

# Increased Parasympathetic Nerve Tone in Tinnitus Patients Following Electrical Promontory Stimulation

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**Abstract:** Cutaneous digital blood flow (CDBF) during electrical promontory stimulation was measured by laser Doppler flowmetry in 46 tinnitus patients. In patients with tinnitus suppression, CDBF was increased. In contrast, patients in whom treatment did not suppress tinnitus experienced no change in digital blood flow. The cutaneous digital blood flow of patients who experienced slight relief did not differ significantly from patients who experienced no relief. The ratio of CDBF before and after treatment did not correlate with patient age, audiogram pattern. Our results suggest that relief of tinnitus was closely related to increased parasympathetic nerve tone.

## INTRODUCTION

Electrical stimulation of the cochlea has been used widely to treat tinnitus of cochlear origin.<sup>1,2,3,4</sup> Charge-balanced alternating current (AC) stimuli do not produce damaging electrochemical reactions and are therefore considered safe.<sup>5</sup> Facial blushing was observed when our electrical promontory stimulation (ES) method fully suppressed patients' tinnitus at an outpatient clinic, suggesting that cutaneous blood flow had increased. Cutaneous blood flow is regulated by the autonomic nervous system. Sympathetic stimulation constricts cutaneous blood vessels but increased parasympathetic tone dilates cutaneous vessels.<sup>6</sup> Laser Doppler flowmetry (LDF) is a conventional method for measuring cutaneous blood flow. Therefore, changes in the blood flow of the skin during ES could be easily detected by LDF.

Our objective is to show that our electrical treatment for tinnitus could cause increased parasympathetic tone in tinnitus patients with tinnitus suppression.

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## SUBJECTS AND METHODS

### Subjects

We used LDF to assess the effects of treatment in 46 patients with tinnitus (46 ears) who received electrical stimulation treatment at least three times between September 1994 and March of 1995. The study group included 26 men (26 ears) and 20 women (20 ears) ages 42-79 years (mean: 61 years). Tinnitus was unilateral in 26 patients and bilateral in 20 patients. In the 20 patients with bilateral tinnitus, ears with louder tinnitus were chosen to be assessed. All patients had variable degrees of hearing loss, the etiology is shown in Table 1.

**Table 1.** Mean value and Std.Dev. of cutaneous digital blood flow as a function of etiology of hearing loss - Std. Dev.: one standard deviation.

Etiology	mean CBFR (%)	Std. Dev.	n
Sudden Deafness	120.2	27.7	8*
Unknown	125.4	26.7	19*
Acoustic Trauma	146.5	41.9	6
Infection	110.4	21.2	6
Head Trauma	114.6	29.3	4
Ménière's Disease	92.0	-	1

\* non significant

## Procedure

The stimulation array was placed on the promontory through a small incision made in the ear drum after local anesthesia with iontophoresis. Current flowed along a tapered, Teflon-insulated Platinum-Iridium (90-10) wire with a diameter of 250  $\mu\text{m}$  along its length and 750  $\mu\text{m}$  at the tip ball. The wire was connected to a stainless steel lead wire that was attached to an electromagnetic coupling system. A plate electrode for recording the electrocardiogram was attached to the post-auricular skin. Stimulation was initiated at 50  $\mu\text{A}$  for 60 seconds, about 30 seconds after the stimulator was switched on. Then, the stimulation intensity level was increased to 60  $\mu\text{A}$  and increased 20  $\mu\text{A}$  every 60 seconds until the stimulus reached 120  $\mu\text{A}$ , even if the tinnitus had not been relieved. Recording LDF was performed at the second or third trial to decrease effects of stress (for example: electrical stimulation and insertion of electrode through the ear drum) on the autonomic nervous system.

Electrical current was supplied by an oscillator and a current amplifier. Amplitude was increased manually from 0 to 120  $\mu\text{A}$  using the amplifier. We used the charge-balanced sinusoidal wave with 10 kHz frequency.

## Laser Doppler Flowmetry

Laser Doppler Flowmetry (LDF) was used to monitor blood flow of the tip of the second finger of the right hand using a laser Doppler flowmetry monitor (Laser-flow, BPM 403, TSI Corp.). The sampling time was 0.2 seconds. The laser light was 0.7 mm in diameter and emitted light at a wavelength of 750 nm. Measurement of blood flow was initiated after patients rested supine for 10 minutes. Measurement was not done at the first stimulation trial because insertion of the electrode through the tympanic membrane was so stressful. Therefore, data from the second or third trial were analyzed in the present study. Figure 1 shows representative LDF pattern in a patient whose tinnitus disappeared. Blood flow started to increase with a stimulation intensity of 50  $\mu\text{A}$  and continued to increase gradually as the intensity of stimulation increased. The ratio of CDBF at the cessation of stimulation to that at the initiation of stimulation (CBFR) was calculated. The value of cutaneous digital blood flow (CDBF) at the initiation of stimulation was defined as the mean value between the maximum and minimum of the blood flow at the point of the initiation on the recording paper. Differences in CBFR were analyzed using the student t-test (two tails).

## RESULTS

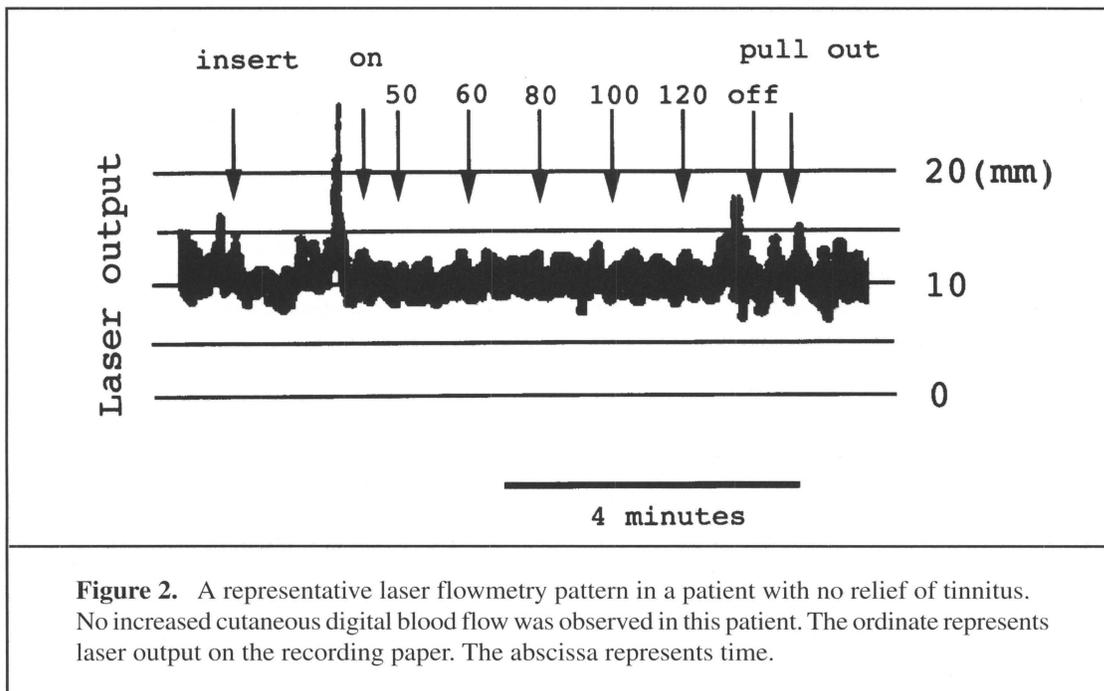
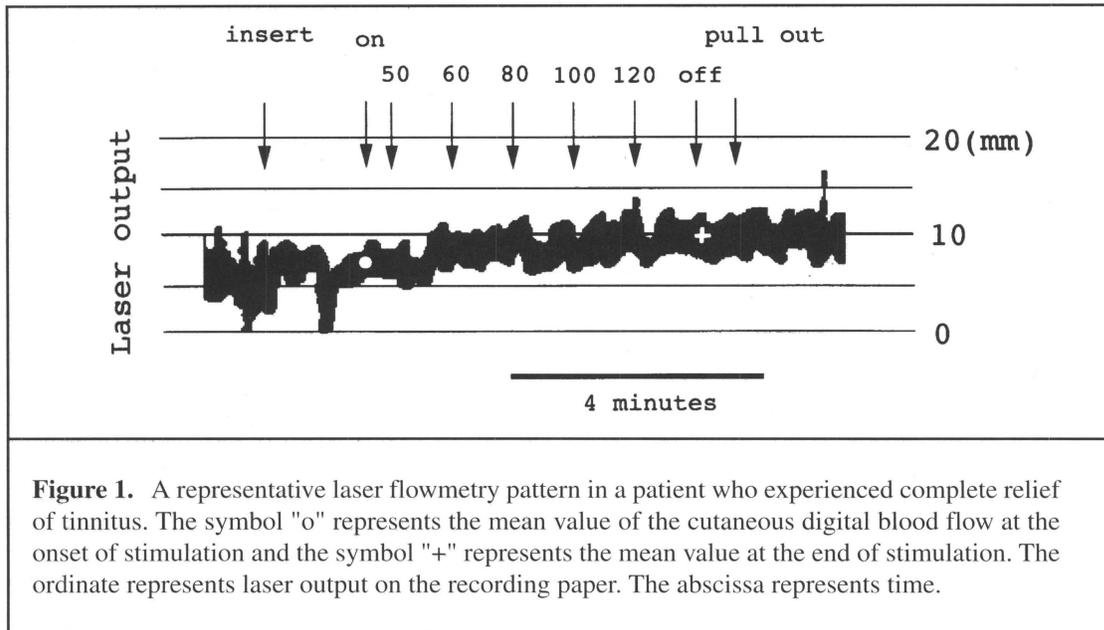
Table 1 shows the mean value and one standard deviation

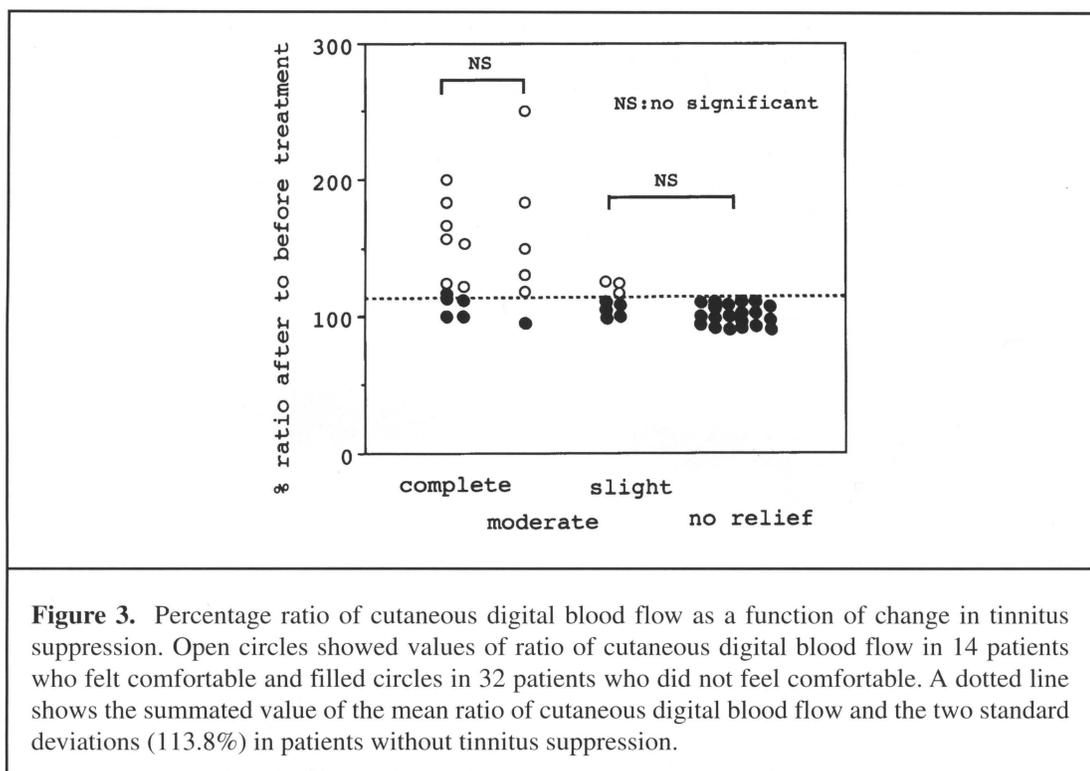
(Std.Dev.) of CBFR in each etiology of hearing loss. Mean CBFR did not differ significantly ( $p>0.4$ ) between patients with sudden deafness and patients with deafness of unknown origin. The number of patients in each etiologic group was too limited to permit a comparison between responsive and unresponsive ears. The difference in the mean hearing level between responsive and unresponsive ears was not significant ( $p>0.1$ ). The most common audiogram pattern was slightly sloped and consistent with that for a high-frequency sensorineural hearing loss ( $n=17$ ). The next most common audiogram illustrated a sharply sloping, high-frequency sensorineural loss pattern ( $n=9$ ). Mean CBFR was 135.2% (Std.Dev.:40.5) in patients with the sharply sloping pattern and 115.9% (Std.Dev.:19.9) in patients with the slightly sloping pattern. Patients with the sharply sloping pattern showed a greater increase in CBFR compared with patients with the slightly sloping pattern. However, the CBFR ratio did not differ significantly between these two groups. The number of patients with other types of audiogram patterns was too small to permit comparison of treatment efficacy. Mean CBFR in patients with high-pitched (3000 to 8000Hz) pre-stimulation tinnitus ( $n=16$ ) did not differ significantly ( $p>0.6$ ) from that of patients whose pre-stimulation tinnitus was classified as a noise (white and band noise,  $n=13$ ). There was no significant difference ( $p>0.4$ ) in mean CBRF between patients with high-pitched tinnitus and patients with low-pitched tinnitus. The number of patients with medium-pitched tinnitus was too small to permit comparison. Blood flow ratio did not correlate with age ( $r=0.32$ ).

Figure 2 shows a representative LDF pattern observed in patients with no relief of tinnitus. No increased CBF was observed in this patient. Figure 3 shows summarized data in each group. There was no significant difference ( $p>0.6$ ) in mean CBFR between the complete relief group (mean:137.2%; Std.Dev.:33.6;  $n=12$ ) and the moderate relief group (mean:154.5%; Std.Dev.:55.4;  $n=6$ ). No significant difference was observed between patients who experienced slight relief (mean:111.1%; Std.Dev.:10.2;  $n=8$ ) and those who had no relief (mean:99.6%; Std.Dev.:7.1;  $n=20$ ). Mean CBFR differed significantly between patients who experienced no relief and other patients who experienced decreased tinnitus (complete, moderate;  $p<0.001$ ,  $p<0.0006$ , respectively). However, mean CBFR of the slight relief group did not differ significantly from that of the moderate group ( $p>0.08$ ). Mean CBFR of the complete relief group differed significantly from that of the slight relief group ( $p<0.05$ ). Figure 3 also shows the relationship of the value of mean CBFR between patients who felt comfortable after tinnitus treatment and those who did not feel comfortable. No patients felt comfortable when tinnitus was unchanged following treatment. However, not all patients reported

that they felt comfortable when tinnitus was relieved. In patients with slight tinnitus suppression, only the three patients with larger CBFR felt comfortable. The other five patients with smaller CBFR did not feel comfortable.

Obviously, CBFR values (mean:153.9%; Std.Dev.:38.8) in 14 patients who felt comfortable are larger ( $p=0.0001$ ) than those (mean:112.1%; Std.Dev.:7.9) in 32 patients who did not feel comfortable.





## DISCUSSION

Electrical stimulation is sometimes associated with an acoustic effect that is similar to the effect produced by a tinnitus-masking device.<sup>7</sup> In the present study, however, tinnitus was relieved without perception of sounds although higher frequency (up to 20 kHz) electrical stimulation evoked cochlear nerve activity even if lower frequency electrical stimulation caused stronger response of cochlear nerve activity.<sup>8</sup> In addition, there has been no report that tinnitus suppression produced increased parasympathetic nerve tone. Therefore, the mechanism of relief following electrical stimulation was not the same as that associated with a tinnitus-masking device. Our previous report<sup>9</sup> showed that response of auditory-evoked magnetic field response was augmented following ES in tinnitus patients with relief of tinnitus. We also showed<sup>10</sup> that word recognition was improved following ES in tinnitus patients with relief of tinnitus. These findings are related to Shulman's comment<sup>11</sup> that tinnitus may be masked secondary to the improvement of hearing. Therefore, these findings may suggest that tinnitus suppression by ES may be caused by a kind of central masking mechanism. However, no previous report about ES showed the relationships between tinnitus suppression and increased parasympathetic nerve tone.

In addition to tinnitus suppression, we reported that some patients with implanted electrical tinnitus suppressor fell asleep on a bed during stimulation,<sup>12</sup> suggesting that ES

using a 10 kHz sinusoidal wave induced sleep. Falling asleep may be the supreme relaxation, suggesting that our method for ES may be a kind of relaxation therapy in addition to masking by improvement of hearing loss which was shown by our preliminary report.<sup>9,10</sup> Our method of using the electrode through the hole on the ear drum was so stressful that some patients actually seemed to feel comfortable after the cessation of the stimulation. However, we did not let patients know the time of stimulation so that the expectancy of cessation of stimulation and pulling the electrode out could not make the parasympathetic nerve tone increased. The gradual increased cutaneous digital blood flow following the start of stimulation, as shown in Figure 1, suggested that ES actually acted on the parasympathetic nerve.

The functional significance of the autonomic nervous system in the inner ear has yet to be elucidated.<sup>13</sup> The fact that a stimulating frequency of 10 kHz was used in this study implies autonomic fibers were not involved, because optimal stimulation of these fibers occurs at much lower frequencies.<sup>14</sup> Electrical stimulation of the guinea pig cochlea has been demonstrated to increase cochlear blood flow.<sup>15</sup> In humans, electrical stimulation causes increased cochlear blood flow, as has been recorded in the promontory of patients.<sup>16</sup> A non-autonomic, neural pathway may be capable of mediating cochlear blood flow (e.g., the olivocochlear efferents). However, electrical stimulation did not affect cutaneous digital blood flow in guinea pig, suggesting that increased

CBF in this study is probably not caused by the same mechanism causing increased blood flow to the cochlea. Increased cholinergic nerve tone dilates the cutaneous vessels, suggesting that parasympathetic tone in tinnitus patients who experienced increased CBF may be augmented by ES.

We showed that tinnitus relief may be associated with increased CDBF. However, the discrepancy between subjective findings and LDF assessment in five patients, who reported complete tinnitus suppression and did not feel comfortable, was observed. The CBFR in these five patients was similar to that detected in patients who reported little or no relief, suggesting a placebo effect. The mean CBFR in the group that was only slightly suppressed did not differ significantly from the group with no relief. CBFR in only three out of eight patients with slight tinnitus suppression exceeded the value of 113.4% (mean + 2 Std.Dev.) of CBFR in patients without suppression. This suggests that tinnitus suppression was not sufficient to increase CBF in patients with slight response or, alternatively, placebo responses are most likely in this group.

Tinnitus suppression by ES is usually temporary. One of our goals for tinnitus suppression by ES is to extend the duration of residual inhibition. We found that there was a close correlation between effectiveness and increased parasympathetic nerve tone. Therefore, we should focus more on the relationship between the autonomic nervous system and tinnitus relief to understand the mechanism of the residual inhibition.

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