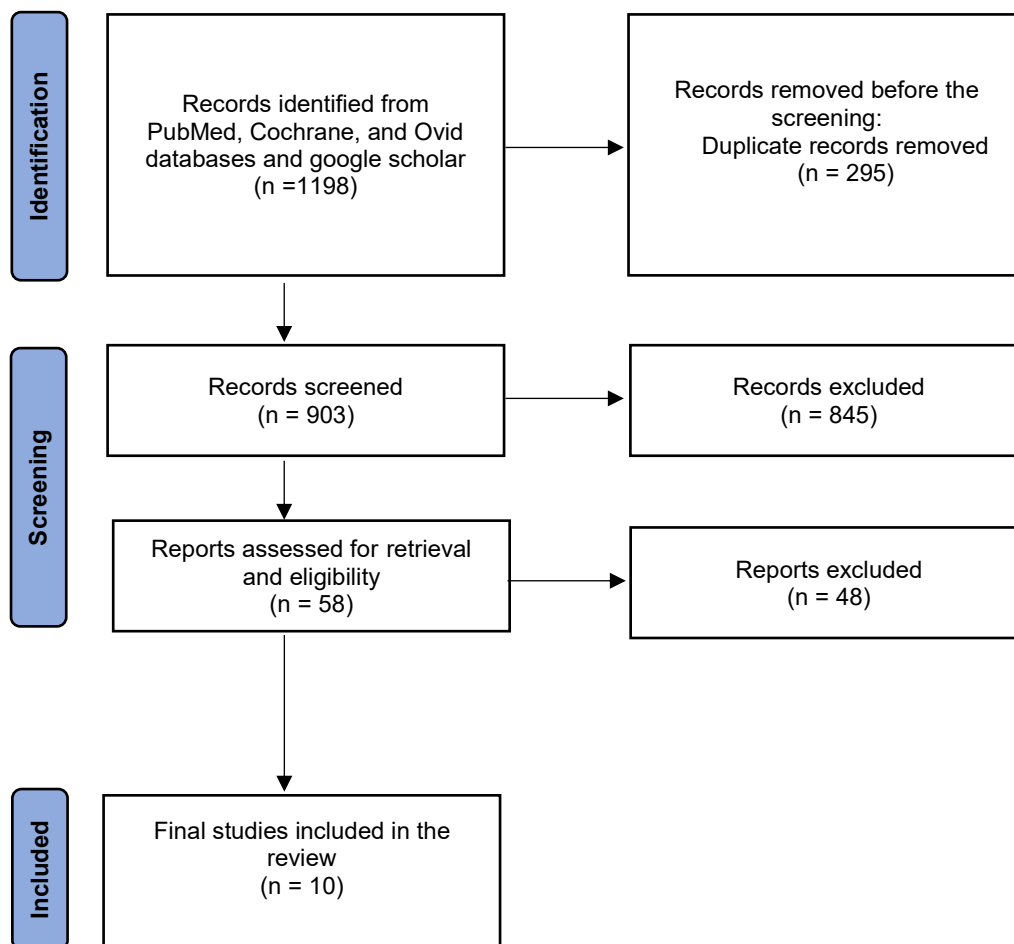


Figure 2. Flow diagram of study selection

### Outcomes

Most studies have investigated and compared the latency and amplitude of ABR waves elicited with the pre and post-gap stimuli. Factors, such as latency shift (the difference of waves latency in response to the pre and post-gap stimulus), and amplitude ratio (the ratio of the amplitude of the pre and post-gap waves) have also been calculated. Studies that have investigated the effect of age-induced hearing changes and age report almost the same results. The latency shift was longer in the aged group compared to the young group [9, 12]. Boetcher et al. reported amplitude ratios with small changes across age groups while Williamson et al. reported that the middle-aged group of mice showed decreased peak amplitude compared to the young group. In the study conducted by Poth et al., older adults showed similar response latencies to younger subjects, but smaller amplitudes were observed. Also, the gap detection thresholds were higher in the aged group in this study [4].

In Lowe et al.'s study a significant reduction in amplitude ratio was observed only near the tinnitus frequency as estimated based on gap pre-pulse inhibition (GPPI) [10]. In the study conducted by Werner et al, a partial correlation (0.39 and  $P=0.011$ ) was reported between the average electrophysiological threshold ( $2.4\pm 0.1$  ms) and the average psychophysical threshold ( $2.9\pm 0.2$  ms) [11]. In contrast, Mori et al. observed that the onset response of ABR was not consistently consistent with behavioral gap detection thresholds, particularly when considering various between-channel and within-channel conditions. [14].

Duda-Miloy et al. reported that the duration of the gap has a suppressive impact on the wave V amplitude in response to post-gap noise burst [5]. On the other hand, Fan et al. found that neither the duration nor depth of the gap influenced response amplitude; however, they observed a significant decrease in response latency with increasing gap duration or depth [17]. Similarly, Grose et al. reported that in conditions where gaps were within-channel, shorter gap durations resulted in increased wave V latency and deteriorated waveform [16].



**Table 1.** Summary of the characteristics of reviewed studies

Article Name	Major Results	ABR Features That Measured	Gap Duration	ABR Stimulus	Hearing Status	Study Groups	Journal	Year	Authors
Auditory evoked potentials in aged gerbils: responses elicited by noises separated by a silent gap	Significantly longer latency shift of wave IV in the aged group than the young group. No notable differences between groups for wave II or CAP. Minimal changes in amplitude ratios across age for both the CAP and ABR waves.	Latency shift, absolute amplitudes, amplitude ratios for the compound action potential (CAP) and waves II and IV of ABR.	1, 2, 4, 8, 16, or 32 ms	Two 50-ms noise bursts WBN Low pass filter: 5 KHz rise-fall: 1-ms 60 and 80 dB SPL	Normal hearing and presbycusis	Mongolian gerbils 10 Young (4-8 m) 10 aged (33-37 m)	Hearing research	1996	Flint A, Boettcher, John H, Mills, Jason L, Swerdloff, Brenda L, Holley [12]
Human auditory brainstem response to temporal gaps in noise	Normal hearing group, the average psychophysical threshold: 2.9±0.2 ms the average ABR threshold: 2.4±0.1 ms partial correlation: 0.39 (P<0.011). HL group, the average psychophysical threshold: 10.7±5.7 ms the average ABR threshold: 12.7±3.7 ms No difference between ABR gap thresholds of adults with normal hearing and 3-month-old infants.	ABR gap threshold Psychophysical gap detection: 2AFC paradigm and go/no-go procedure	0-125 ms	Two 15- ms noise bursts WBN Low-pass filter: 7 KHz 10, 30 or 50 dB SPL/Hz Psychophysical: Two 3,000-ns WBN bursts, at 30 dB	Normal hearing: passed screening audiometry at 15 dB HL (0.5 to 8 KHz) and the presence of click-evoked ABR at 20 dB nHL Sensorineural hearing loss: to 65 dB HL	35 young adults with normal hearing (18-30y) 3 listeners with sensorineural hearing loss (58-64y) 10 infants (3-6m)	Journal of speech, language, and hearing research	2001	Lynne A, Werner, Richard C, Folsom, Lisa R, Mancl, Connie L, Syapin [11]
Auditory brainstem responses in younger and older adults for broadband noises separated by a silent gap	No measurable post-gap responses in 4 and 8 ms gap duration for 3 of 8 older adults and in 4 ms gap duration for young subjects. Similar latencies for older and younger subjects when responses were present, and smaller amplitudes in older adults.	Wave V amplitude and latency presence of wave V in response to the second noise burst	4, 8, 32, or 64 ms	Two 50-ms noise bursts WBN rise-fall: 0.7-ms	Young subjects: PTT ≤ 20 dB HL (0.25 - 8 KHz) aged subjects: PTT ≤ 25 dB HL	8 young (19-32 y) 8 aged (60-72 y)	Hearing research	2001	Elizabeth A, Poth, Flint A, Boettcher, John H, Mills, Judy R, Dubno [4]
Frequency asymmetry and gap duration discrimination in auditory brainstem responses	Within-channel condition: Increase in wave V latency, and deterioration in waveform morphology with the decrease in gap duration. No latency shift or morphology change with gap duration, in response to the secondary tone in the frequency-asymmetric trailing marker. Larger wave V amplitude with the two-tone trailing marker than with a single-tone.	Wave V latency, amplitude and morphology	0.4, 8, 16, 32, 64 ms	Frequency-asymmetric markers: A single primary tone and a two-tone trailing marker (2285/4000Hz) Duration of each marker: 100ms Zms rise/8ms fall 65dB SPL	PTT ≤ 20 dB HL (0.25–8 KHz)	6 adult (19-39 y)	Journal of the acoustical society of America	2007	John H, Grose, Joseph W, Hall III, and Emily Buss [16]

Article Name	Major Results	ABR Features That Measured	Gap Duration	ABR Stimulus	Hearing Status	Study Groups	Journal	Year	Authors
Auditory brainstem gap responses start to decline in mice in middle age: a novel physiological biomarker for age-related hearing loss	Prolonged post-gap wave latency and decreased amplitude in the middle-age group in comparison with the young group.	Peak amplitude and peak latency (peak I and IV), the smallest detected gap duration	0, 1, 2, 4, 8, 16, 32 and 64 ms	Two 25 ms noise bursts WBN low-pass cutoff: 5 KHz 0.5 ms rise-fall times 80dB SPL rate: 21/s	Normal function of the outer hair cell according to DPOAEs.	CBA/Cal mice 8 young adult (3-4 m) 8 middle age (15-18 m)	Cell tissue research	2015	Tanika T. Williamson, Xiaoxia Zhu, Joseph P. Walton, and Robert D. Frisina [9]
Alterations in peripheral and central components of the auditory brainstem response: A neural assay of tinnitus	Increased post SS gap detection threshold at 16 KHz measuring with peak1 and at 12, 16, and 20 KHz measuring with peak4 and with The behavioral PPI. A significant decrease in peak1 amplitude ratio at 16 KHz, reflects the frequency range of tinnitus.	Peak 1,2,3,4 latency and amplitude ratios, gap detection threshold	2, 4, 8, 12, 16, 25, and 50 ms	150-ms NBN with or without a silent gap Center frequencies: 6/ 12/ 16/ 20/ 24/ 36 KHz 70 dB	Before sodium salicylate (SS): Normal hearing, no tinnitus Post SS: Elevated ABR thresholds, tinnitus	CBA/Cal mice 12 young adult (2-4 m) 4 men	PLOS One	2015	Andrea S. Lowe, Joseph P. Walton [10]
Auditory brainstem responses to silent gaps in across-channel conditions	No correspondence was observed between ABR results and the behavioral gap thresholds. Consistent low wave V amplitudes until the gap duration of 6-7 ms. sharp amplitudes increment to a high level beyond this threshold, across all frequency combinations.	Presence of wave V wave V amplitude	0.05, 1, or 1.5 times of behavioral gap detection threshold at every frequency combination.	Two 50-ms One-half octave band of center frequency Rise/fall: 3ms Center frequencies in Hz: between channels: 3 200/800, 1 600/800, 800/3 200, and 800/1 600 within channel: 800/800	Normal hearing	10 male students (22 – 25 y)	Acoustical science and technology	2016	Shuji Mori, Keiji Iramina [14]
Auditory brainstem, middle and late latency responses to short gaps in noise at different presentation rates	Present of all components at 1 Hz. Disappearing of N1 and P2 at higher rates.	Latency/amplitude of major ABR, MLR and LLR components (V, Na, Pa, Nb, Pb, N1 and P2)	12 ms rates: 0.5, 1, 5 and 40 Hz	White noise signal low-pass filter: 5KHz	PTT ≤ 25 dB HL (0.25–8 kHz)	14 Young adults (21 to 31 y) (10 men)	International Journal of audiology	2018	Khalid Alhussaini, Jorge Bohorquez, Rafael E. Delgado, and Ozcan Ozdamar [15]

Article Name	Major Results	ABR Features That Measured	Gap Duration	ABR Stimulus	Hearing Status	Study Groups	Journal	Year	Authors
Using the auditory brainstem response elicited by within-channel gaps to measure temporal resolution	Suppressive effect of gap duration on the post-gap wave V amplitude. A significant difference between the amplitude of pre and post-gap wave V for gap durations $\leq 20$ ms for 750 Hz and $\leq 5$ ms, for 3750 Hz.	The amplitude of wave V (pre and post-gap)	2, 5, 10, 20, 30, 40 or 50 ms	Two 15 ms NBN Center frequency: 3750 or 750 Hz. 1000db pesPL	PTT $\leq 15$ dB HL (0.25–8-KHz)	15 adult participants (18-30 y) (7 men)	Canadian acoustics	2019	Victoria Duda-Millooy, Eric Zorbas, Daniel L. Benoit, and Aminesh Koravand [5]
Auditory brainstem responses to successive sounds: Effects of gap duration and depth	Significant decrease in latency with an increase in depth or duration of the gap. No changes in the amplitude of the responses by changing the duration or depth of the gap.	Peak latency and amplitude of wave V	Experiment 1: 0.5 and 10 ms Experiment 2: a continuous background noise was added. The gap depth: Target signal level minus continuous noise level.	Leading signal: Signal 1 Following target signal: Signal 2 Signal 1: A complex consisting of ten harmonics spanning from 200 to 2 kHz with frequency increments of 200 Hz. Duration: 50 ms Rise/fall: 10 ms Signal 2: A tone at a frequency of 1 kHz, which corresponds to the fifth harmonic of signal 1. Duration: 10 ms Rise/fall: 5 ms 70db SPL	PTT $\leq 25$ dB HL (0.25–8-KHz)	12 adults (18-35 y) (6 men)	Audiology research	2021	Fan-Yin Cheng and Craig A. Champlin [17]

Abbreviations: m: months old; y: years old; WBN: Wide band noise, DPOAEs: Distortion product otoacoustic emissions; NBN: Narrow band noise, PPI: Pre-pulse inhibition, ms: millisecond; HL: Hearing loss; PTT: Pure tone thresholds; ABR: Auditory brainstem response; MLR: Middle-latency responses; LLR: Late latency responses.

## Discussion

The GIN-ABR is a relatively novel assessment technique that holds promise for clinical applications. It has been extensively studied across a range of contexts, including age-related hearing loss and tinnitus [4, 9-12]. Additionally, researchers have focused on exploring the correlation between GIN-ABR results and subjective evaluations, as well as investigating the influence of various factors on different components of this test [5, 11, 14-17].

### Age

GIN-ABR has been used to investigate the effects of age on auditory temporal processing across different age periods. Two studies showed that the latency of the post-gap ABR waveform increases with age, indicating a decline in the speed of neural processing with age, suggesting that it can be an innovative physiological marker in case of age-related hearing changes even in the very early stages [9, 12]. Also, some other studies found that the post-gap ABR responses start to decline with increas-

ing age [4, 9], and gap detection thresholds increase [4]. The results indicated that age-related gap detection deficits exist at the brainstem level among older individuals without hearing threshold changes [4]. Gap detection thresholds, using ABR, in 3-month-old infants showed no difference from those of adults with normal hearing in Werner et al.'s study [11].

The age-related decline in amplitude levels has been attributed to various factors, such as diminished temporal synchronization among neurons, declined number of responsive neurons, and decreased endocochlear potential [18, 19]. Spiral ganglion (SG) cells, located in the modiolus, send excitatory signals to the central auditory system, particularly to the cochlear nucleus. In this interaction, SG excitatory neurons interact with neurons that utilize inhibitory neurotransmitters, such as glycine or gamma-aminobutyric acid [19, 20]. Age-related reduction in responsive nerve fibers in SG disturbs the balance between inhibition and excitation. This decline in neural coding capabilities within the central auditory system is associated with age-related changes at hair cell/SG neu-



ron synapses and reductions in hair cell and neuron numbers. Consequently, studies have suggested that post-gap ABR peak latency and amplitude are compromised or degraded due to impaired temporal processing and inhibitory functions [9].

### Hearing loss

GIN-ABR has been used to investigate the effects of hearing loss on temporal processing, just like the conventional subjective gap in noise tests. In Werner et al's study, participants with hearing loss exhibited an average psychophysical threshold of 10.7 ms compared to normal hearing participants (2.6 ms). Similarly, the ABR threshold averaged 12.7 ms for those with hearing loss and 2.7 ms for those with normal hearing. These results indicated that sensorineural hearing loss has the same effect on both psychophysical and ABR thresholds, while the psychophysical gap detection threshold is slightly higher than the ABR gap threshold [11]. Studies that have used behavioral and psychophysical gap detection tests also showed that the gap detection threshold is higher in individuals with hearing loss than in individuals with normal hearing, indicating a decline in auditory temporal processing with hearing loss. The mechanisms underlying sensorineural hearing loss seem to impact both behavioral and electrophysiological gap thresholds. This suggests that peripheral factors associated with sensorineural hearing loss limit the ability of individuals with hearing loss to detect gaps. Consequently, ABR may serve as a valuable tool to investigate temporal resolution in individuals with hearing loss [11].

### Tinnitus

Lowe et al. found a notable reduction in amplitude ratio (recovery time) specifically around the frequency associated with sodium salicylate (SS)-induced tinnitus, which was measured using the reliable gap pre-pulse inhibition (GPPI) method [10]. This study highlights the effectiveness of GIN-ABRs as a non-invasive approach to detect the presence of tinnitus and or approximate pitch in mouse models objectively. Furthermore, it suggests that GIN-ABR can potentially be applied to human subjects and reveals distinct impairments in temporal processing within peripheral and brainstem pathways, affected in drug-induced tinnitus. In a review article on ABR in tinnitus, GIN-ABR was recognized as one technique capable of objectively assessing the presence of tinnitus [8].

In the studies conducted in recent years, it has been found that people with tinnitus have shown higher thresholds in tests related to temporal processing, such

as types of GIN and gap detection tests [10, 21-24]. Contemporary research articles explore the question of whether the elevation in gap detection thresholds observed in individuals with tinnitus is attributed to a general impairment in temporal resolution [21-23, 25] or if tinnitus itself masks the silent gap between two stimulus components [10, 24, 26]. Evidence has been presented supporting both theories, indicating that further investigation is necessary to gain deeper insights into this area of study.

### Clinical application

So far, gap in noise has been electrophysiologically investigated using methods, such as ABR, auditory middle latency responses (MLR), event-related potentials (ERP), and mismatch negativity in studies.

As mentioned, GIN-ABR is a method that has been investigated in animal and human studies and in people with normal hearing, sensorineural hearing loss, and tinnitus, as well as in infants and the elderly. The results of these studies have shown the appropriate use of this test in experimental groups. Also, in recent studies, the effect of various factors, such as the frequency of the stimulating noise, gap length, and depth on the amplitude and latency of waves has been investigated [5, 16, 17]. This is a big step towards bringing GIN-ABR closer to clinical application.

In the study of Alhussaini et al., a detailed comparison was made between the characteristics of ABR, mid-range, and late auditory responses in response to GIN stimuli [15]. In this study, the effect of the stimulation presentation rate on these responses was investigated, showing that most of these electrophysiological responses to the gap stimulus in noise can be obtained at a rate of 1 Hz; meanwhile, at higher stimulation presentation rates, only ABR and middle latency responses (MLR) can be recorded, indicating the greater priority of the GIN-ABR test in clinical routine evaluations compared to late responses. This priority can be due to the higher speed and shorter test time.

The use of ABR as a clinical electrophysiological tool for gap detection has other advantages. Among them, we can mention non-invasiveness, cost-effectiveness, and the possibility of using a large number of audiologists [5]. Meanwhile, providing the necessary environment, equipment, expertise and experience for the implementation of event-related potentials (ERP) tests in clinics will not be easy. In addition, unlike late responses and other electrophysiological tests of hearing, ABR is less affect-

ed by alertness, depth of sleep, and medications taken by people [27]. Another advantage of using electrophysiological GIN compared to studies that investigate conventional electrophysiological tests to find an objective clinical evaluation of hearing system function is that the effect of complications on the amplitude or latency of waves in electrophysiological GIN is eliminated. Thus, any potential effects of interindividual variation on amplitude, waveform, latency, or other characteristics of waves is replicated twice, pre-gap and post-gap. As a result, the possibility of interfering with the purpose of the test, which is the gap detection threshold, is reduced.

To develop electrophysiological tests in line with behavioral gap detection tests, studies have been conducted that behavioral GIN thresholds in various groups of patients are closely related to gap detection thresholds in noise, which are determined by GIN-ABR [11, 28]. Also, The GIN-ABR holds promise in providing frequency-specific information to investigate temporal resolution in individuals with diverse hearing disorders [5].

## 5. Conclusion

The GIN-ABR is a valuable assessment tool for auditory temporal processing, offering non-invasive and objective measurements that encompass the entire auditory system from the cochlea to the brainstem. This method has been extensively utilized in investigating various factors, including age-related effects, hearing loss, tinnitus, and auditory processing disorders. Notably, GIN-ABR has several clinical advantages, such as cost-effectiveness, shorter test duration compared to other electrophysiological methods to assess gaps in noise perception, independence from alertness levels, attention span variations, sleep depth fluctuations, or medication influences commonly encountered among individuals. Additionally, it has been shown to be compatible with psychophysical tests.

Despite its strengths and applications, it is essential to acknowledge certain limitations associated with GIN-ABR that warrant careful interpretation of results. Ongoing research efforts are needed to comprehensively explore the potential clinical implications of this technique and elucidate its precise role within the broader context of evaluating auditory system function. Further deepening our understanding of these aspects through rigorous investigation and studies conducted on larger populations across diverse settings and conditions ultimately enhances our ability to leverage GIN-ABR effectively for diagnostic purposes and treatment planning.

## Limitations

GIN-ABR has limitations that should be considered when interpreting the results. One limitation is that GIN-ABR only measures auditory temporal processing up to the brainstem. Other auditory temporal processing measurement tools, such as gap detection using behavioral measures, can evaluate higher levels of the auditory temporal processing system. Another limitation is that GIN-ABR uses a broadband noise stimulus, which may not be representative of real-world listening situations. Finally, GIN-ABR requires specialized equipment and expertise, which may limit its availability in some clinical settings.

## Future directions

Future research on GIN-ABR may focus on developing new methods of data analysis to improve the accuracy and reliability of the results. For example, machine learning algorithms may be used to analyze the GIN-ABR waveform to identify patterns that are associated with specific auditory disorders or use frequency-specific stimuli to obtain detailed information from different parts of the auditory pathway by region. Future research may also focus on developing new applications of GIN-ABR testing, such as using it to assess the efficacy of hearing loss treatments or to predict the risk of developing auditory disorders before the onset of clinical symptoms.

## Ethical Considerations

### Compliance with ethical guidelines

This research did not involve the use of human volunteers or animals, ensuring compliance with ethical guidelines.

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### Authors' contributions

All authors equally contributed to preparing this article.

### Conflict of interest

The authors declared no conflict of interest.

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## مقاله مروری



### پاسخ‌های شنیداری ساقه مغز برانگیخته‌شده با محرک شکاف در نویز؛ یک مرور نظام‌مند

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## چکیده

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**مقدمه:** پاسخ‌های شنیداری ساقه مغز برانگیخته‌شده با محرک شکاف در نویز یک ابزار ارزیابی ارزشمند برای سنجش پردازش زمانی سیستم شنوایی است. این ابزار یک روش غیرتهاجمی و عینی را ارائه می‌کند که کل سیستم شنوایی از حلازون تا ساقه مغز را دربر می‌گیرد. در مطالعات پیشین اثر عوامل مختلف از جمله افزایش سن، کاهش شنوایی و وزوز گوش بر این آزمون بررسی شده است. در این مطالعه یک مرور نظام‌مند روی شکاف در نویز با استفاده از پاسخ‌های شنیداری ساقه مغز، شامل روش شناسی، کاربردها و محدودیت‌های ذاتی آن انجام شد.

**مواد و روش‌ها:** این مطالعه براساس دستورالعمل‌های موارد گزارش‌دهی ترجیحی برای مرور نظام‌مند و متآنالیز (PRISMA) انجام شد. پایگاه‌های اطلاعاتی PubMed، Cochrane، Ovid برای استخراج مقالات انگلیسی از سال ۱۹۹۰ تا ژوئن ۲۰۲۳ استفاده شدند. کلیدواژه‌های مورد استفاده جهت جست‌وجو عبارت بودند از: «شکاف در نویز پاسخ شنیداری ساقه مغز»، «تشخیص شکاف در ABR»، «طول شکاف در ABR»، «آستانه تشخیص شکاف در ABR» و «پردازش زمانی و ABR». مقالاتی که پتانسیل‌های برانگیخته آن‌ها شامل امواج ABR نبود، حذف شدند. در جست‌وجو مقالاتی مدنظر بودند که پاسخ‌های شنوایی ساقه مغز برانگیخته‌شده با انواع محرک شکاف‌دار در گروه‌های مختلف شرکت‌کننده را بررسی کرده بودند.

**یافته‌ها:** در مجموع ۱۰ مطالعه، مناسب تشخیص داده شد. مقالات از نظر جمعیت مورد مطالعه، روش به کار گرفته‌شده و نتایج حاصل بررسی و مقایسه شدند. در جمع‌بندی نتایج مطالعات با وجود تنوع در این نتایج، افزایش زمان تأخیر و کاهش دامنه امواج در افراد مسن نسبت به گروه جوان در بیشتر مطالعات گزارش شد. مطابقت آستانه‌های رفتاری با پاسخ‌های شنیداری ساقه مغز برانگیخته‌شده با محرک شکاف در نویز نیز در مطالعات ذکر شده است.

**نتیجه‌گیری:** روش پاسخ‌های شنیداری ساقه مغز برانگیخته‌شده با محرک شکاف در نویز به‌طور گسترده در بررسی عوامل مختلف از جمله اثرات مربوط به سن، کاهش شنوایی و وزوز گوش استفاده شده است. از جمله مزایای بالینی استفاده از این روش می‌توان به مقرون به‌صرفه بودن، مدت‌زمان کمتر تست، عدم وابستگی به سطح هوشیاری، توجه، نوسانات عمق خواب یا دارو اشاره کرد. علاوه بر این، این ابزار تطابق خود را با آزمون‌های رفتاری در مطالعات نشان داده است. جهت بررسی تأثیر عوامل مختلف بر اجزای این پاسخ‌ها پژوهش‌های بیشتری مورد نیاز است. در نتیجه، با یافته‌های امیدوارکننده و تحقیقات رو به رشد، آزمون پاسخ‌های شنیداری ساقه مغز برانگیخته‌شده با محرک شکاف در نویز این پتانسیل را دارد که به‌تدریج در مجموعه ارزیابی‌های بالینی شنوایی‌شناسی ادغام شود.

## کلیدواژه‌ها:

پاسخ‌های شنوایی ساقه مغز، شکاف در نویز، تشخیص شکاف، الکتروفیزیولوژی، مرور

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