

# Enhancing Sensation in Diabetic Neuropathic Foot With Mechanical Noise

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**OBJECTIVE** — Localized low-level mechanical or electrical noise can significantly enhance tactile sensitivity in healthy young subjects and older adults. This phenomenon is termed stochastic resonance (SR). In this study, we examined the effect of SR on vibratory and tactile sensation in patients with moderate to severe diabetic peripheral neuropathy.

**RESEARCH DESIGN AND METHODS** — A total of 20 subjects were included in the study. The vibration perception threshold (VPT) test and the Semmes-Weinstein filament (SWF) threshold at the plantar surface of the left foot and the big toe were determined under two mechanical noise stimulus conditions: null (no noise) condition and at 10% lower than each subject's mechanical noise threshold of perception.

**RESULTS** — The baseline values (mean  $\pm$  SD) were as follows: Neuropathy Symptom Score (NSS)  $5.2 \pm 2.5$ , Neuropathy Disability Score (NDS)  $5.0 \pm 2.1$ , VPT  $24 \pm 11$  V, and SWF threshold  $5.6 \pm 0.8$  at the plantar surface of the foot and  $5.3 \pm 0.9$  at the big toe. The VPT improved significantly from  $24 \pm 11$  under null condition to  $19 \pm 10$  V with mechanical noise ( $P < 0.0001$ ). Mechanical noise also significantly increased the number of detections of the SWF at the plantar surface of the foot (detection rate  $66 \pm 11$  vs.  $59 \pm 15\%$ ,  $P < 0.02$ ) but not at the big toe ( $63 \pm 10$  vs.  $61 \pm 16\%$ ,  $P = \text{NS}$ ).

**CONCLUSIONS** — Mechanical noise stimulation improves vibration and tactile perception in diabetic patients with moderate to severe neuropathy. Additional studies are required to examine the effect of long-term noise stimulation on parameters of nerve function.

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**D** iabetic neuropathy is the most common neuropathy in western countries. This condition is estimated to occur in 20–50% of diabetic patients, depending on the patient population studied and the criteria used for diagnosis (1–5). When compounded by peripheral

vascular disease and impaired wound healing, the result is a classic cascade of skin and other medical problems in the affected areas (6). Seemingly innocuous circumstances such as ill-fitting shoes and minor skin lacerations progress into serious medical problems such as slow-

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**Abbreviations:** NDS, Neuropathy Disability Score; NSS, Neuropathy Symptom Score; SR, stochastic resonance; SWF, Semmes-Weinstein filament; VPT, vibration perception threshold.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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healing skin ulcers. Peripheral neuropathy can also lead to deformity of the foot and Charcot arthropathy (7,8). In severe cases, which are all too common, amputation of the affected extremity becomes necessary. In the U.S., >50,000 amputations are performed annually for these reasons (9). The cost to the U.S. health care system for diabetic foot problems exceeds \$3,000,000,000 annually.

Recently, a wide range of studies from computer models to human experiments have shown conclusively that low-level mechanical or electrical noise presented directly to sensory neurons can significantly enhance their ability to detect weak stimuli. This phenomenon of noise improving system performance is termed stochastic resonance (SR) and has been seen to occur in a variety of physical and biological systems. From a clinical perspective, one particularly important finding is that subsensory mechanical noise (very low amplitude deflections applied to the skin) can improve the ability of cutaneous sensory cells to detect mechanical stimuli such as pressure and vibration. Similarly, mechanical noise can also make sensory cells, which are responsible for joint angle and muscle force senses (proprioception), more sensitive.

Noise, whether audio or visual, is generally considered to interfere with perception. Static on a radio station and ancillary conversations in a crowded room tend to obscure or distract from the desired information. However, a wide range of studies in a variety of systems, including global climates, radiofrequency communication, and sensory neurons, have shown that the presence of certain kinds of noise can actually enhance information transmission. The low-level noise sensitizes the system so that small signals or stimuli, which in a no-noise environment would not be discernible, are now apparent. Human tactile and proprioceptive sensory networks are examples of such systems.

The role this phenomenon can play in biological systems has been well studied. SR-type effects have been demonstrated experimentally in a wide variety of neurophysiological and perceptual systems

(10–12), including crayfish mechanoreceptors (13), rat cutaneous afferents (14), and the feeding behavior of fish (15). Of greater importance to this study, however, are SR studies in humans. Studies by Collins et al. (16–20) have shown that SR significantly lowers the threshold of sensation of tactile and proprioceptive systems in healthy adults, elderly subjects with aged-related cutaneous impairment, and a small group of patients with sensory deficits. Interestingly, they have established that both electrical and mechanical modalities of noise increase sensitivity. Furthermore, several of these experiments (18,19,21) have shown that SR can also result in functional benefit in humans.

In the present study, we investigated the effect of SR in patients with moderate to severe diabetic peripheral neuropathy. Specifically, we hypothesized that fine touch and vibratory sensitivity in this group of patients can be improved by introducing a low level of mechanical noise.

## RESEARCH DESIGN AND METHODS

### Subjects

A total of 20 diabetic patients (10 with type 1 diabetes and 10 with type 2 diabetes) were included in the study. The inclusion criteria were established diagnosis of type 1 or type 2 diabetes, defined according to the recommendations of the American Diabetes Association Expert Committee, and presence of moderate to severe peripheral neuropathy. Subjects were excluded from the study if they had a history of seizures or fainting or if they had open lesions or poor skin condition on the feet.

The study protocol was approved by the Institutional Review Board of Beth Israel Deaconess Medical Center, and all participants gave written informed consent.

### Methods

**Clinical evaluation.** The medical history evaluation included age, sex, weight, height, BMI, history of alcohol consumption, smoking, type and duration of diabetes, and presence of other microvascular and macrovascular complications. The neuropathic symptoms were assessed using a modified Neuropathy Symptom Score (NSS) (22). More specifically, patients were asked whether they had the following

symptoms in the feet or legs: 1) muscular cramps; 2) numbness; 3) abnormally hot or cold sensation; 4) tingling or prickling sensation; 5) sharp, shooting pain; 6) burning pain; and 7) irritation caused by bedclothes. These symptoms were scored with 1 point if present, and 2 points were assigned for nocturnal exacerbation.  $NSS \geq 3$  was considered abnormal. The Neuropathy Disability Score (NDS) was obtained from physical examination, based on the examination of tendon reflexes and sensory modalities (5). The evaluation of clinical signs was quantified using the NDS, which represented the sum of the reflex and sensory scores. For determination of the reflex score, the knee and ankle reflexes for both legs were tested and scored with 0 points if normal, 1 point if the reflexes were elicited by reinforcement, and 2 points if the reflexes were absent. The sensory score was determined by testing the sensations of pain, light touch, vibration, and cold perception. Each modality was scored according to the anatomic location at which first feeling occurred, as follows: tip of the toe, 0 points; base of the toe, 1 point; midfoot, 2 points; ankle, 3 points; midleg, 4 points; knee, 5 points. The average of both feet was calculated and the sum of all four modalities represented the sensory score. The NDS was the sum of the sensory and motor score.  $NDS \geq 5$  indicated the existence of moderate to severe neuropathy.

The vibration perception threshold (VPT) was determined using a biothesiometer (Biomedical Instruments, Newbury, OH). The lowest voltage at which the patient could perceive the vibration stimulus on the pulp of the toe was recorded, and the mean of three readings for each foot was entered for final data analysis. The Semmes-Weinstein filament (SWF) threshold was also determined using a set of 20 SWFs (Touch Test; North Coast Medical, Morgan Hill, CA) to apply a force from 1 to 100 g. Each filament is individually calibrated so when applied against the skin to its bending point, it delivers a targeted force within a 5% SD. Each test was repeated three times for every SWF used. The lowest pressure the subject could feel consistently, at every application, was considered that subject's SWF threshold. The log of the perceived force was entered for data analysis, e.g., 5.07 was recorded when the patient could feel a filament applied with 10 g of pressure. The mean of these values is presented in RESULTS.

Subjects were eligible for the study if they had moderate to severe diabetic peripheral neuropathy, defined as VPT of 20–45 V, or were able to feel a 5.07 SWF (10 g of pressure) at the big toe and the plantar surface of the foot but were unable to feel any filament of smaller diameter.

**Protocol.** We used an apparatus that incorporated mechanical actuators called tactors (C-2; Engineering Acoustics, Winter Park, FL) into a pair of insoles to deliver mechanical stimulation to the specific areas of the foot, specifically the heel, ball, and big toe regions. The perforations in the insole allow access of the SWFs to the plantar surface of the foot.

The level of vibration was set independently for each subject in a threshold ranging experiment. The subjects were seated with their bare left foot resting on the vibrating insole, and the level of vibration was independently raised. The level of vibration on the insole device could be varied between 0 and 1,000 arbitrary units. The level at which the subject first feels the vibration was termed the threshold. Because the level of noise imparting the greatest benefit has been lower than the threshold, meaning it was not felt by the subject, the level of vibration for each experiment was then set 10% less than the threshold level for the duration of the experiment and was recorded.

The SWFs at the plantar surface of the left foot and the big toe and VPT tests were then repeated in two mechanical noise conditions; stimulation device in place but not active (null condition) and stimulation device in place and active. The sequence of noise presentations was randomized. All measurements were made 30–60 s after the stimulation device was switched on. We used the SWFs subjects were able to feel, but not consistently ( $>0$  but  $<100\%$  of the time SWFs were presented to the subjects). The detection rate (the percentage of the number of the correct detection over the total number of filament presentations) was calculated. To reduce bias, the investigator performing the sensory tests was also blinded to the stimulus condition. In addition, subjects were not aware of the mechanical noise condition because the stimulating device was set below the threshold level. Subjects served as their own controls because the mechanical stimulation has only acute benefit when applied in this manner.

**Table 1—Characteristics of the study population**

Total subjects (n)	20
Race	
White (n)	17
Black (n)	3
Age (years)	53 ± 9
Sex (male/female)	13/7
BMI (kg/m <sup>2</sup> )	28.8 ± 5.5
Type of diabetes (1/2) (n)	10/10
Duration of diabetes (years)	23.5 ± 13
NSS	5 ± 2
NDS	5 ± 2
VPT (V)	24 ± 11
SWF (big toe)	5.33 ± 0.86
SWF (plantar surface)	5.58 ± 0.82

Data are means ± SD unless otherwise indicated.

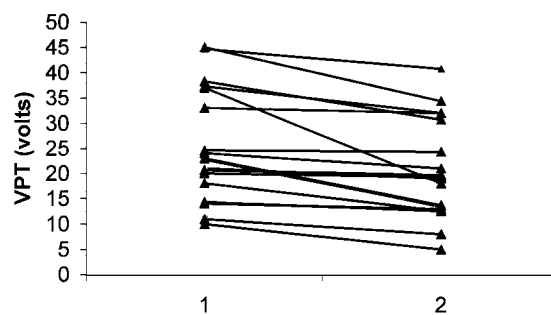
**Statistical analysis**

The Minitab statistical package (Minitab, State College, PA) for personal computers was used for the statistical analysis. To compare the sensory tests between the two mechanical noise conditions, we used a paired Student's *t* test. Data are presented as mean ± SD. The results are considered significant if *P* < 0.05.

**RESULTS**

The demographic characteristics of all subjects are summarized in Table 1. A total of 10 patients with type 1 diabetes and 10 patients with type 2 diabetes were included in the study. The mean duration of diabetes was 23.5 ± 13 years. The baseline values (mean ± SD) were as follows: NSS 5.2 ± 2.5, NDS 5.0 ± 2.1, VPT 24 ± 11 V, and SWF 5.6 ± 0.8 fiber size at the plantar surface of the foot and 5.3 ± 0.9 at the big toe. The VPT that was recorded using the noise device was 286 ± 251 (range 34–875). The mean subthreshold vibratory mechanical noise was 258 ± 225 (31–788).

The results of VPT and SWF with and without mechanical noise are shown in Figs. 1 and 2, respectively. All patients tested showed improvement in vibratory sensation with mechanical noise. When all patients were considered as one group, the VPT of the big toe improved from 24 ± 11 V under null conditions to 19 ± 10 V with mechanical noise (*P* < 0.0001). Improvement in the SWF detection rate at the plantar surface was noticed in 12 patients (60%). The SWF detection rate also improved at the plantar surface of the foot with mechanical noise when compared with the rate without stimulation (59 ±



**Figure 1—VPT in all subjects without (1) and with (2) mechanical noise stimulation.**

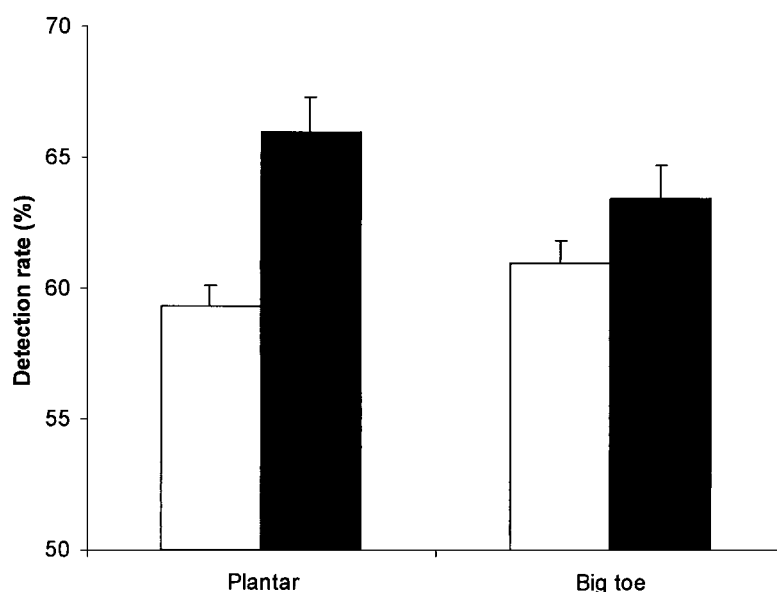
15 vs. 66 ± 11%, *P* < 0.02). On the contrary, we found no differences in SWF detection rates at the big toe between those two conditions (61 ± 16 vs. 63 ± 10%, *P* = NS).

**CONCLUSIONS**

In this study, we have shown that low levels of mechanical noise significantly improved vibratory and fine-touch sensitivity of the foot in patients with moderate to severe diabetic neuropathy. The improvement in vibratory sensation was consistent in all subjects tested, whereas the improvement of tactile sensation was seen in only 60% of the subjects. In addition, applying mechanical noise to the plantar surface of the foot seems to improve the fine-touch sensitivity only at the plantar surface of the foot but not at the big toe.

Previous studies have shown that reduced vibrotactile sensitivity in older adults, patients with stroke, and patients with diabetic neuropathy can be significantly

improved with mechanical noise. In one study (23), mechanical noise reduced the vibratory threshold at both the fingertip and the first metatarsal of the foot in all eight patients with diabetic neuropathy, and the mean detection thresholds were reduced by 34% at the fingertip and 31% at the foot. It is of interest that the improvement noticed in the present study was similar to that was seen in the elderly nondiabetic subjects in that previous study. In contrast, a smaller response was noticed in patients with stroke, suggesting that the noise-enhanced effect was at the peripheral level. Our result showed a slighter reduction in the threshold (20%), but it should be emphasized that in contrast to the previous study, we did not add mechanical noise directly to the site at which the VPT was evaluated. In the present study, the noise was applied to the plantar surface of the foot while the VPT was tested at the great toe. Finally, we observed an improvement in the func-



**Figure 2—SWF detection rate at the plantar surface of the foot and the big toe without (□) and with (■) mechanical noise stimulation.**

tion of the SWFs at the plantar surface of the foot, indicating that application of SR improves the function of nerve fibers that are not directly stimulated by the device used. This may be very important, because it indicates that stimulation of one type of nerve fiber can have beneficial effects on other fibers. The lack of definitive effect at the great toe using the SWFs might be a result of the physical separation between the vibration source and the testing location. When the separation was minimal, i.e., at the plantar surface, improved sensation was noted. To show an effect at the great toe, the apparatus design may need to be modified to allow more efficient vibration transmission to the toe region.

The pathways via which SR improves nerve function are not clearly understood, but various mechanisms have been proposed (18). First, the vibratory noise may add mechanical energy to the vibratory stimulus, thus enhancing the vibration transmission through the dermal tissue. In addition, the vibratory noise may stimulate nerve receptor endings directly by affecting the permeability of ion channels. A direct effect of SR on the muscle spindle receptor has also been proposed (16). Another possible mechanism that can explain the improvement of the small fibers may be related to the gate-control theory of pain that was proposed in 1965 by Melzack and Wall (24). According to this hypothesis, the impulse transmission from the body into the central nervous system is gated (changed) in the spinal cord. Gating is affected by the degree of activity in the large-diameter and the small-diameter nerve fibers. Impulses along the larger fibers tend to block pain transmission (close the gates), whereas activity in the smaller fibers tends to facilitate transmission (open the gates). Further studies will be required to fully explore the effect of SR on gating.

On a clinical level, confirmation that mechanical noise stimulation can improve nerve function may have important therapeutic implications. More specifically, more studies will be necessary to examine whether long-term noise stimulation can improve vibration and tactile perception or prevent its deterioration in diabetic patients. Mechanical stimulation

can be easily applied through using specifically designed insoles. Further studies will be required to examine whether such techniques can prevent the development of foot ulceration or reduce the risk of injuries related to gait instability and falling.

In conclusion, we showed that vibratory and fine-touch sensitivity in patients with diabetic neuropathy can be improved by application of mechanical noise. This technique may be helpful in improving nerve function, restoring tactile sensitivity, and reducing incidence of foot ulceration.

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