

## Auditory efferent dysfunction in normal-hearing chronic idiopathic tinnitus

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**Key-words.** Otoacoustic emissions; contralateral suppression; auditory brainstem responses; medial olivocochlear bundle

**Abstract.** *Auditory efferent dysfunction in normal-hearing chronic idiopathic tinnitus.* **Objective:** To investigate the function of the auditory efferent system in patients with chronic idiopathic tinnitus, but normal pure-tone audiograms.

**Methods:** We studied 15 subjects with normal hearing that had experienced either unilateral or bilateral persistent tinnitus for at least 3 months. The ears of the 15 subjects were classified into tinnitus-positive-ear (TPE) and tinnitus-negative-ear (TNE) groups. The control-ear group (CE) comprised the ears of 15 subjects with normal hearing and no tinnitus. We measured different types of otoacoustic emissions (OAEs), including spontaneous (SOAEs), transient evoked (TEOAEs), and distortion product (DPOAEs). We also analyzed contralateral suppression of OAEs and auditory brainstem responses (ABRs). Data were compared among TPE, TNE, and CE groups.

**Results:** The data associated with cochlear mechanics, including the prevalence of SOAEs, the number of SOAE peaks, and the overall TEOAE responses in the absence of a contralateral stimulus, were not significantly different among the TPE, TNE, and CE groups. In the TPE group, contralateral stimuli failed to significantly suppress overall TEOAEs, and contralateral suppression of DPOAEs was significantly reduced over a limited frequency range. Furthermore, the TPE group showed prolonged latencies in waves III and V of ABRs.

**Conclusion:** This study demonstrated that abnormal contralateral suppression of OAEs and ABRs indicated a dysfunction in the ipsilateral efferent medial olivocochlear system; this might play a role in normal-hearing tinnitus.

### Introduction

Tinnitus, an auditory perception experienced in the absence of any external acoustic stimulus, may be triggered by a lesion in the auditory pathway. The mechanisms underlying tinnitus tend to be abstruse, with no single, concise, widely-agreed-upon scientific explanation. This situation presents a challenge for clinical audiologists in treating patients with tinnitus.<sup>1</sup>

The measurement of auditory brainstem responses (ABRs) is one of various methods for assessing tinnitus and facilitating a topographical diagnosis of auditory pathway lesions that cause tinnitus. Among the five ABR signals (peaks I-V), Møller *et al.*<sup>2</sup> showed that patients with high-frequency hearing loss and intractable tinnitus exhibited shorter peak V latencies than patients with similar hearing loss, but no tinnitus. They also recorded compound action potentials from the exposed eighth cranial nerves (the vestibulocochlear nerves) of these pa-

tients, and found that the two patient groups had indistinguishable mean latencies in the negative polarity peaks, N1 and N2. This suggested that tinnitus might result from abnormalities in the superior olivary complex.

Otoacoustic emissions (OAEs), the energy emitted by the outer hair cells in the cochlea, are recordable as acoustic vibrations in the external auditory canal. The olivocochlear efferent system is divided medially into the medial olivocochlear (MOC) bundle, which arises from neurons of the medial superior olivary nucleus complex, and the medial nucleus of the trapezoid body, which is of particular importance in the modulation of cochlear activity. Cochlear activity can be reflected through OAEs, but the amplitude of OAEs can be suppressed when contralateral sound stimulation is applied. This suppression of OAEs is mediated through the MOC system.<sup>3,4</sup> Thus, OAEs are related to both cochlear integrity and the status of the MOC system. Abnormalities in these structures may be structural (e.g.,

a demonstrated morphological lesion) or functional (e.g., an imbalance in central neurotransmitters).<sup>5</sup> Another study demonstrated that ipsilateral pontine lesions could suppress abnormal transient evoked OAEs (TEOAEs).<sup>6</sup> Therefore, OAEs and their suppression by contralateral acoustic stimulation might serve as an objective, noninvasive, clinical test for the status of the outer hair cells, the auditory brainstem, and the efferent MOC bundle.

Previously, cochlear mechanical activity was suggested to be an objective correlate of tinnitus. Results from a study by Norton *et al.*<sup>7</sup> argued against the OAEs as the source of tinnitus; however, they indicated that oscillating evoked OAEs and tinnitus were related to a common underlying pathology. Patients with hearing-impairments and tinnitus due to various etiologies exhibited reduced MOC bundle effectiveness.<sup>8-10</sup> Recently, Riga *et al.*<sup>11</sup> showed that audiological dysfunction of the efferent auditory system could occur in affected or unaffected ears of patients with normal hearing and acute tinnitus (duration of tinnitus <3 weeks). They suggested that efferent nerve dysfunction should be considered a generalized, bilateral phenomenon in patients with acute tinnitus. However, no studies have investigated whether auditory efferent dysfunction also occurred in affected and unaffected ears of patients with normal hearing and chronic or idiopathic tinnitus. Recent neuroimaging studies demonstrated lateralization of nerve dysfunction in patients with lateralized tinnitus. Furthermore, in patients with lateralized tinnitus, Smits *et al.*<sup>12</sup> showed that functional MRI activation was lateralized towards the side of perceived tinnitus in the primary auditory cortex, inferior colliculus, and medial geniculate body. Schneider *et al.*<sup>13</sup> also demonstrated that subjects with chronic tinnitus exhibited a significant reduction in the gray matter volume of Heschl's gyrus exclusively in the hemisphere ipsilateral to the affected ear. Therefore, in this study, we used various OAEs and other auditory measurements to investigate the function of the auditory efferent system in patients with chronic idiopathic tinnitus, but normal pure-tone audiograms.

## Materials and methods

This study recruited 15 consecutive, patients with normal hearing that experienced at least 3 months of either unilateral (7 patients) or bilateral (8 patients)

persistent tinnitus of unknown etiology. We also recruited 15 individuals with normal hearing that had no auditory complaints to serve as control subjects. To exclude any possible psychological, neurological, or otological abnormalities, all study participants underwent a protocol that included an interview (to obtain relevant clinical information), an otoscopy examination, standard pure tone audiometry, tympanometry, a static compliance measurement, an acoustic reflex test, an ABR survey, and various OAE examinations. Informed consent was obtained from all participants, and the Internal Review Board approved the study in advance.

In addition to normal middle ear function and normal stapedial reflexes, every participant had normal hearing, validated with a flat-pattern, pure-tone audiogram, and by the observation that thresholds among all octave frequencies differed by less than 10 dB. Normal hearing was defined as a set of hearing thresholds  $\leq 25$  dB hearing level (HL) for pure tones at octave step frequencies from 0.25 to 8 kHz, according to the American National Standards Institute 1969 criteria, and thresholds  $\leq 25$  dB HL for click ABRs.

We excluded subjects that had systemic diseases, a history of head injury, other neurological or otological complaints, a long-term history of noise exposure, or a family history of congenital hearing impairment. We also excluded subjects with psychological comorbidities, including sleep disorders, depression, mania, bipolar disorders, anxiety/panic disorders, somatoform disorders, and psychotic disorders.

### Ear groupings

The ears were classified into the following 3 groups: (1) the tinnitus-positive-ear group (TPE), which comprised 23 tinnitus-affected ears from patients with bilateral or unilateral tinnitus, (2) the tinnitus-negative-ear group (TNE), which comprised 7 tinnitus-unaffected ears from patients with unilateral tinnitus, and (3) the control-ear group (CE), which comprised 30 ears from 15 volunteers with normal hearing and without any auditory complaints.

### Pitch-matching test

A series of sound stimuli, either pure tones or narrow-band noises, were presented to patients to determine which sound matched the pitch of the tinnitus. Sounds were presented with a GSI 61

clinical audiometer (Grason-Stadler, Madison, WI, USA) over TDH-50p earphones. In patients with unilateral tinnitus, sounds were presented to the unaffected ear. In patients with equal tinnitus in both ears or with central tinnitus, the right ear was arbitrarily preselected for sound presentation. When a patient gave a subjective indication of hearing different pitches in the two ears, the sounds were applied to both ears.

Subjects were asked to choose the sound (pure tone or narrow-band noise) that was most similar to their tinnitus. Then, the selected sound was presented among a set of frequencies with center frequencies of 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000, and 8000 Hz, and the series was presented from the lowest to the highest frequency at 15 dB above the patient's hearing threshold. These sound series sweeps were performed until the patient selected same frequency on three consecutive occasions. The final selection was determined to be the pitch of the tinnitus.

#### *ABR survey*

An ABR system (GN Otometrics; Schaumburg, IL, USA) was used to measure the hearing thresholds, and to make topographical diagnoses of the auditory pathway lesions. For topographical diagnoses, we delivered click stimulations at an intensity level of 80 dB above normal hearing level (nHL) and a stimulation rate of 11.1/s. All ABRs were two-channel recordings from electrodes placed on the high forehead and on each earlobe; another electrode on the glabella served as ground. Each recorded ABR waveform was replicable, and the averaged result was obtained from 1024 sweeps. The parameters studied were the absolute latencies of waves I, III, and V, and the intervals between these waves (interpeak latencies, IPLs), indicated as IPLs for I–V, I–III, and III–V.

#### *OAE examinations*

OAEs were recorded with an ILO292 OAE system, version 5 (Otodynamics Inc., Hatfield, Herts, UK).

#### *Spontaneous OAE (SOAE) recordings*

Synchronized SOAEs were recorded after stimulation with single 80- $\mu$ s clicks at 54–60 dB sound pressure level (SPL), presented at 80-ms intervals. The TEOAEs elicited by clicks persisted less than

20 ms, but the synchronized SOAEs, time-locked to the stimulus, were continuous. A spectral analysis of the waveform captured in the 60 to 80-ms time window confirmed the presence of the synchronized SOAEs. We calculated the average of 260 responses, and we performed fast Fourier transformation analysis in the spectral band from 0 to 6250 Hz, with a resolution of 12.3 Hz. Meaningful SOAEs were spectral peaks with amplitudes of at least 5 dB above the noise floor in the frequency range from 1000 to 2000 Hz.<sup>14</sup>

#### *Transient Evoked OAE (TEOAE) recordings*

TEOAE recording was performed as described by Kemp *et al.*<sup>15</sup> The stimuli were presented in a non-linear mode, where 4 clicks were delivered, and every fourth click had reversed polarity and three times the amplitude of the first 3 clicks. Thus, the 4<sup>th</sup> click cancelled the linear portion of the stimulus, and the responses were non-linear OAEs. The peak reception level of the stimuli was approximately 60 dB SPL. We rejected random noise contamination (sounds below 47.3 dB SPL), which mainly arose from low-frequency biological noise from the patient and ambient noise. We collected 260 sweeps during the test period. The parameters measured included the overall TEOAE response, residual noise contamination, wave reproducibility, and the signal-to-noise ratio in the frequency bands centered at 1, 1.5, 2, 3, and 4 kHz. Two repeated tests were performed and the data were averaged.

#### *Medial olivocochlear suppression test with TEOAEs*

TEOAEs were recorded with simultaneous contralateral stimulation of 40 dB SL white noise. This was delivered from the B channel of an Otodynamics ILO292 OAE analyzer via a contralateral earphone. The difference between TEOAE responses with and without contralateral stimulation was taken as the MOC suppression effect.

#### *Distortion Product OAE (DPOAE) recordings*

The DPOAEs were recorded with two stimuli (F1 and F1), where the frequencies of stimulus 2 (F2) were 1001, 1257, 1587, 2002, 2515, 3174, 4004, 5042, 6348 Hz and the F2/F1 ratio was set at 1.22. The intensities of stimuli 1 and 2 (L1 and L2) were automatically set at 70 dB SPL by the Otodynamics ILO292 OAE analyzer. The DPOAE responses

(DP level) and noise floor (NF) were measured at various cubic difference frequencies, 2F1–F2. Two repeated tests were performed and the data were averaged.

*Medial olivocochlear suppression test with DPOAEs*

DPOAEs were recorded with simultaneous contralateral stimulation of 65 dB HL white noise,<sup>8</sup> which was delivered from the GSI 61 clinical audiometer via a contralateral TDH-50p earphone. The difference in DPOAE responses with and without contralateral stimulation represented the MOC suppression effect.

*Statistical analysis*

All data were analyzed with STATA software (STATA Corp., College Station, TX, USA). The results in the TPE, TNE, and CE groups were compared with the two-sample *t*-test, the Fisher exact test, the two-sample Wilcoxon rank-sum test, and the Wilcoxon signed-rank test. The significance level was set at  $P < 0.05$ .

**Results**

There were no significant differences in gender (Fisher exact test,  $P = 0.710$ ) or age (two-sample *t*-test,  $P = 0.4692$ ) between the tinnitus group (7 men

Table 1

Significant variation of DPOAEs and tinnitus pitches in the tinnitus-positive ears of 15 subjects with chronic idiopathic tinnitus

Patient no. (Ear)	Sex/ Age (y)	Stimulus frequency (2F1–F2) (Hz)								Tinnitus Pitch (Hz)	
		635	819	1025	1270	1611	2026	2564	3210		4052
1 (L)	M/34										8000 PT
2 (L)	F/52										250 PT
3 (R)	M/44					▼	▼	▼	▼		6000 PT
3 (L)	M/44					▼	▼				6000 PT
4 (R)	M/55				▼	▼	▼				1500 PT*
5 (R)	F/35							▲	▲		8000 PT
6 (R)	F/20										125 PT
6 (L)	F/20										3000 PT
7 (L)	M/39	▼						▼	▼		6000 PT
8 (R)	F/64					▼					3000 PT
8 (L)	F/64					▼	▼				3000 PT
9 (R)	F/29	▼							▼		1500 PT
9 (L)	F/29										1500 PT
10 (R)	F/38					▼					1500 PT*
10 (L)	F/38										1500 PT
11 (R)	M/41					▼					8000 NB
11 (L)	M/41		▼			▼	▼	▼			8000 NB
12 (R)	F/55							▼			8000 NB
12 (L)	F/55							▼			8000 NB
13 (L)	M/44							▲			6000 NB
14 (R)	M/18			▲		▲					8000 PT
14 (L)	M/18					▲		▲			8000 PT
15 (R)	F/48					▼					250 PT

DPOAE: Distortion Product Otoacoustic emission; R: right ear; L: left ear; PT: pure tone; NB: narrow band noise. ▼: decrease in DPOAE (the DPOAE amplitude was less than “the CE mean –2 SD”). ▲: increase in DPOAE (the DPOAE amplitude was more than “the CE mean +2 SD”).

\*: tinnitus pitch was within or near the frequency range where the DPOAEs were decreased or increased.

Table 2  
Mean (SD) of pure tone audiometric thresholds (dB HL) for all groups

Frequency (Hz)	250	500	1000	2000	4000	8000
TPE (n = 23)	9.1 (5.6)	9.1 (4.2)	9.8(5.7)	9.8 (7.1)	10.7 (7.0)	9.8 (8.0)
TNE (n = 7)	10 (5.8)	10 (8.2)	11.4 (4.8)	10.7 (7.3)	9.3 (5.3)	12.1 (5.7)
CE (n = 30)	10.5 (5.1)	7.2 (3.9)	9.5 (4.8)	6.7 (4.8)	11.2 (7.2)	7.5 (7.6)

Comparisons between groups at each frequency showed no significant differences;  $p > 0.05$ ; two-sample Wilcoxon rank-sum test. TPE: tinnitus-positive ear; TNE: tinnitus-negative ear; CE: control ear.

and 8 women, age  $41.1 \pm 12.9$  years) and the control group (5 men, 10 women, age  $37.9 \pm 10.9$  years). The pitches of the tinnitus in the tinnitus-positive ears of 15 patients (23 ears) are listed in Table 1.

The mean thresholds of octave frequencies ranged from 9.1 to 10.7 dB HL in the TPE group, 9.3 to 12.1 dB HL in the TNE group, and 6.7 to 11.2 dB HL in the CE group (Table 2). There were no significant differences between groups in the mean threshold levels at the audiometric frequencies 0.25, 0.5, 1, 2, 4, and 8 kHz (two-sample Wilcoxon rank-sum test,  $P > 0.05$ ).

*ABR survey*

The ABR measurements showed significantly prolonged latencies for waves III and V in the TPE group compared to those of the CE group. However, the IPLs for III–V were not significantly different between the two groups (Table 3). A significant difference was detected between the mean latencies of wave I in the TPE and TNE groups. Nevertheless, no statistically significant differences were exhibited in any ABR parameters between the TNE and CE groups.

*SOAE recordings*

There prevalence of SOAEs was not significantly different among groups (TPE, 7/23, 30.4%; TNE,

1/7, 14.3%; CE, 13/30, 43.3%; Fisher exact test,  $P > 0.05$ ). Also, the average number of SOAE peaks was not significantly different among the three groups (TPE, 0.48/ear; TNE, 0.14/ear; CE, 0.7/ear; two-sample Wilcoxon rank-sum test,  $P > 0.05$ ).

*TEOAE recordings and medial olivocochlear suppression test*

The three groups showed similar mean overall TEOAE responses (Table 4) and similar mean suppression effects on TEOAEs ( $0.92 \pm 2.04$  dB in TPE,  $1.91 \pm 1.77$  dB in TNE, and  $0.92 \pm 1.23$  dB in CE) (two-sample Wilcoxon rank-sum test,  $P > 0.05$ ). However, the overall TEOAE responses recorded without contralateral acoustic stimulation were significantly larger than those recorded with contralateral stimulation in both the TNE and CE groups, but not in the TPE group (Table 4).

*DPOAE recordings and medial olivocochlear suppression test*

The mean DPOAE amplitudes were equivalent at each frequency in the TPE and TNE groups. However, compared to the CE group, the mean DPOAE amplitudes were significantly reduced at 635 and 1611 Hz in the TPE group ( $P = 0.0201$  and  $0.0086$  respectively) and at 1611 Hz in the TNE group

Table 3  
Mean (SD) of auditory brainstem response latencies (ms) for all groups and differences between groups

	I	III	V	I–V	I–III	III–V
TPE (n = 23)	1.50*	3.69**	5.59***	4.10	2.19	1.91
	(0.14)	(0.14)	(0.16)	(0.22)	(0.16)	(0.15)
TNE (n = 7)	1.37*	3.61	5.63	4.26	2.24	2.02
	(0.07)	(0.17)	(0.22)	(0.22)	(0.15)	(0.15)
CE (n = 30)	1.44	3.60**	5.53***	4.09	2.16	1.93
	(0.19)	(0.15)	(0.18)	(0.22)	(0.20)	(0.14)

\*:  $P = 0.0148$ , \*\*:  $P = 0.0490$ , \*\*\*:  $P = 0.0410$ ; two-sample Wilcoxon rank-sum test. TPE: tinnitus-positive ear; TNE: tinnitus-negative ear; CE: control ear.

Table 4

Comparison among the three ear groups of mean (SD) overall transient evoked otoacoustic emission responses (dB SPL) with and without contralateral stimulation

	Without CS	With CS
TPE (n = 23)	-1.55* (5.44)	-1.57* (4.72)
TNE (n = 7)	-1.84** (5.09)	-2.92** (4.39)
CE (n = 30)	0.41*** (4.92)	-0.51*** (5.16)

CS: contralateral acoustic stimulus.

\*:  $P = 0.0701$ , \*\*:  $P = 0.0464$ , \*\*\*:  $P = 0.0009$ ; Wilcoxon signed-rank test.

TPE: tinnitus-positive ear; TNE: tinnitus-negative ear; CE: control ear.

( $P = 0.0028$ ) (two-sample Wilcoxon rank-sum test) (Figure 1).

More ears showed decreased DPOAEs (amplitudes below “the CE mean - 2 SD”) in the TPE group (56.5%, 13 of 23 ears) and the TNE group (57.1%, 4 of 7 ears) compared to the CE group (20%, 6 of 30 ears). More ears also showed increased DPOAEs (amplitudes above “the CE mean + 2 SD”) in the TPE (17.4%, 4 of 23 ears) and TNE (28.6%, 2 of 7 ears) groups compared to the CE group (3.3%, 1 of 30 ears). Decreases and increases in DPOAEs in tinnitus-positive ears are shown in Table 1.

There were no significant differences in the MOC suppression of DPOAEs between the TPE and TNE groups. However, in comparison with the

CE group, the efferent suppression of DPOAE amplitudes were significantly decreased at 3210 Hz in the TPE group (two-sample Wilcoxon rank-sum test,  $P = 0.0444$ ), but not in the TNE group (Table 5).

## Discussion

We found three interesting audiologic findings related to the function of the MOC bundle in patients with chronic tinnitus, but normal pure-tone audiograms. The first was a significant reduction of overall TEOAE responses during contralateral acoustic stimulation in both the TNE and CE groups, but not in the TPE group. The second was that, compared to the CE group, suppression of DPOAEs was significantly reduced over a limited frequency range in the TPE group, but suppression was not reduced in the TNE group. The last was the significantly prolonged latencies of waves III and V in the TPE group compared to the CE group.

Afferent auditory fibers from the cochlear nuclei project mainly to the contralateral medial superior olivary nuclei. Most efferent MOC fibers exit from the brainstem, then cross, and terminate at the outer hair cells of the contralateral cochlea; the others remain uncrossed and terminate at the outer hair cells of the ipsilateral cochlea. The combined crossed and uncrossed efferent fibers travel within the inferior vestibular nerve.<sup>16</sup> Therefore, there is a neural

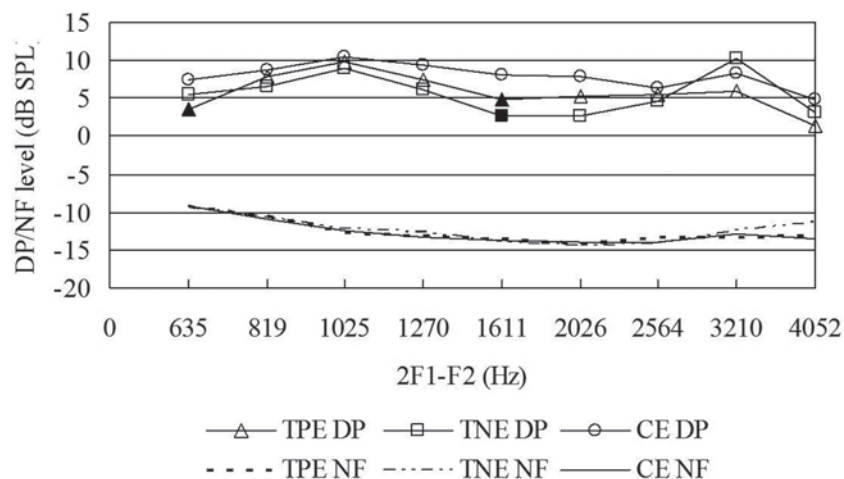


Figure 1

Mean levels of distortion product otoacoustic emissions (DP) or noise floors (NF) for controls or subjects with normal hearing and chronic idiopathic tinnitus.  $\blacktriangle$ : significantly decreased (two-sample Wilcoxon rank-sum test,  $P < 0.05$ ), compared to the CE group;  $\blacksquare$ : significantly decreased (two-sample Wilcoxon rank-sum test,  $P < 0.05$ ), compared to the CE group; the open symbols ( $\Delta$ ,  $\square$ ) indicate no significant difference from CE. TPE: tinnitus-positive-ear group; TNE: tinnitus-negative-ear group; CE: control-ear group; 2F1-F2: cubic distortion difference, used for the stimulation frequency.

Table 5

Mean (SD) medial olivocochlear bundle suppression effects (dB) on the distortion product otoacoustic emissions for all groups

2F1–F2 (Hz)	635	819	1025	1270	1611	2026	2564	3210	4052
TPE (n = 23)	4.3 (5.1)	3.4 (4.1)	2.4 (2.5)	1.1 (3.4)	1.5 (3.5)	0.8 (3.4)	0.3 (1.5)	0.1* (2.0)	2.9 (5.8)
TNE (n = 7)	3.4 (3.3)	3.1 (2.8)	0.6 (2.3)	0.4 (1.9)	-0.5 (2.9)	-1.6 (2.6)	-0.3 (1.2)	0.9 (1.6)	0.3 (1.9)
CE (n = 30)	4.5 (5.1)	2.2 (3.7)	2.1 (3.3)	0.3 (2.4)	0.6 (1.9)	0.0 (1.4)	0.7 (3.3)	0.6* (1.2)	0.6 (1.6)

\*:  $P = 0.0444$ ; two-sample Wilcoxon rank-sum test.

2F1–F2 (Hz): the cubic difference frequency used for stimulations.

TPE: tinnitus-positive ear; TNE: tinnitus-negative ear; CE: control ear.

pathway that extends from one cochlea, via the afferent auditory system, primarily to the contralateral medial superior olivary nuclei, and from there to the other cochlea, via the MOC efferent pathway. Williams *et al.*<sup>4</sup> demonstrated that, following unilateral vestibular neurectomy, contralateral acoustic stimulation could no longer inhibit evoked OAEs on the sectioned side. That result suggested that the contralateral auditory suppression of OAEs was mediated by the ipsilateral MOC efferent nerves. In the present study, we found that the efficacy of the efferent auditory system was reduced in the TPE group. This was demonstrated by the insignificant contralateral suppression of overall TEOAEs and the significantly reduced contralateral suppression of DPOAEs over a limited frequency range. This suggested that the tinnitogenic lesion may be located in the ipsilateral MOC bundle and the superior olivary complex. However, these results should be interpreted with caution, because the reduced suppression of DPOAEs was noticed only within a limited frequency range (3210 Hz), and the TPE group had a small number of patients.

Although the IPLs for III–V were not statistically different among patient groups, the ABRs showed significantly prolonged latencies in waves III and V in the TPE, but not in the TNE group, compared to the CE group. However, the TPE group showed a latency in wave I similar to that of the CE group. Although there was a significant difference between the mean latencies of wave I between the TPE and TNE groups, this was due to the shortened latency in the TNE group, not an extended latency in the TPE group. Our data also showed significant reductions in TEOAEs in the presence, compared to the absence, of contralateral acoustic stimulation for both the TNE and CE groups, but not for the TPE group. However, the

mean of overall TEOAE responses without contralateral stimulus were not significantly different among the three groups. This indicated that the cochlear integrity was intact in patients with normal hearing, despite chronic idiopathic tinnitus. Consequently, we inferred from the ABR and TEOAE findings that the lesion in the TPE group was located mainly in the brainstem or auditory nerve. Currently, ABR components are thought to result from superimposed action potentials from several generators in the brainstem that are predominantly ipsilateral to the stimulated ear.<sup>17</sup> Generally, wave III is thought to originate within the structures of the ipsilateral caudal pons, including the cochlear nucleus, trapezoid body, and superior olivary complex. In humans, waves IV and V are often fused into a single, broad IV/V complex, which was suggested to originate within the ipsilateral pons, midbrain, the medial geniculate in the thalamus, and in auditory radiations. In the present study, topographic analyses of ABR parameters in the TPE group suggested that the prolonged latencies in waves III and V with normal IPLs for III–V indicated a potential dysfunction in the caudal pontine area, mainly ipsilateral to the tinnitus-affected ear.

Shiomi *et al.*<sup>18</sup> investigated cochlear activity in tinnitus and found significant decreases in DPOAE amplitudes over a limited frequency range (4–7 kHz) in 93.3% of patients with normal-hearing and tinnitus. That indicated a dysfunction in the outer hair cells in that frequency range. They also demonstrated that a number of cases had pitch-matched tinnitus frequencies out of the dysfunctional frequency range. They suggested that the cochlear dynamic properties changed in tinnitus, but the mechanism of tinnitogenesis remained obscure. In the present study, the three groups showed

similar cochlear mechanics, including the prevalence of SOAEs, the numbers of SOAE peaks, and the mean overall TEOAE responses in the absence of a contralateral stimulus. This may indicate that cochlear integrity is maintained in patients with normal-hearing and tinnitus. However, significant decreases in the DPOAE amplitudes were observed over a limited frequency range in both the TPE (635 and 1611 Hz) and TNE (1611 Hz) groups, compared to the CE group. In addition, both the TPE and TNE groups had higher percentages of ears with low DPOAE amplitudes (below “the CE mean - 2 SD”) or elevated DPOAE amplitudes (above “the CE mean + 2 SD”) than the percentages observed in the CE group. These results suggested the possibility that the ears with tinnitus may have had less-than-optimal outer hair cell function or some sort of degradation in auditory nerve fibers (both afferent and efferent). The present study also showed that the matched tinnitus pitch was out of the frequency range of decreased or increased DPOAEs in 4 of 6 ears (67%) with tinnitus frequencies below 4052 Hz (the highest DPOAE frequency in this study).

Riga *et al.*<sup>11</sup> showed that contralateral white noise could not significantly suppress the DPOAEs over all test frequencies in both tinnitus-affected and tinnitus-unaffected ears. This indicated that the auditory efferent system was ineffective in both tinnitus and non-tinnitus ears. They suggested that efferent nerve dysfunction may be considered a generalized, bilateral phenomenon in patients with acute tinnitus. In the present study, we found that contralateral noise could significantly suppress most DPOAEs in both the TPE and TNE groups, but this suppression failed over a limited frequency range in the TPE group. However, we found that contralateral suppression could not significantly suppress TEOAEs in the TPE group, but suppression was normal in the TNE group. The discrepancy between our results and those of Riga *et al.* may be partially attributed to the differences in tinnitus duration (<3 weeks vs. >3 months) or differences in etiologies. In the study by Riga *et al.*,<sup>11</sup> tinnitus was caused by the exposure to loud noise in 5 subjects. In contrast, the cause of chronic tinnitus was unknown for our subjects.

In the present study, lateralized central auditory dysfunction was demonstrated by the prolonged latencies of ABR waveforms. This was consistent with recent studies that found neuroimaging laterali-

zation in patients with lateralized tinnitus.<sup>12,13</sup> In addition, numerous recent studies have concurred with the hypothesis that the dorsal cochlear nucleus and the inferior colliculus may be involved in the generation and modulation of tinnitus.<sup>19,20</sup> The present study showed prolonged latencies of waves III and V in the TPE, but not in the TNE group; this provided audiologic evidence in support of possible pathology in the dorsal cochlear nucleus and the inferior colliculus. Our findings did not support the suggestion by Riga *et al.*<sup>11</sup> that auditory efferent pathway dysfunction may occur bilaterally in tinnitus; instead, we suggest that, in subjects with normal hearing and chronic idiopathic tinnitus, the dysfunction may occur ipsilateral to tinnitus-positive ear.

Based on the results from this preliminary study, lateralization of a dysfunction in the auditory efferent system may occur in patients with normal hearing and chronic idiopathic tinnitus. Because patients with normal pure-tone hearing and tinnitus are rare, it was difficult to study a large sample size. Future studies with larger populations may strengthen the conclusions of the present study.

## Conclusion

OAE recordings and the MOC suppression test with contralateral acoustic stimulation have potential value in neuro-otological topographic assessments of tinnitus. Our data provided audiologic evidence that suggested that the dysfunction in the efferent auditory pathway (MOC system) may occur ipsilateral to tinnitus-positive ears in subjects with normal hearing and chronic idiopathic tinnitus. However, further investigation is required to clarify the complex mechanism that underlies dysfunction in the MOC system, alterations in cochlear micromechanics, and tinnitogenesis.

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