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Transtympanic Electrical Stimulation for Immediate and Long-Term Tinnitus Suppression

Walter Di Nardo, Francesca Cianfrone, Alessandro Scorpecci, Italo Cantore, Sara Giannantonio, and Gaetano Paludetti

Institute of Otorhinolaryngology, Catholic University of the Sacred Heart, A. Gemelli University Hospital, Rome, Italy

Abstract: Tinnitus is a common symptom which often becomes disabling, affecting the emotional and psychosocial dimensions of life. There are many reports describing tinnitus suppression or attenuation through electrical stimulation of the ear, provided either by cochlear implants or by transtympanic stimulation. Our study project aims to assess the effects of electrical promontory stimulation (EPS) on persistent disabling tinnitus.We enrolled 11 patients affected by postlingual monoaural or binaural profound hearing loss and disabling tinnitus in the worse ear. EPS was performed with direct continuous positive current delivered by an active platinum-iridium needle electrode connected to a promontory stimulator device. The short-term effect on tinnitus was assessed during and immediately after the stimulation. Long-term effects were estimated after one month by comparing pre- and post-EPS Tinnitus Handicap Inventory (THI) scores. Immediately after EPS, five patients (45.4%) reported complete suppression and four (36.4%) reported attenuation of tinnitus. Two patients (18.2%) said it was unchanged. After one month, the THI score was reduced in five patients (45.4%) and remained unchanged in the other six patients (54.6%). The beneficial effects of EPS on tinnitus might be explained by interference with tinnitus generating circuits such as the dorsal cochlear nucleus and the inferior colliculus and by modification of cortical activity. EPS is to be considered a worthwhile attempt at tinnitus suppression, and could help select candidates for the positioning of an implantable electrical stimulator that might provide longer-term beneficial effect on tinnitus.

Key Words: electrical stimulation; promontory; tinnitus; treatment

Tinnitus is a quite common symptom, not infrequently reported by patients as a bothersome and upsetting experience severely affecting the emotional and psychosocial dimensions of life and sometimes impairing the patients' ability to perform daily life activities. Etiological factors and neural mechanisms for tinnitus remain challenging topics.

As reported by basic and clinical research, lesions are more often localized within the auditory periphery and concern hairy cells. The subsequent change in the acoustic nerve fiber excitation pattern triggers an immediately successive elaboration by neural centers and then, after some time, the priming of neural plasticity phenomena. Therefore, tinnitus could be due to central nervous system reorganization as a long-term consequence of a peripheral alteration [1,2].

To date, only a few effective tinnitus treatments are available. Many studies have described attempts at suppressing tinnitus by means of electrical stimulation, delivered both transcutaneously [3–9] and transtympanically [10–12]. Recently, attempts have been made at relieving chronic intractable tinnitus by delivering electrical stimuli directly to the auditory cortex [13,14]. Nonetheless, given the invasiveness of cortical stimulation and the uncertainty of its beneficial effect on tinnitus, and also considering the as-yet-undefined criteria of patient selection for such a treatment option, we believe that electrical promontory stimulation (EPS) still

Reprint requests: Alessandro Scorpecci, MD, Institute of Otorhinolaryngology, Catholic University of the Sacred Heart, A. Gemelli University Hospital, Largo F.Vito 1, 00168, Rome, Italy. E-mail: alessandroscorpecci@virgilio.it

deserves attention on account of its good rate of success and of its low invasiveness. Furthermore, the assumption that peripheral stimulation can effectively achieve tinnitus suppression is strengthened by the common observation that sensorineurally deaf patients undergoing cochlear implantation often experience reduction or even utter suppression of their tinnitus [15–18]. Our study project aims to assess the effectiveness of EPS as a treatment of persistent tinnitus induced by cochlear lesions and to try to define the most effective electrostimulation type.

MATERIALS AND PATIENTS

Our methods for patient enrollment, informed consent, psychoacoustic testing, placement of a transtympanic electrode, electrical stimulation, data analysis, and follow-up were reviewed and approved by our institutional review board and are in accordance with the Helsinki Declaration.

In our clinic, we enrolled 11 patients (7 women and 4 men) affected by postlingual monaural or binaural profound hearing loss and with severe and disabling tinnitus in the worse ear. Each of the patients had been suffering from tinnitus for at least 1 year. The patients' ages ranged between 34 and 64. We obtained from each patient a complete history and ear, nose, and throat physical examination. In particular, we focused on tinnitus features, such as day, month, and year in which it started; type and characteristics of sound; loudness as represented on a visual analog scale; and the way it affected common daily life activities, sleep, and emotions. Eventually, each patient was asked about tinnitus or hearing loss (or both) in his or her family. We performed a complete audiological assessment (pure-tone audiometry, speech audiometry, and transitory evoked otoacoustic emissions) and a study of tinnitus pitch, loudness, and minimum masking level (MML) on the day of the EPS session.

When the hearing loss was gradual in onset, patients underwent auditory brainstem response (ABR) recordings before their deafness became profound, and results were consistent with a peripheral origin of their disease. In other cases, we used ABR to exclude anomalies of the contralateral ear and malingering. Furthermore, to exclude the most common central causes of tinnitus (acoustic neuroma, vascular lesion, neurovascular conflict), all patients underwent brain magnetic resonance imaging with gadolinium.

Overall, the test battery suggested a cochlear origin of tinnitus in all patients. Finally, immediately before EPS and 1 month afterward, we had the study subjects complete the Tinnitus Handicap Inventory (THI), a 25-question test dealing with the social and neuropsychological consequences of tinnitus (e.g., disabilities, emotional reactions to the symptom, difficulty in concentrating). The questionnaire was introduced into the tinnitus assessment battery in order to give the clinician a quick and effective tool for evaluating tinnitus and for classifying patients clinically [19]. THI has been validated worldwide and can be completed by patients in a very short time.

The stimulation system we used is a Cochlear Promontory Stimulator Z10012 (Cochlear Ltd., Lane Cove, NSW, Australia), an active platinum-iridium needle electrode and a silver surface electrode located on the ipsilateral mastoid region. The anesthetic procedures consisted in careful cleansing of the external auditory canal and local administration of lidocaine to anesthetize the tympanic membrane for 5 minutes. We performed transtympanic electrical stimulation with direct continuous positive current at levels ranging from 0 to 500 μA. Pulse rates available were 50, 100, 200, 400, 800, and 1,600 Hz. We started by delivering current at the lowest pulse rate (50 Hz) and proceeded to increase the pulse rate. For each presented frequency of stimulation, current intensity was slowly increased to find threshold first and then the discomfort level, and we asked patients about the effect of stimulation on tinnitus. Having learned from the patients the frequency causing the best tinnitus suppression, we delivered continuous stimulation at that frequency for at least 60 seconds. At the end of the procedure, we asked patients whether tinnitus was still present or had abated or disappeared.

RESULTS

Characteristics of the study population, including age, cause of hearing loss, and duration of tinnitus, are shown in Table 1; tinnitus pitch, loudness, and MML as measured immediately before the electrical stimulation

Table 1. Characteristics of the Study Population

Patient	Age (yr)	Cause of Hearing Loss	Duration of Tinnitus (yr)
1	73	Idiopathic	2
2	34	Genetic	16
3	44	Sudden hearing loss	2
4	50	Sudden hearing loss	4
5	57	Sudden hearing loss	1
6	60	Sudden hearing loss	3
7	62	Idiopathic	17
8	48	Idiopathic	20
9	32	Idiopathic	12
10	52	Iatrogenic (stapedotomy complication)	2
11	46	Autoimmune	16

Table 2. Tinnitus Pitch, Loudness, and MML in the Study Patients Immediately Preceding Electrical Stimulation

Patient	Pitch (Hz)	Loudness (dB HL)	MML (dB HL)
1	4,000	50	60
2	1,000	60	70
3	8,000 and 1,000	60	60
4	250 and 3,000	70 and 90	90
5	125	75	80
6	1,000 and 3,000	65	75
7	250	60	70
8	250	80	NM
9	250	80	90
10	250	70	90
11	4,000	60	65

MML = minimum masking level; NM = not masked by any intensity of sound stimulus.

session are shown in Table 2. Table 3 lists data concerning the modalities and the effects of EPS, such as pulse rate of the delivered stimulus, threshold, discomfort level, and best tinnitus-suppressing frequencies for each patient. Overall tinnitus evaluation immediately after EPS showed that five patients (45.4%) reported complete suppression of tinnitus, four (36.4%) reported tinnitus attenuation, and two (18.2%) said it was unchanged; no one reported tinnitus worsening. On the whole, 9 of the 11 patients (81.8%) had immediate benefit from EPS relative to their tinnitus.

The most effective frequencies of electrical stimulation for tinnitus suppression or reduction were 50 Hz and 100 Hz. For lower frequencies of stimulation, electrical intensity for tinnitus suppression or attenuation was just above auditory threshold, whereas for high frequencies of stimulation, it was quite near maximum acceptable

Table 3. Effects of Electrical Promontory Stimulation on Tinnitus

Patient	Pulse Rate of Stimulus (Hz)	Threshold (μA)	Discomfort Level (μA)	Effective Pulse Rates and Intensities*
1	50	150	250	50 and 100 Hz
	100	200	250	at threshold
2	50	40	70	Tinnitus unchanged
	100	40	80	
	200	60	80	
	400	No sound	130	
	800	No sound	70	
	1,600	No sound	70	
3	50	70	350	50 and 100 Hz; 300 μA,
	100	300	350	200, 400, 800 Hz;
	200	No sound	500	400 μA (for both
	400	No sound	500	tinnitus components)
	800	No sound	500	
	1,600	No sound	500	
4	50	80	80	50 Hz, 80 μA (250 Hz
	100	220	300	component of
	200	90	500	tinnitus)
	400	No sound	500	3,000 Hz component
	800	No sound	500	unchanged
	1,600	No sound	500	
5	50	70	250	Tinnitus unchanged
	100	400	500	
	200	No sound	500	
	400	No sound	500	
	800	No sound	500	
	1,600	No sound	500	
6	50	36	75	50, 100, 200 Hz;
	100	20	68	60 μA
	200	15	80	
	400	No sound	80	
	800	No sound	80	
	1,600	No sound	80	
7	50	225	380	50 Hz, 300 μA
	100	150	250	100 Hz, 200 μA
	200	200	250	200 Hz, 200 μA
	400	No sound	250	
	800	No sound	250	
	1,600	No sound	250	
8	50	370	500	50 Hz, 440 μA
	100	No sound	500	(3,000 Hz
	200	No sound	500	component
	400	No sound	500	of tinnitus)
	800	No sound	500	1,000 Hz component
	1,600	No sound	500	unchanged
9	50	80	270	50, 100 Hz, 230 μA
	100	230	390	200 Hz, 400 μA
	200	No sound	700	
	400	No sound	850	
	800	No sound	900	
	1,600	No sound	900	
10	50	215	400	800 Hz, 300 μA
	100	250	400	
	200	250	500	
	400	250	500	
	800	250	500	
	1,600	No sound	500	
11	50	30	120	50, 100 Hz; 100 μA
	100	70	140	
	200	220	220	
	400	No sound	220	
	800	No sound	220	
	1,600	No sound	220	

* Describes the most effective tinnitus-suppressing pulse rates, with the respective intensity of stimulation. Patient 1 could be stimulated only with 50-Hz and 100-Hz pulse rates, because other pulse rates gave him painful sensations.

level in the majority of patients. Remarkably, three patients reported tinnitus attenuation with subthreshold stimulation (i.e., stimulation with a pulse rate that did not elicit any sounds). Three patients (patients 3, 4, and 8) had a double tinnitus. In these cases, the effect of EPS was considered separately for the two components. Patient 3 reported suppression of both tinnitus components, whereas patients 4 and 8 said that only one of the components had been reduced or suppressed, the other one remaining unchanged (see Table 3). After 1 month, among the eight patients who had benefited from EPS, five (45.4%) said their tinnitus was still present but that its intensity was much lower than before. The remaining six patients (54.6%) reported that tinnitus was unchanged or had progressively returned to its former loudness. No patient reported tinnitus worsening.

Evaluation of the emotional, affective, and psychosocial impact of tinnitus performed through the THI showed the following: THI reduction in five patients (45.4%) and THI unchanged in the remaining six patients (54.6%). THI scores obtained immediately before and 1 month after EPS are shown in Table 4, which also provides information about pre- and poststimulation partial scores relative to the three categories (emotional, functional, and catastrophic) comprising the THI. No association was found among tinnitus pitch and loudness, MML, and effect of electrical stimulation.

Conversely, factors such as tinnitus duration and patient's age appear to be associated with the THI outcome: Four of the six patients having had tinnitus for less than 5 years had a complete or partial benefit from the procedure, whereas only one of five patients with more than 5 years of tinnitus showed a THI score reduction after 1 month. As for patients' age, four of the five subjects reporting longer-lasting benefit from the procedure were younger than 50 years. Finally, there seemed to be no association between the cause of hearing loss and the benefits derived from EPS.

DISCUSSION

The effectiveness of electrical stimulation on tinnitus is well-known, thanks to studies on groups of patients affected by bilateral profound sensorineural hearing loss and undergoing cochlear implantation, the majority of whom report suppression or attenuation of tinnitus after device hookup [15–18]. Our short-term and long-term results are consistent both with the evidence provided by such studies on cochlear implants and with recent works on transtympanic electrical stimulation [20–22].

Mechanisms Underlying the Immediate Effects of EPS on Tinnitus

Despite the remarkable amount of evidence pointing to a beneficial and lasting effect of EPS on tinnitus, studies generally describe the clinical effects of the procedure rather than focusing on the mechanisms underlying tinnitus suppression, so that at present there are many questions—and no certainty—as to how EPS should work. The "masking" hypothesis, which was among the earliest proposed [23], has long been considered too simplistic and insufficient, because in some cases tinnitus reduction can be obtained by means of subliminal electrical pulse rates. Consistent with reports by Rubinstein et al. [20] and Okusa et al. [22], our results indicate that in two patients (patients 3 and 9), suppression of tinnitus occurred at a pulse rate and at an intensity of stimulation that did not elicit any sound sensations (see Table 3). So, even if a role for masking cannot be completely ruled out, it appears that other mechanisms play a role. One of the theories about peripheral tinnitus suggests that its origin lies in an alteration of spontaneous firing by acoustic nerve fibers. In a number of animal studies, this abnormal activity was brought back to a spontaneous-type nerve firing by application of an electrical stimulus [24,25].

Table 4. Tinnitus Handicap Inventory (THI) Scores Before and After Electrical Promontory Stimulation (EPS)

	Pre-EPS THI				THI One Month After EPS			
Patient	**Functional**	**Emotional**	**Catastrophic**	**Total**	**Functional**	**Emotional**	**Catastrophic**	**Total**
1	28	10	8	46	6	4	0	10
2	34	28	6	68	34	28	6	68
3	18	14	6	38	10	6	0	16
4	36	32	20	88	18	16	8	46
5	34	16	14	64	34	16	14	64
6	14	20	12	46	14	20	12	46
7	8	6	6	20	4	6	8	18
8	10	4	4	18	10	4	4	18
9	28	32	12	72	28	32	12	72
10	22	16	18	56	0	0	4	4
11	12	8	4	24	4	4	0	8

Whether EPS can restore some degree of normal firing in the cochlear nerve of humans affected by tinnitus is at present unknown. Very few reports are currently available about a real-time monitoring of nerve fiber activity during and immediately after peripheral electrical stimulation. Watanabe et al. [26] registered compound action potentials (CAP) through electrocochleography during promontory stimulation: Patients reporting tinnitus suppression during the procedure were also found to have greater CAP amplitudes as compared to patients whose tinnitus remained unchanged, but whether this is a neural correlate of tinnitus suppression is still a matter of debate.

Alternatively, suggested mechanisms through which a positive current delivered to the promontory or to the cochlea may work on nerve fibers include hyperpolarization of axons, with subsequent inhibition of spontaneous discharge rates [27], and even a reflex increase in microcirculation in the auditory pathway [21].

Mechanisms Underlying Long-Term Effects of EPS on Tinnitus

A temporary alteration of acoustic nerve firing cannot account for the long-term effect (at least 1 month) of a 60-second promontory stimulation such as the one we administered to our study patients. In fact, the lasting residual inhibition we observed in some of them implies that central stations along the auditory pathway are likely to be involved as well. The dorsal cochlear nucleus (DCN) and the inferior colliculus (IC) could be plausible candidates, given the amount of evidence pointing to them as tinnitus generators [28,29], although there is currently a paucity of direct evidence of their role in humans [30]. In vivo monitoring of electrical activity in these centers during and after electrical stimulation delivered to the promontory or to the cochlea would be an optimal method to ascertain whether changes occur in the DCN and IC in response to EPS.

Finally, a possible effect of EPS on the cortical reorganization [31–34] underlying tinnitus must be assumed, as a positron emission tomography (PET) study has shown that electrical stimulation delivered to the promontory and round-window region causes activation of the primary auditory cortex and some of the surrounding association areas [35]. Other PET studies report that the electrical stimulation produced by a cochlear implant can reduce the signs of abnormal activity supposed to be associated with tinnitus in the primary auditory and associated cortices and in brain areas of the limbic system [36]. To confirm this, functional brain imaging should be improved so as to reliably identify central areas of tinnitus-related activity. No other reports address the central effects of electrical stimulation on tinnitus in humans, though other noninvasive, promising techniques, such as quantitative electroencephalography, could well serve the purpose of a precise monitoring of EPS brain effects as long as they become more reliable in defining central correlates of tinnitus [37].

As for the tinnitus-associated psychosocial impairment, THI administration allowed us to appreciate a reduction of the THI score in five patients 1 month after transtympanic stimulation, which means most of the negative emotional, affective, and psychosocial impacts of tinnitus abated. This outcome seems to suggest that electrical stimulation also affects the activity of association areas (limbic system) that are notoriously closely intertwined with the neural pathways involved in tinnitus pathogenesis and play a very important role in producing negative emotional correlates of tinnitus, such as anxiety and annoyance.

Toward Optimization of EPS

Considering our preliminary results, we think more expansive series are necessary to precisely define the features that the electrical stimulation should possess to suppress tinnitus. However, even the results on our small series seem to indicate that tinnitus suppression occurs mostly at lower pulse rates (50 and 100 Hz) and at an intensity of stimulation between threshold and minimum discomfort level, although in two of our patients, tinnitus suppression was achieved through subthreshold stimuli. In particular, the issue of using subthreshold or suprathreshold electrical stimulation should be addressed with special attention in future studies: Subthreshold stimulation would be better, avoiding replacement of tinnitus with an unpleasant and intrusive sound, just as often happens with maskers.

Aside from the optimal parameters of stimulation, clinical features that predict EPS success should be outlined more precisely for a correct selection of candidates who could derive the utmost benefit from the procedure. Our results suggest that recent onset of tinnitus and a patient's age can be predictive of tinnitus suppression, although selection criteria deserve deeper investigations in larger series.

In conclusion, we assume that EPS is to be considered per se a worthwhile attempt at tinnitus suppression, being quite easy to administer and successful in the majority of cases. Certain parameters of EPS (e.g., lower frequencies of stimulation) seem more effective and should be taken into account for future use of this procedure. Specific features, such as recent onset of tinnitus and patients' young age, appear to be associated with a better outcome and should therefore be considered as major factors for patient selection.

EPS results could help predict tinnitus response to the positioning of an implantable electrical stimulator: Patients for whom EPS proves to be effective could benefit from the implantation of an intratympanic stimulator that could be controlled by radiofrequencies from the outside. Considering the recent achievements of cochlear implant "soft surgery," which allows preservation of residual hearing, cochlear implants could definitely be used to suppress intractable tinnitus in patients with unilateral profound hearing loss [38].

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