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**MAIN ARTICLE**

# Comparison of auditory electrophysiological responses in normal-hearing patients with and without tinnitus

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## Abstract

*Introduction*: Tinnitus is a disturbing symptom and is often the main reason for otology referral. It is usually associated with hearing loss of varying aetiology, and is thought to begin in the cochlea, with later abnormal central activity. We hypothesise that tinnitus without hearing loss may be caused by central and subcortical abnormalities and altered outer hair cell function.

*Aim*: To compare the auditory brainstem responses, middle latency responses and otoacoustic emissions in normal-hearing individuals with and without tinnitus.

*Methodology*: The audiological test results of 25 normal hearing subjects with tinnitus (age 18–45 years) were determined, and compared with those of a control group.

*Results*: A statistically significant difference was found between study group tinnitus ears *vs* control group ears, as regards wave I latency prolongation, shortening of wave V and absolute I–III and I–V interpeak latency, enlargement of wave Na and Pa amplitude, and distortion product and transient evoked otoacoustic emission signal-to-noise ratios. There was no statistically significant difference between unilateral *vs* bilateral tinnitus ears.

*Conclusion*: The pathogenesis and optimum management of tinnitus are still unclear. It often occurs with primary ear disease, usually associated with hearing loss, but may occur in patients with normal hearing. Observed changes in auditory brainstem and middle latency responses indicate central auditory alterations. Tinnitus involves both peripheral and central activity, and complete audiological and neurophysiological investigation is required. Management should be based on both audiological and neurophysiological findings.

**Key words:** Tinnitus; Audiometry; Pure Tone Audiometry; Spontaneous Otoacoustic Emissions; Evoked Potentials; Auditory; Brainstem

## Introduction

Tinnitus is a disturbing symptom and is often the main reason for referral to an otology clinic. It is usually associated with hearing loss of varying aetiology.[1]

Although tinnitus may be associated with abnormality at any level of the auditory pathway, it very often begins in the cochlea.[2] Jastreboff considered that tinnitus usually starts in the cochlea and later generates abnormal activity in the central pathways, perpetuating the symptoms.[3] The central auditory pathways do not need to be structurally altered.

In our clinical practice, we have often encountered patients complaining of tinnitus who are found to have a normal hearing sensitivity on pure tone audiometry. We hypothesise that tinnitus without hearing loss may be caused by abnormalities at the central and subcortical level, together with changes in outer hair cell function. If this hypothesis is valid, tinnitus patients with normal hearing should have abnormal auditory brainstem responses (ABRs), middle latency responses, transient evoked otoacoustic emissions (TEOAEs) and distortion product otoacoustic emissions (DPOAEs).

### *Objective*

Our study aimed to evaluate the function of the central auditory pathway and cochlear outer hair cells by means of ABR, middle latency response, TEOAE and DPOAE testing in patients with tinnitus and normal hearing, and to compare this group of patients with an age- and gender-matched control group with normal hearing and no tinnitus.

### *Need for the study*

The presence of hearing loss often precludes the search for the origin of concomitant tinnitus. We believe that the evaluation of tinnitus occurring in the absence of

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hearing loss will assist the development of better diagnostic and management practices.

## Methods and materials

### *Methodology*

The study group comprised 25 normal-hearing patients with tinnitus, aged 18 to 45 years (mean 32 years; standard deviation (SD) 7.8 years).

These patients were audiologically examined in the Speech and Hearing Unit of the Postgraduate Institute of Medical Education and Research, Chandigarh, India. Normal hearing sensitivity was defined as a hearing level of less than 25 dB at each frequency examined, from 250 Hz to 8 kHz.[4] A type A impedance audiometry tympanogram was defined as normal.[5]

A control group was also studied, comprising 20 patients with normal hearing and no tinnitus, who were age- and sex-matched to the study group.

None of the patients in the study or control groups had any history of occupational noise exposure. We also excluded from the study any patients with previous otological disease, neurological disease, acoustic trauma, vascular disease, metabolic problems, previous ototoxic drug use or middle-ear problems.

### *Apparatus and procedure*

A detailed physical examination was conducted, including a complete otorhinolaryngological examination. Following this, audiological assessment was performed, including pure tone audiometry, tympanometry, and assessment of otoacoustic emissions (OAEs), ABRs and middle latency responses.

Audiological assessment was conducted in sound-treatment rooms. A commercially available audiometer (Madsen Orbiter 922, Taastrup, Denmark) was used, together with TDH39 ear phones (Madsen Electronics, Taastrup, Denmark).

A Siemens SD 30 tympanometer (Siemens, Danplex A/S, Copenhagen, Denmark) was used for tympanometry and acoustic reflex testing. A 226 Hz probe tone was used for tympanometry, with pressure varying from +200 to −300 dapa.

Otoacoustic emissions, ABRs and middle latency responses were measured using systems developed by Intelligent Hearing System (Miami, Florida, USA). Transient evoked OAEs (TEOAEs) were measured using a wide band click in continuous mode, with an intensity of 90 dB SPL. When measuring distortion product gram, the frequency separation of the primaries was f2/f1 = 1.22, with L1 and L2 set to 65 and 55 dB SPL, respectively.

The parameter of interest during TEOAE testing was a signal-to-noise ratio of more than 3 dB in at least three consecutive test frequencies (i.e. of 1, 1.5, 2, 3 and 4 kHz).

The parameter of interest during distortion product OAE testing was a signal-to-noise ratio of more than 3 dB in at least three consecutive test frequencies, as well as the amplitude of the signal in the 90th percentile of the normal distribution for the following test frequencies: 357, 499, 704, 1003, 1409, 2000, 2822, 3991 and 5649 Hz.

During ABR assessment, wave peaks I, III and V were identified. The absolute latencies of waves I, III and V, and the interpeak latencies of waves I–III, III–V and I–V, were also calculated.

Auditory brainstem responses and middle latency responses were measured using the same instrumentation. Middle latency response testing identified the Na, Pa and Nb wave peaks, and measured the amplitude of waves Na and Pa. The voltage differential between the Na and Pa waves was taken as the amplitude of the Na wave, and the voltage differential between the Pa and Nb waves was taken as the amplitude of the Pa wave. The criteria used to define middle latency response wave abnormalities were: (1) an Na wave amplitude of less than 0.50 μV, and (2) a Pa wave amplitude of less than 0.50 μV.

Results for unilateral and bilateral tinnitus ears were compared. Unilateral tinnitus was present in 19 patients and bilateral tinnitus in six patients.

Results for the study group (tinnitus ears) and control group were also compared. For the purposes of comparison, the study group comprised 31 tinnitus ears while the study group comprised 40 normal ears. In patients with unilateral tinnitus, hearing thresholds in the two ears were symmetrical.

Statistical analysis was performed using the unpaired *t*-test. A *p* value of less than 0.05 was considered statistically significant.

## Results

Comparison of unilateral versus bilateral tinnitus ears identified no statistically significant differences for ABR, middle latency response or OAE results.

However, statistically significant differences were observed between the study group tinnitus ears and the control group normal hearing ears, as follows.

Table I compares the absolute latencies of waves I, III and V, and the wave I–III, III–V and I–V interpeak latencies, in the study group tinnitus ears and control group normal ears. In the study group tinnitus ears,

TABLE I
ABR RESULTS FOR TINNITUS AND NORMAL EARS

| Parameter | Tinnitus ears* | | Normal ears† | | *t* |
|---|---|---|---|---|---|
| | Mean (ms) | SD | Mean (ms) | SD | |
| Wave I latency | 1.59 | 0.11 | 1.53 | 0.14 | 2.013‡ |
| Wave III latency | 3.62 | 0.16 | 3.68 | 0.15 | 1.375 |
| Wave V latency | 5.43 | 0.22 | 5.54 | 0.21 | 2.197‡ |
| Wave I–III IPL | 2.03 | 0.16 | 2.14 | 0.15 | 2.939** |
| Wave III–V IPL | 1.80 | 0.20 | 1.86 | 0.15 | 1.499 |
| Wave I–V IPL | 3.83 | 0.20 | 4.01 | 0.19 | 3.673** |

*$n = 31$; †$n = 40$. ‡$p < 0.05$; **$p < 0.01$. ABR = auditory brainstem response; SD = standard deviation; IPL = interpeak latency

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we found a statistically significant prolongation of wave I latency, and also a statistically significant shortening of wave V and of absolute wave I–III and I–V interpeak latencies, compared with the control group ($p < 0.05$). No significant difference was observed for the wave III–V interpeak latency ($p > 0.05$).

Table II compares the latencies and amplitudes of waves Na and Pa, in the study group tinnitus ears and control group normal ears. No statistically significant difference was observed for wave Na or Pa latencies ($p > 0.05$). However, there was a statistically significant enlargement in the amplitude of the Na and Pa waves in the study group tinnitus ears, compared with the control group ($p < 0.05$).

Table III shows the amplitude of the distortion product OAEs (DPOAEs) detected in the study and control groups. No statistically significant difference was observed for this parameter, comparing the study group tinnitus ears versus control group normal ears ($p > 0.05$).

Table IV compares the DPOAE signal-to-noise ratio, across the 357–5649 Hz frequency range, in the study and control groups. A statistically significant difference was found for DPOAE signal-to-noise ratio in the study group tinnitus ears compared with the control group normal ears, for all frequencies ($p < 0.05$) except 5649 Hz ($p > 0.05$).

Table V shows the transient evoked OAE (TEOAE) signal-to-noise ratio, across the 1–4 kHz frequency range, in the study and control groups. A statistically significant difference was found for TEOAE signal-to-noise ratio in the study group tinnitus ears compared with control group normal ears, across all frequencies ($p < 0.05$).

To conclude, there was a statistically significant difference between the study group tinnitus ears and the control group normal ears, for most of the parameters studied.

No statistically significant difference was observed for ABR parameters in unilateral versus bilateral tinnitus ears. However, a significant difference was observed for wave Na latency in this respect, upon middle latency response testing ($p < 0.05$). No statistically significant differences were observed for wave Pa latency or for wave Na or Pa amplitude, comparing unilateral versus bilateral tinnitus ears.

TABLE II
MLR RESULTS FOR TINNITUS AND NORMAL EARS

| Parameter | Tinnitus ears* | | Normal ears† | | $t$ |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Wave Na latency (ms) | 18.76 | 1.42 | 19.42 | 1.78 | 1.444 |
| Wave Pa latency (ms) | 29.92 | 3.18 | 29.98 | 2.61 | 0.083 |
| Wave Na ampl (μA) | 1.13 | 0.54 | 0.66 | 0.46 | 3.862‡ |
| Wave Pa ampl (μA) | 1.17 | 0.52 | 0.71 | 0.29 | 4.379‡ |

*$n = 31$; †$n = 40$. ‡$p < 0.001$. MLR = middle latency response; SD = standard deviation; ampl = amplitude

TABLE III
DPOAE AMPLITUDE FOR TINNITUS AND NORMAL EARS

| Freq (Hz) | Tinnitus ears* (dBSPL) | | Normal ears† (dBSPL) | | $t$ |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| 357 | 5.03 | 10.85 | 3.00 | 10.16 | 0.804 |
| 499 | 7.52 | 12.49 | 2.18 | 9.00 | 1.113 |
| 704 | 2.55 | 13.79 | −1.52 | 9.68 | 1.399 |
| 1003 | 0.52 | 11.91 | −1.78 | 9.26 | 0.883 |
| 1409 | −4.06 | 9.63 | −6.78 | 10.46 | 1.132 |
| 2000 | −6.74 | 10.71 | −6.72 | 8.84 | 0.007 |
| 2822 | −12.81 | 9.32 | −12.92 | 9.16 | 0.054 |
| 3991 | −10.97 | 6.39 | −11.00 | 9.07 | 0.045 |
| 5649 | −12.52 | 10.92 | −15.00 | 5.47 | 1.158 |

*$n = 31$; †$n = 40$. DPOAE = distortion product otoacoustic emission; freq = frequency; SD = standard deviation

No statistically significant differences were observed for DPOAE and TEOAE parameters, comparing unilateral versus bilateral tinnitus ears.

## Discussion

Tinnitus is the perception of sound in the absence of any external acoustic source. This sound has been described variously by patients as a constant tone, ringing, chirping, hissing or buzzing, or as a noise like 'whizzing air', crickets, a water fall, an engine, etc.

The pathogenesis and site of origin of tinnitus have yet to be clearly established. Tinnitus is often a feature of primary ear disease associated with hearing loss, but it may also occur in patients with normal hearing.

A review of the literature revealed that tinnitus can arise from cochlear damage or from changes in central pathways. We used transient evoked OAE (TEOAE) and distortion product OAE (DPOAE) testing to verify cochlear dysfunction in patients with normal hearing and tinnitus, as these tests are the most commonly used OAE investigations in clinical practice and have a more standardised methodology than other, less frequently used investigations.

TABLE IV
DPOAE SNR FOR TINNITUS AND NORMAL EARS

| Freq (Hz) | Tinnitus ears* | | Normal ears† | | $t$ |
|---|---|---|---|---|---|
| | Mean (dBSPL) | SD | Mean (dBSPL) | SD | |
| 357 | 0.16 | 6.45 | 3.62 | 6.67 | 2.209‡ |
| 499 | 0.84 | 5.91 | 4.60 | 7.10 | 2.432‡ |
| 704 | −2.77 | 7.61 | 5.68 | 6.98 | 4.806** |
| 1003 | −1.13 | 5.86 | 8.85 | 7.10 | 6.476** |
| 1409 | −0.29 | 6.27 | 8.75 | 10.14 | 4.611** |
| 2000 | 2.35 | 6.05 | 10.52 | 8.79 | 4.628** |
| 2822 | 0.52 | 5.72 | 6.52 | 10.13 | 3.157§ |
| 3991 | 0.42 | 7.65 | 7.40 | 8.18 | 3.697** |
| 5649 | 1.61 | 6.31 | 3.40 | 5.14 | 1.280 |

*$n = 31$; †$n = 40$. ‡$p < 0.05$; **$p < 0.001$; §$p < 0.01$. DPOAE = distortion product otoacoustic emission; SNR = signal-to-noise ratio; freq = frequency; SD = standard deviation

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TABLE V
TEOAE SNR FOR TINNITUS AND NORMAL EARS

| Freq (kHz) | Tinnitus ears* | | Normal ears† | | $t$ |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| 1 | 1.03 | 2.61 | 4.43 | 3.88 | 4.396‡ |
| 1.5 | 1.92 | 3.11 | 6.09 | 6.13 | 3.726‡ |
| 2 | 1.16 | 2.90 | 7.96 | 6.22 | 6.106‡ |
| 3 | 2.44 | 3.17 | 10.09 | 5.87 | 7.025‡ |
| 4 | 0.45 | 2.25 | 4.33 | 5.55 | 4.011‡ |

*$n = 31$; †$n = 40$. ‡$p < 0.001$. TEOAE = transient evoked otoacoustic emission; SNR = signal-to-noise ratio; freq = frequency; SD = standard deviation

We used ABR and middle latency response testing to distinguish between central and peripheral tinnitus. Auditory brainstem response testing provides an objective electrophysiological measure of cochlear functioning and the brainstem auditory pathway. Middle latency response testing provides an objective electrophysiological measure of the central auditory system, especially the auditory pathway of the subcortical region.

In contrast to previous studies, we found prolongation of wave I latency in the tinnitus ears of the study group, compared with controls. A shortening of wave V latency and wave I–III and I–V interpeak latencies was also found in the tinnitus ears, compared with controls.

Prolongation of wave I latency occurs in ears with cochlear hearing loss, and was first reported in 1977.[6] Previous studies have reported a prolongation of wave I which also affects the late ABR waves, in ears with tinnitus and normal hearing.[7–9] Moller *et al.* studied compound action potentials and brainstem evoked potentials from exposed VIIIth nerves in patients with tinnitus, and reported an unchanged wave III absolute latency but a significantly shorter wave V latency. This shortening of wave V latency was interpreted as indicating hyperactivity of some structures in the ascending auditory pathway.[10]

In our study, we found increased wave Na and Pa amplitudes in the study group tinnitus ears, compared with controls. This indicates an alteration in the middle latency response generators. In contrast, when Gerken *et al.* compared ABR and middle latency response recordings in tinnitus patients with recordings in elderly patients and those with hearing loss and normal hearing, they found significant differences only for ABR wave latencies.[11] These authors also reported that middle latency response amplitude was affected, but in very few patients.[11] None of the patients in these authors' study group had clinically abnormal ABR or middle latency response parameters.

We did not find any statistically significant difference between the DPOAE amplitude of the study group tinnitus ears versus the control group normal ears. However, we did find statistically significant differences in this respect for DPOAE and TEOAE signal-to-noise ratios. These abnormal DPOAE and TEOAE results indicate the presence of outer hair cell dysfunction in patients with tinnitus and normal hearing. The degree of outer hair cell dysfunction detected in this way would not seem to be sufficient to cause tinnitus. However, normal-hearing individuals with tinnitus have significantly more abnormal TEOAE and DPOAE results than normal-hearing individuals without tinnitus. One explanation for this phenomenon would be the existence of different levels of sensitivity of higher auditory pathways to outer hair cell dysfunction. In some patients, levels of dysfunction may not be sufficient to cause symptoms. In this way, we would agree with Jastreboff, who stated that all levels of the auditory pathway may be involved in the production of tinnitus, but that the trigger is probably at the outer hair cell level, at least in the majority of cases.[3]

Our comparison of unilateral and bilateral tinnitus ears did not reveal any statistically significant differences between the study and control groups as regards ABR, TEOAE and DPOAE parameters. However, tinnitus ears had a significantly prolonged wave Na latency compared with normal ears, indicating an effect of tinnitus on the central auditory pathways at a primary auditory cortex level.

There was no statistically significant difference between the hearing thresholds of the study and control groups. This suggests that the study group tinnitus ears and control group normal ears had equivalent hearing sensitivity.

- **Tinnitus is a disturbing symptom usually associated with hearing loss of varying aetiology, but may occur with normal hearing**
- **Tinnitus without hearing loss may be caused by central and subcortical abnormalities and by changes in outer hair cell function**
- **The pathophysiology of tinnitus is still unclear**

We believe that patients with normal hearing and no tinnitus but with abnormal TEOAE and DPOAE results should be followed up due to the possibility of tinnitus development. However, it is difficult to state conclusively whether such patients are at higher risk of tinnitus development, as the aetiology of tinnitus seems to involve an interaction between cochlear abnormalities and increased central pathway sensitivity.

### *Study limitations*

One limitation of our study was that patients with tinnitus did not undergo magnetic resonance imaging.

## Conclusion

Tinnitus involves activity in both the peripheral and central neural pathways. Therefore, the investigation

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of tinnitus requires complete audiological and neurophysiological testing.

The optimal management of tinnitus patients is still elusive. However, it would seem advisable to base patient management upon both audiological and neurophysiological findings.

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