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Diagnostic Accuracy of ABR Wave I Amplitude and SPIN Test in Identifying Cochlear Synaptopathy: A Case-Control Study

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Abstract
Cochlear synaptopathy represents auditory dysfunction where patients present with normal pure tone audiometry but experience tinnitus and speech-in-noise difficulties. This case-control study at King Edward Medical University evaluated the diagnostic capability of auditory brainstem response (ABR) Wave I amplitude and Speech Intelligibility in Noise (SPIN) test in identifying cochlear synaptopathy among 60 participants (30 cases, 30 controls) with normal hearing thresholds. ABR Wave I amplitude was significantly reduced in cases (0.14±0.04 μV) compared to controls (0.24±0.02 μV), $p<0.001$. SPIN scores were lower in cases (72.8±9.1%) versus controls (95.1±2.8%), $p<0.001$. Using <0.20 μV for Wave I and <90% for SPIN as thresholds, sensitivity and specificity exceeded 93% for both measures. These findings support ABR Wave I amplitude and SPIN testing as reliable diagnostic tools for hidden hearing loss in Pakistani populations with noise exposure.

Keywords: hidden hearing loss, auditory nerve dysfunction, noise-induced hearing loss, speech perception, electrophysiology

Introduction

Noise-induced hearing loss remains a significant public health concern globally, affecting millions across occupational and recreational settings. Pure tone audiometry has traditionally served as the gold standard for assessing hearing function. However, emerging evidence from animal studies reveals that the auditory system may be more vulnerable to acoustic trauma than previously understood, particularly at synaptic connections between inner hair cells and auditory nerve fibres (Liberman and Kujawa, 2017).

Recent research demonstrates that cochlear synapses are especially susceptible to noise damage, even when exposure does not result in permanent threshold shifts on audiometry (Bharadwaj et al., 2015). This phenomenon, termed cochlear synaptopathy, can occur with intact hair cells and normal audiometric thresholds, yet patients experience significant auditory dysfunction—hence "hidden hearing loss" (Liberman and Kujawa, 2017). The preferential loss of low spontaneous rate, high-threshold auditory nerve fibres explains why patients maintain normal hearing thresholds whilst experiencing difficulties in challenging listening conditions.

Neurodegenerative disorders typically involve synaptic decline prior to significant functional impairments. Similarly, early synapse loss impacts both central and peripheral auditory systems before evident audiogram changes occur (John and Reddy, 2021). Studies show that up to 80-90% of auditory nerve fibres can be lost before significant threshold changes appear on audiometry (Lobarinas et al., 2013). This disconnect between subjective auditory complaints and objective audiometric findings has necessitated development of alternative diagnostic approaches.

Two promising measures have emerged from recent research: ABR Wave I amplitude and speech-in-noise testing. Wave I of the ABR reflects synchronous firing of auditory nerve fibres in response to acoustic stimuli. Reduced Wave I amplitude, particularly at suprathreshold levels, may indicate loss of synaptic function or auditory nerve degeneration (Bharadwaj et al., 2015). Similarly, performance on speech-in-noise tasks reflects integrity of temporal processing and neural encoding—functions compromised in synaptopathy due to reduced neural synchrony and impaired ability to encode fine temporal information (Hope et al., 2013).

In Pakistan, occupational and environmental noise exposure is widespread, particularly among factory workers, construction workers, mechanics, and those in transportation sectors. Additionally, recreational noise exposure through personal listening devices and attendance at loud venues has increased among younger populations. According to the World Health Organization, one-third of all hearing damage is attributable to loud sounds (Le et al., 2017). Despite normal audiometric findings, many individuals present with tinnitus and difficulty understanding speech in noisy environments—complaints that pure tone audiometry fails to adequately explain.

The primary challenge in diagnosing cochlear synaptopathy lies in the insensitivity of conventional audiometric measures to synaptic loss. Pure tone audiometry may fail to identify individuals with hearing impairments who have normal thresholds but experience hearing problems, such as diminished ability to understand conversation in loud surroundings and ear ringing

(Tremblay et al., 2015). Speech audiometry has low sensitivity, making it difficult for audiologists to diagnose patients' listening impairments effectively.

Despite growing international evidence for these diagnostic approaches, limited research has been conducted in the Pakistani population to establish their clinical utility. Furthermore, the specific characteristics of cochlear synaptopathy in individuals with occupational and recreational noise exposure in the South Asian context remain inadequately explored.

This study was undertaken to evaluate the diagnostic accuracy of ABR Wave I amplitude and SPIN test performance in identifying cochlear synaptopathy among individuals with normal hearing thresholds at King Edward Medical University and Mayo Hospital, Lahore. By establishing the sensitivity and specificity of these measures in a local population, we aim to provide clinicians with evidence-based tools for detecting hidden hearing loss and guiding appropriate management strategies.

Methodology

Study Design and Setting

This case-control study was conducted in the ENT Department of Mayo Hospital, affiliated with King Edward Medical University (KEMU), Lahore, Pakistan, over a period of five months from March 2024 to May 2024. The study received approval from the KEMU Institutional Review Board (IRB), and written informed consent in Urdu was obtained from all participants prior to enrolment.

Participants

The study enrolled 60 participants, comprising 30 cases and 30 controls, aged 15-55 years of both genders.

Inclusion Criteria for Cases: Age 15-55 years; presence of tinnitus (unilateral or bilateral) AND difficulty understanding speech in noisy environments; normal hearing thresholds (PTA ≤25 dB HL across frequencies 250-8000 Hz); normal otoscopic examination; Type A tympanogram bilaterally; history of noise exposure (occupational, recreational, or environmental).

Inclusion Criteria for Controls: Age 15-55 years; no auditory complaints (no tinnitus, no speech-in-noise difficulties); normal hearing thresholds (PTA ≤25 dB HL); normal otoscopic examination; Type A tympanogram bilaterally; no significant history of noise exposure.

Exclusion Criteria (both groups): Any degree of hearing loss (PTA >25 dB HL); chronic ear disease; tinnitus due to systemic diseases; history of ototoxic medication use; abnormal otoscopic findings; Type B or C tympanograms; history of head trauma or neurological disorders; conductive hearing loss or middle ear pathology.

Procedures

Clinical Assessment: All participants underwent comprehensive otological evaluation including detailed history with noise exposure assessment, otoscopic examination, pure tone audiometry, and tympanometry with acoustic reflex testing.

Pure Tone Audiometry: Air conduction thresholds were obtained at octave frequencies from 250 to 8000 Hz using calibrated audiometer (Interacoustics AC40) with TDH-39 headphones. Four-frequency pure tone average (PTA) was calculated using thresholds at 500, 1000, 2000, and 4000 Hz.

Tympanometry: Middle ear function was assessed using impedance audiometry (Interacoustics AA2) to ensure normal middle ear status (Type A tympanogram) and presence of acoustic reflexes.

Auditory Brainstem Response (ABR): ABR testing was conducted in a quiet, electrically shielded room with participants in a relaxed, reclined position. Testing parameters included: click stimuli (rarefaction polarity, 100 μs duration); intensity 90 dB nHL; presentation rate 21.1 clicks/second; filter settings 150-3000 Hz; analysis time 10 ms; 1000 sweeps; electrode montage vertex (Cz) to ipsilateral mastoid. Waveforms were analysed for Wave I and Wave V absolute latencies and amplitudes. Wave I amplitude was measured from the preceding trough to the Wave I peak. Recordings were performed binaurally, starting with the right ear. Testing was conducted by two trained examiners (HA and TA) to ensure reliability.

Speech Intelligibility in Noise (SPIN) Test: The SPIN test was administered using phonetically balanced Arabic word lists (adapted for Urdu speakers) presented binaurally through headphones at 70 dB HL with multi-talker babble background noise at 0 dB signal-to-noise ratio. Two randomly selected lists of 25 words each were presented to each ear. Participants were instructed to repeat each word, disregarding background noise. Scoring was based on percentage of correctly repeated words for each ear.

Data Collection and Analysis

Demographic information, occupational history, and noise exposure details were recorded for all participants. Clinical findings from otoscopy, audiometry, tympanometry, ABR, and SPIN testing were systematically documented using standardised data collection forms.

Primary Outcome Measures: (1) ABR Wave I amplitude (right and left ears); (2) ABR Wave I latency (right and left ears); (3) SPIN test scores (right and left ears, percentage correct).

Statistical Analysis: Data were analysed using IBM SPSS Statistics version 28. Descriptive statistics included means and standard deviations for continuous variables and frequencies with percentages for categorical variables. Independent samples t-test was used to compare continuous variables between case and control groups. Receiver operating characteristic (ROC) curve analysis was performed to determine diagnostic accuracy, with area under the curve (AUC) calculated for both ABR Wave I amplitude and SPIN test. Optimal cut-off values were determined using Youden's index. Pearson correlation analysis was performed to examine relationships between noise exposure duration, ABR parameters, and SPIN scores. Statistical significance was set at $p<0.05$.

Research Findings

Participant Characteristics

Sixty participants were enrolled in the study, with 30 in the case group and 30 in the control group. The mean age was 34.6±6.7 years for cases (range: 25-52 years) and 28.9±3.8 years for controls (range: 22-36 years), representing a statistically significant difference ($p<0.001$). The case group consisted of 21 males (70%) and 9 females (30%), whilst the control group included 14 males (46.7%) and 16 females (53.3%), reflecting the higher occupational noise exposure among male participants in our study population (Table 1).

Table 1. Participant Demographics and Baseline Characteristics

Characteristic	Controls (n=30)	Cases (n=30)	p-value
Age (years), mean±SD	28.9±3.8	34.6±6.7	<0.001
Age range (years)	22-36	25-52	-
Male, n (%)	14 (46.7%)	21 (70%)	0.067
Female, n (%)	16 (53.3%)	9 (30%)	-
Education: Graduate/Postgraduate, n (%)	26 (86.7%)	14 (46.7%)	<0.001
Education: Primary/Secondary, n (%)	4 (13.3%)	16 (53.3%)	-
PTA right ear (dB HL), mean±SD	19.9±2.7	21.3±2.9	0.063
PTA left ear (dB HL), mean±SD	19.8±2.9	21.5±2.8	0.029
Noise exposure duration (years)	None	10.9±5.8	-
Tinnitus present, n (%)	0 (0%)	30 (100%)	<0.001
Speech-in-noise difficulty, n (%)	0 (0%)	30 (100%)	<0.001

Baseline Audiological Parameters

All participants in both groups demonstrated normal hearing thresholds and middle ear function, as required by inclusion criteria. Mean PTA was 21.4±2.9 dB HL for cases (range: 16-25 dB HL) and 19.9±2.8 dB HL for controls (range: 15-25 dB HL), with no statistically significant difference between groups when considering the normal threshold criterion ($p=0.052$). All participants (100%) in both groups exhibited Type A tympanograms bilaterally, indicating normal middle ear pressure and compliance, with present acoustic reflexes.

Auditory Complaints in Case Group

All 30 case participants (100%) reported both tinnitus and speech-in-noise difficulty, as per inclusion criteria. Tinnitus distribution: bilateral tinnitus 24 cases (80%); unilateral right tinnitus 3 cases (10%); unilateral left tinnitus 3 cases (10%). Speech-in-noise difficulty distribution: bilateral difficulty 27 cases (90%); predominantly right ear difficulty 2 cases (6.7%); predominantly left ear difficulty 1 case (3.3%).

Noise Exposure History

All case participants reported significant noise exposure through occupational or recreational activities. The mean duration of noise exposure was 10.9±5.8 years (range: 3-22 years). Occupational categories associated with noise exposure are presented in Table 2.

Table 2. Occupational Distribution in Case Group (n=30)

Occupational Category	n	%	Examples
Industrial Workers	12	40%	Factory workers, textile, foundry, welding, power plant
Transportation	6	20%	Truck drivers, bus drivers, rickshaw drivers, airport workers
Music/Entertainment	7	23.30%	Musicians, DJs, sound engineers, event coordinators
Service Sector	3	10%	Call centre agents, security guards, kitchen managers
Other	2	6.70%	Gym instructors, printing operators

Control participants reported no significant occupational or recreational noise exposure history, with professions including healthcare professionals, educators, engineers, business professionals, and other office-based occupations.

ABR Findings

Highly significant differences were observed in Wave I amplitudes between case and control groups (Table 3). In the right ear, controls demonstrated mean amplitude of 0.241±0.023 μV (range: 0.20-0.28 μV) compared to cases with 0.140±0.035 μV (range: 0.08-0.21 μV), representing a mean difference of 0.101 μV ($p<0.001$, Cohen's $d=3.4$). In the left ear, controls showed 0.242±0.024 μV (range: 0.20-0.28 μV) versus cases with 0.143±0.034 μV (range: 0.08-0.21 μV), mean difference 0.099 μV ($p<0.001$, Cohen's $d=3.4$).

Table 3. ABR Wave I Amplitude and Latency Results

Parameter	Controls mean±SD	Cases mean±SD	Mean Difference	p-value	Cohen's d
Wave I Amplitude					
Right Ear (μV)	0.241±0.023	0.140±0.035	0.101	<0.001	3.4
Left Ear (μV)	0.242±0.024	0.143±0.034	0.099	<0.001	3.4
Wave I Latency					
Right Ear (ms)	1.619±0.044	1.718±0.049	0.099	<0.001	2.1
Left Ear (ms)	1.612±0.050	1.712±0.053	0.1	<0.001	1.9

No statistically significant difference was found between right and left ears within each group (controls: p=0.864; cases: p=0.735). Using the threshold of <0.20 μV as indicative of abnormal Wave I amplitude, 28 of 30 case participants (93.3%) demonstrated reduced Wave I amplitude in at least one ear: 25 cases (83.3%) showed bilateral reduction and 3 cases (10%) showed unilateral reduction. Two cases (6.7%) had Wave I amplitudes at the borderline (0.20-0.21 μV range). Only one control participant (3.3%) showed Wave I amplitude below 0.21 μV (0.20 μV in right ear), whilst all other controls demonstrated amplitudes above 0.21 μV.

Wave I latencies showed slight but statistically significant differences between groups. Right ear latencies were 1.619±0.044 ms for controls (range: 1.54-1.71 ms) and 1.718±0.049 ms for cases (range: 1.62-1.81 ms), p<0.001. Left ear latencies were 1.612±0.050 ms for controls (range: 1.54-1.71 ms) and 1.712±0.053 ms for cases (range: 1.64-1.80 ms), p<0.001. The mean latency difference of approximately 0.1 ms, whilst statistically significant due to sample size, was of limited clinical significance.

SPIN Test Results

Marked differences in speech-in-noise performance were observed between groups (Table 4). In the right ear, controls scored 95.1±2.5% (range: 90-99%) compared to cases with 72.7±9.4% (range: 55-89%), representing a mean difference of 22.4% (p<0.001, Cohen's d=3.2). In the left ear, controls scored 95.1±2.9% (range: 89-99%) versus cases with 72.9±9.0% (range: 56-87%), mean difference 22.2% (p<0.001, Cohen's d=3.1).

Table 4. SPIN Test Results

Parameter	Controls mean±SD	Cases mean±SD	Mean Difference	p-value	Cohen's d
Right Ear (%)	95.1±2.5	72.7±9.4	22.4	<0.001	3.2
Left Ear (%)	95.1±2.9	72.9±9.0	22.2	<0.001	3.1
Average (%)	95.1±2.4	72.8±9.1	22.3	<0.001	3.3

Using the threshold of <90% as indicative of impaired speech-in-noise performance, all 30 case participants (100%) scored below 90% in both ears. One control participant (3.3%) scored exactly 89% in the left ear, whilst all other controls scored 90% or above in both ears.

Correlation Analysis

Significant correlations were observed in the case group between noise exposure duration and audiological parameters (Table 5). Noise exposure duration correlated negatively with Wave I amplitude in the right ear (r=-0.687, p<0.001) and left ear (r=-0.694, p<0.001), indicating that longer duration of noise exposure was associated with greater reductions in Wave I amplitude. Similarly, noise exposure duration correlated negatively with SPIN scores in the right ear (r=-0.742, p<0.001) and left ear (r=-0.751, p<0.001), indicating poorer SPIN test performance with longer exposure.

Table 5. Correlation Analysis in Case Group (n=30)

Variables	Pearson Correlation (r)	p-value	Interpretation
Noise exposure duration vs Wave I amplitude (right)	-0.687	<0.001	Strong negative
Noise exposure duration vs Wave I amplitude (left)	-0.694	<0.001	Strong negative
Noise exposure duration vs SPIN score (right)	-0.742	<0.001	Strong negative
Noise exposure duration vs SPIN score (left)	-0.751	<0.001	Strong negative
Wave I amplitude vs SPIN score (right)	0.821	<0.001	Very strong positive
Wave I amplitude vs SPIN score (left)	0.834	<0.001	Very strong positive

Additionally, Wave I amplitude showed significant positive correlation with SPIN scores in both the right ear (r=0.821, p<0.001) and left ear (r=0.834, p<0.001). This suggests that reduced neural synchrony, as reflected in Wave I amplitude, is strongly associated with impaired speech perception in noise.

Diagnostic Performance

ROC curve analysis revealed excellent diagnostic accuracy for both measures (Table 6). For ABR Wave I amplitude (averaged across both ears), the area under the curve (AUC) was 0.984 (95% CI: 0.949-0.999, p<0.001), indicating excellent diagnostic accuracy. Using Youden's index, the optimal cut-off value was ≤0.195 μV, yielding sensitivity of 93.3% (28/30 cases) and specificity of 96.7% (29/30 controls).

For SPIN test performance (averaged across both ears), the AUC was 0.997 (95% CI: 0.981-1.000, p<0.001), indicating outstanding diagnostic accuracy. Using Youden's index, the optimal cut-off value was ≤89.5%, yielding sensitivity of 100% (30/30 cases) and specificity of 96.7% (29/30 controls).

Table 6. Diagnostic Performance: ROC Analysis

Measure	AUC	95% CI	Optimal Cut-off	Sensitivity	Specificity	PPV	NPV
ABR Wave I Amplitude (μV)	0.984	0.949-0.999	≤0.195	93.30%	96.70%	96.60%	93.50%
SPIN Test (%)	0.997	0.981-1.000	≤89.5	100%	96.70%	96.80%	100%
Combined Criteria	-	-	Both abnormal	93.30%	100%	100%	93.80%

Note: AUC = Area under the curve; PPV = Positive predictive value; NPV = Negative predictive value

When applying combined criteria (both ABR Wave I amplitude ≤0.195 μV and SPIN score ≤89.5%), sensitivity was 93.3% and specificity was 100%, as 28 of 30 cases showed both abnormalities whilst all 30 controls showed normal findings on both measures.

Both ABR Wave I amplitude and SPIN test demonstrated excellent diagnostic performance, with SPIN test showing marginally superior AUC (0.997 vs. 0.984, p=0.156). The difference in AUC between the two tests was not statistically significant, suggesting comparable diagnostic utility.

Discussion

This study demonstrates the excellent diagnostic capability of ABR Wave I amplitude and SPIN test in identifying cochlear synaptopathy among individuals with normal hearing thresholds. The findings provide important evidence for the clinical utility of these non-invasive measures in detecting hidden hearing loss, particularly in populations with significant noise exposure.

Principal Findings

Our results revealed marked differences between case and control groups across both electrophysiological and behavioural measures. Wave I amplitude was reduced by approximately 42% in cases compared to controls, whilst SPIN scores were diminished by nearly 23 percentage points. These findings are consistent with the hypothesis that cochlear synaptopathy results in reduced neural output from the cochlea and impaired temporal processing, manifesting as decreased ABR Wave I amplitude and poor speech-in-noise performance despite normal audiometric thresholds (Mekki et al., 2024).

The excellent diagnostic accuracy observed for both measures (AUC >0.98 for both tests) suggests that these tests may serve as reliable diagnostic tools for cochlear synaptopathy. The strong correlation between Wave I amplitude reduction and SPIN score impairment (r>0.82) further supports the notion that these measures assess related aspects of auditory dysfunction stemming from synaptic loss.

The dose-response relationship observed between noise exposure duration and both ABR Wave I amplitude (r≈-0.69) and SPIN performance (r≈-0.75) provides compelling evidence for the cumulative impact of noise exposure on auditory nerve function, supporting the causal relationship between occupational noise exposure and cochlear synaptopathy.

Comparison with Previous Research

Our findings align well with the broader literature on hidden hearing loss. Mekki and colleagues recently reported that individuals with noise exposure and auditory complaints demonstrated significantly reduced ABR Wave I amplitudes and impaired SPIN test performance compared to controls, despite normal audiograms (Mekki et al., 2024). Similarly, studies by Liberman and colleagues have shown that noise-induced synaptopathy in animal models results in reduced suprathreshold ABR amplitudes, particularly at Wave I, without affecting hearing thresholds (Liberman et al., 2016).

The magnitude of Wave I amplitude reduction observed in our study (approximately 0.10 μV difference between groups) is comparable to or greater than differences reported by Valderrama and colleagues in individuals with lifetime noise exposure (Valderrama et al., 2018). Their study found that Wave I amplitude decreased progressively with increasing cumulative noise exposure, a pattern we clearly observed through significant negative correlations (r≈-0.69) between exposure duration and Wave I amplitude.

Regarding speech perception, our finding of substantially reduced SPIN scores (mean 72.8% versus 95.1%) in cases with normal audiograms mirrors results from multiple studies. Vijayasarathy and colleagues reported significantly impaired speech-in-noise performance in noise-exposed individuals with normal hearing (Vijayasarathy et al., 2021), whilst Maruthy and colleagues demonstrated progressive decline in SPIN scores with increasing noise exposure even among those with normal thresholds (Maruthy et al., 2018). The 23-percentage-point difference observed in our study represents a clinically significant impairment that would substantially impact daily communication function.

Interestingly, we found statistically significant but clinically modest differences in Wave I latency between groups (approximately 0.1 ms), which aligns with some studies but contrasts with others showing that synaptopathy primarily affects response amplitude rather than timing (Ahmadpour et al., 2022). This suggests that severe synaptic loss may affect both neural synchrony (amplitude) and conduction velocity (latency), though amplitude changes remain the more sensitive marker.

Pathophysiological Implications

The pattern of results observed in our study can be understood through current knowledge of cochlear synaptopathy pathophysiology. Noise exposure preferentially damages the synaptic connections between inner hair cells and auditory nerve fibres, particularly those with low spontaneous rates and high thresholds (Liberman and Kujawa, 2017). These high-threshold

fibres are crucial for encoding sounds at moderate-to-high intensity levels and for maintaining precise temporal information in challenging acoustic conditions.

Loss of these synapses results in several auditory consequences. First, it reduces the overall neural output from the cochlea at suprathreshold levels, manifesting as decreased ABR Wave I amplitude. Second, it impairs the auditory system's ability to encode fine temporal details and maintain robust neural representations in the presence of background noise, leading to poor speech-in-noise performance (Bharadwaj et al., 2015). Third, it may contribute to tinnitus generation through aberrant neural activity resulting from reduced peripheral input—all 30 of our case participants reported tinnitus.

The preserved hearing thresholds in synaptopathy reflect the fact that threshold detection primarily depends on the most sensitive auditory nerve fibres (high spontaneous rate, low threshold fibres), which remain relatively intact in early synaptopathy (Lobarinas et al., 2013). This dissociation explains the clinical paradox of normal audiograms coexisting with significant auditory complaints—a phenomenon observed universally in our case group.

The diminished electrical impulses passing via the auditory nerves can impact the cerebral auditory cortex, potentially resulting in impairments in comprehending speech. Due to the decrease of low spontaneous rate fibres, both the acoustic and olivocochlear reflexes have been diminished, and consequently, a cochlear response that appears to be stronger could potentially result in elevation of summating potential levels (Ting et al., 2022).

Clinical Implications

The findings of this study have important implications for clinical practice in Pakistan and similar settings with high rates of occupational and recreational noise exposure. Current clinical practice relies heavily on pure tone audiometry for hearing assessment. However, our results demonstrate that audiometry alone misses significant auditory dysfunction in patients with synaptopathy.

We propose that clinicians consider incorporating ABR Wave I amplitude measurement and speech-in-noise testing into the assessment of patients who present with tinnitus or speech perception difficulties despite normal audiograms, particularly those with noise exposure history. The combination of reduced Wave I amplitude (≤0.195 μV) and impaired SPIN performance (≤89.5%) appears to be highly indicative of cochlear synaptopathy, with combined sensitivity of 93.3% and specificity of 100%, and can help explain patients' symptoms whilst guiding appropriate counselling and management.

Management strategies for patients with diagnosed synaptopathy should focus on: counselling regarding the nature of their condition and validation of their symptoms; strict hearing protection to prevent further synaptic loss; communication strategies to improve function in noisy environments; consideration of assistive listening devices or personal amplification systems in severe cases; and regular monitoring to detect any progression to threshold-level hearing loss.

It is crucial to validate a method for identifying clinical outcomes that cochlear synaptopathy primarily influences at the clinical level. Establishing a clinical testing procedure that can detect noise-induced cochlear synaptopathy occurring before the loss of sensory hair cells in humans provides a basis to anticipate the development of a reliable set of tests that can detect and consequently manage hidden hearing loss (Mekki et al., 2024).

Occupational and Public Health Considerations

The high prevalence of auditory complaints among noise-exposed workers in our study highlights the need for improved occupational health standards and hearing conservation programmes in Pakistan. Our case group included individuals from diverse noise-exposed occupations: 40% from industrial settings (factories, textile mills, foundries, welding), 20% from transportation, and 23% from music and entertainment industries. Current regulations may focus primarily on preventing threshold shifts, but our findings demonstrate that significant auditory damage occurs even when audiometric thresholds remain normal.

The inclusion of diverse occupational groups in our study reveals that cochlear synaptopathy affects not only traditional industrial workers but also modern service sector employees (call centre agents), entertainment professionals (DJs, musicians, sound engineers), and even educators exposed to chronic classroom noise. This broader occupational spectrum suggests that current noise exposure guidelines may need revision to account for cumulative effects leading to synaptopathy.

Workplace noise exposure assessments should account for the risk of synaptopathy, and hearing conservation efforts should emphasise consistent use of hearing protection even in environments where noise levels may not be considered hazardous by traditional standards. Additionally, screening programmes for high-risk occupations might benefit from including ABR and speech-in-noise testing alongside standard audiometry.

The presence of synaptopathy-related complaints among younger participants with recreational noise exposure (musicians, DJs, sound engineers, event coordinators, gym instructors) also raises concerns about the long-term hearing health consequences of lifestyle factors increasingly common among urban Pakistani youth. Public health campaigns addressing the risks of loud music through personal audio devices and attendance at loud venues may be warranted. Individuals at risk should undergo regular screening to detect auditory abnormalities exceeding the normal threshold.

Study Limitations

Several limitations should be acknowledged. First, whilst our sample size (n=60) was adequate for detecting the large effect sizes observed, larger multi-centre studies would be valuable for establishing population-specific normative data and validating diagnostic thresholds across diverse Pakistani populations.

Second, the absence of histological confirmation of synaptopathy represents an inherent limitation of human research in this area. Whilst the pattern of findings (normal thresholds, reduced Wave I amplitude, impaired speech-in-noise performance in noise-exposed individuals) is consistent with animal models of synaptopathy (Liberman et al., 2016), we cannot definitively confirm synaptic loss in our participants. Future studies incorporating additional measures such as envelope-following

responses, electrocochleography, or middle ear muscle reflex measurements may provide converging evidence for synaptic dysfunction.

Third, the noise exposure assessment relied on self-report and occupational history rather than quantified dosimetry with sound level measurements. Whilst we documented exposure duration and occupational categories, the actual sound pressure levels and temporal patterns of exposure varied across participants and occupations. More detailed noise exposure characterisation using standardised instruments such as the Noise Exposure Structured Interview (NESI) would strengthen future investigations (Guest et al., 2018).

Fourth, we did not assess extended high-frequency audiometry systematically or perform comprehensive distortion product otoacoustic emissions (DPOAEs) analysis in this study. Whilst all participants had normal standard audiometry and were required to have present acoustic reflexes for inclusion, more comprehensive characterisation of cochlear function across the full frequency range might have provided additional insights into the relationship between hair cell status and synaptic function.

Fifth, the cross-sectional design precludes assessment of the longitudinal trajectory of synaptopathy or its relationship to future development of permanent threshold shifts. Prospective studies following noise-exposed individuals over time would be valuable for understanding the natural history of synaptopathy and its potential role as a precursor to conventional hearing loss.

Finally, the age difference between groups (mean 34.6 years for cases versus 28.9 years for controls), whilst reflecting realistic differences in occupational exposure duration, could potentially confound results. However, the age range overlapped substantially (controls: 22-36 years; cases: 25-52 years), and the magnitude of differences observed far exceeds what would be expected from age effects alone in this range**.**

Future Directions

Several avenues for future research emerge from this study. First, larger multi-centre studies involving diverse populations are needed to establish normative data and diagnostic cut-offs for ABR Wave I amplitude and SPIN test performance in the Pakistani population, accounting for age, gender, ethnicity, and regional variations.

Second, investigation of additional electrophysiological measures such as envelope-following responses, electrocochleography, middle ear muscle reflexes, and auditory steady-state responses may provide complementary information about synaptic function and improve diagnostic accuracy (Ahmadpour et al., 2022). Similarly, behavioural measures including temporal processing tests (gap detection, amplitude modulation detection) and dichotic listening tasks may enhance the assessment battery for synaptopathy.

Third, research into potential therapeutic interventions for synaptopathy is critically needed. Whilst hearing protection can prevent further damage, no current treatments exist to reverse synaptic loss. Emerging therapies based on neurotrophic factors, stem cell approaches, or pharmacological agents targeting synaptic regeneration represent promising areas for translational research (Wang et al., 2021).

Fourth, longitudinal studies examining the relationship between synaptopathy and subsequent development of age-related hearing loss would help clarify whether early synaptic damage predisposes individuals to accelerated hearing decline with ageing—a question with important implications for lifespan hearing health. Following our cohort prospectively could provide valuable insights into progression patterns.

Fifth, development of automated, accessible screening tools for synaptopathy could facilitate large-scale surveillance in high-risk populations and enable early identification of individuals who would benefit from intervention. Integration of ABR and speech-in-noise testing into mobile or portable platforms could make such screening feasible in occupational settings, particularly in resource-limited environments common in Pakistan.

Finally, economic analyses examining the cost-effectiveness of implementing synaptopathy screening programmes in high-risk occupational settings would provide important evidence for policy-makers considering expansion of hearing conservation efforts beyond traditional audiometry.

Conclusion and Recommendations

This study provides robust evidence that ABR Wave I amplitude and SPIN test performance serve as highly sensitive and specific markers for identifying cochlear synaptopathy in individuals with normal hearing thresholds. Among our cohort of 30 noise-exposed participants with tinnitus and speech-in-noise complaints, 93-100% demonstrated reduced Wave I amplitudes ($\leq$0.195 μV) and impaired SPIN scores ($\leq$89.5%) despite normal pure tone audiometry, with excellent discrimination from 30 control participants (specificity 96.7-100%).

These findings support the concept that hidden hearing loss represents a distinct clinical entity requiring assessment beyond conventional audiometry. The strong correlations observed between noise exposure duration, Wave I amplitude reduction ($r\approx-0.69$), and SPIN score impairment ($r\approx-0.75$) underscore the cumulative impact of noise exposure on auditory nerve function even in the absence of threshold shifts.

For clinical practice, we recommend that patients presenting with tinnitus or speech perception difficulties in noise undergo evaluation with ABR Wave I amplitude measurement and speech-in-noise testing, particularly when they have a history of occupational or recreational noise exposure. The combination of these measures provides objective evidence of auditory dysfunction that validates patients' symptoms, guides counselling, and informs management strategies. The excellent diagnostic performance observed (AUC >0.98 for both measures) supports their implementation in clinical protocols.

From a public health perspective, these findings highlight the urgent need for enhanced hearing conservation efforts in Pakistan, targeting both traditional occupational settings (40% of cases from industrial sectors) and emerging risk groups in music, entertainment, and service industries (33% of cases). Preventing synaptopathy through consistent use of hearing

protection may preserve not only audiometric thresholds but also the suprathreshold auditory function essential for communication in real-world listening environments.

It is recommended that COVID-19 protocols—or in this context, hearing protection protocols—should be strictly adhered to prevent the spread of auditory damage that may necessitate further medical intervention. Workplace noise exposure guidelines must be revised to account for the risk of synaptopathy occurring before threshold shifts, and screening programmes should incorporate suprathreshold measures alongside conventional audiometry.

Due processes and diligence must be taken by healthcare authorities to assist individuals who may be affected by noise-induced synaptopathy, particularly those in high-risk occupations. Regular screening programmes should be established for workers in industrial, transportation, and entertainment sectors to enable early detection and intervention.

Further research with longitudinal designs, investigation of therapeutic approaches, and development of accessible screening tools will be essential for advancing our understanding and management of this increasingly recognised form of auditory dysfunction. The establishment of reliable diagnostic tools for cochlear synaptopathy represents an important step towards identifying and managing hidden hearing loss in vulnerable populations, potentially preventing progression to more severe hearing impairment.

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