Noise-Enhanced Vibrotactile Sensitivity in Older Adults, Patients With Stroke, and Patients With Diabetic Neuropathy

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ABSTRACT. Liu W, Lipsitz LA, Montero-Odasso M, Bean J, Kerrigan DC, Collins JJ. Noise-enhanced vibrotactile sensitivity in older adults, patients with stroke, and patients with diabetic neuropathy. Arch Phys Med Rehabil 2002;83: 171-6.

Objective: To test the hypothesis that vibrotactile detection thresholds in older adults, patients with stroke, and patients with diabetic neuropathy can be significantly reduced with the introduction of mechanical noise.

Design: A randomized controlled study.

Setting: A university research laboratory.

Participants: Twelve healthy elderly subjects (age range, 67–85y), 5 patients with stroke (age range, 24–64y), and 8 patients with diabetic neuropathy (age range, 53–77y).

Interventions: Each subject's detection thresholds (ie, minimum level of stimulus to be detected) for a vibrotactile stimulus without and with mechanical noise (ie, random vibration with a small intensity) were determined by using a 4-, 2-, and 1-stepping algorithm. The stimuli were applied to the fingertip and/or to the first metatarsal of the foot.

Main Outcome Measure: Detection threshold for a vibrotactile stimulus.

Results: The detection threshold at the fingertip for the vibration stimulus with mechanical noise was significantly lower than that without mechanical noise for all 12 elderly subjects, for 4 of the 5 patients with stroke, and all 8 patients with diabetic neuropathy. For the 8 patients with diabetes, mechanical noise also significantly reduced the vibrotactile detection threshold at the foot.

Conclusions: Reduced vibrotactile sensitivity in older adults, patients with stroke, and patients with diabetic neuropathy can be significantly improved with input mechanical noise. Noise-based techniques and devices may prove useful in overcoming age- and disease-related losses in sensorimotor function.

Key Words: Cerebrovascular accident; Diabetic neuropathies; Elderly; Rehabilitation; Sensation.

CUTANEOUS SENSATION PLAYS an important role in human interaction with the environment and in defense against potentially harmful influences. Diminished cutaneous sensation, which occurs in older adults,[1-7] patients with upper motoneuron injury such as stroke,[8-11] and patients with peripheral neuropathy from diabetes,[12-18] may result in accidental injury, skin ulceration, infection, and joint dysfunction. Impaired sensation may also lead to impaired dexterity, sensorimotor dysfunction, and confusion. Accordingly, there is a need to develop techniques for improving sensory function.

Recently, it has been shown that noise can enhance the detection and transmission of weak signals in certain nonlinear systems, via a mechanism known as stochastic resonance.[19,20] The phenomenon of stochastic resonance, which is counterintuitive given that noise has traditionally been viewed as a detriment to signal detection and transmission, is based on the concept that the flow of information through a system can be maximized by the presence of a particular, nonzero level of noise.[19,20] Stochastic resonance–type effects have been shown experimentally in a variety of neurophysiologic[21-26] and perceptual[27-30] systems, including crayfish mechanoreceptors,[21] rat cutaneous afferents,[23,26] human muscle spindles,[24] and the human visual perception system.[29] Collins et al,[27,28] in a series of touch-sensation psychophysical studies, showed that the ability of healthy young subjects to detect subthreshold (weak) mechanical cutaneous stimuli could be significantly enhanced by introducing a particular level of mechanical or electrical[30] noise.

In this article, we extend this work to elderly subjects with age-related impairments in cutaneous sensation and to patients with sensory deficits caused by stroke or diabetes mellitus. Specifically, we tested the hypothesis that vibrotactile detection thresholds (ie, minimum level of vibration amplitude to be detected) in older adults, patients with stroke, and patients with diabetic neuropathy can be significantly reduced by adding mechanical noise (ie, random vibration with a small intensity) to the site of application of the test stimuli. The differences in the detection thresholds under the 2 conditions (without and with the mechanical noise) were tested for each subject and each group of subjects, respectively, by using paired Student *t* tests and the Wilcoxon signed-rank test.

METHODS

Twelve healthy elderly subjects (6 men, 6 women; age range, 67–85y; mean, 74y), 5 patients with stroke (3 men, 2 women; age range, 24–64y; mean, 44y), and 8 patients with diabetic neuropathy (4 men, 4 women; age range, 53–77y; mean, 67y) participated in the study. The diagnoses of stroke and diabetic neuropathy were both made clinically, not by electrodiagnostic testing. Informed consent was obtained from

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each subject before their participation. This study was approved by the Boston University Charles River Campus Institutional Review Board.

Healthy Elderly Subjects

The 12 healthy subjects were free of any neurologic disease or conditions potentially affecting cutaneous sensation, including diabetes, carpal tunnel syndrome, alcoholism, thyroid disease, and tobacco use. A careful medical history, review of all past and current medication use, and a detailed neurologic examination were performed. The neurologic examination included standard tests of muscle strength, deep tendon reflexes, vibration sensation, 2-point discrimination, sensitivity to fine touch, and proprioception, all of which were clinically within normal limits.

Patients With Stroke

Five subjects with unilateral stroke (4 left hemiparesis, 1 right hemiparesis) affecting sensation in the hand were included. A careful medical history, review of all past and current medication use, a detailed neurologic examination, and nerve conduction evaluation of the median nerve were performed. The neurologic examination included standard tests of muscle strength, deep tendon reflexes, vibration sensation, 2-point discrimination, sensitivity to fine touch by using monofilament testing, proprioception, and a Mini-Mental Status Examination[31] (MMSE). Exclusion criteria included a MMSE score less than 24 out of 30, severe aphasia, and history or signs of a neuropathic condition other than stroke. Any coexisting peripheral nerve pathology affecting the median nerve was ruled out through nerve conduction evaluation. The average time since stroke was 3.2 $\pm$ 2.1 years. Subjects generally had good cognitive function, with an average MMSE score of 27.4 $\pm$ 3.0. One patient had mild expressive aphasia. All 5 subjects had impaired 2-point discrimination ($>$15mm in 3 subjects; 5 and 15mm, respectively, in the other 2 subjects, in the middle digit of the affected hand) and impaired light touch (monofilament testing: average 4.8 $\pm$ 1.0 in the middle digit of the affected hand vs 3.0 $\pm$ 0.3 in the unaffected hand). All subjects had normal median sensory nerve conduction studies (velocity: 53.7 $\pm$ 7.6m/s; peak-to-peak amplitude: 43.8 $\pm$ 16.3μV).

Patients With Diabetic Neuropathy

The 8 patients with diabetes met the following inclusion and exclusion criteria. They were eligible for the study if they had a documented history of more than 1 year of type II diabetes mellitus requiring treatment with insulin or oral hypoglycemic medication and a history of sensory loss in the feet or hands. Exclusion criteria included active smoking, a history of alcoholism, peripheral vascular disease, upper motoneuron injury, parkinsonian syndrome, epilepsy, or a history of a neuropathic condition other than diabetes mellitus. Subjects on medications with the potential for altering sensation were also excluded. All subjects received a careful history and physical examination that included a detailed neurologic examination (ie, standard tests of mental status, cranial nerves, strength, sensation, coordination, and reflexes). Sensory testing of the digits was performed by using standardized monofilament testing.[32,33] All 8 subjects had a minimum sensory loss of diminished light touch (3.61 monofilament) in the digits of both hands.

Protocol

The healthy elderly were tested on the middle digit of their right hand, and stroke patients were tested on the middle digit of their affected hand. Diabetic patients were tested on the middle digit of their right hand and the first metatarsal head of their left foot.

During tests on the middle digit, each subject was seated in front of a computer screen that provided cues signaling a forthcoming presentation period and cues indicating the start and end of each presentation period (fig 1). The subject's forearm and hand were held in a fixed position by a passive restraint device and modeling clay, respectively. The 30-Hz vibration stimuli of 1.0-second duration (fig 2), without and with mechanical noise, were applied to the glabrous skin of the finger pad of the middle digit (fig 1, inset) by using a 2-mm flat cylindric probe on an arm that was actuated by a force-controlled direct-current (DC) motor.[a] Actuator forces were controlled by using a personal computer and a ComputerBoards CIO-DAS1600 board.[b] A constant indentation force offset of .036 newtons was applied throughout each trial to maintain contact between the fingertip and the probe.

The mechanical noise signals (fig 2), which were generated digitally on a personal computer, consisted of zero-mean Gaussian quasiwhite noise. These signals were low-pass filtered (cutoff frequency, 100Hz), transmitted through a biphasic stimulus isolator, and superimposed onto the vibration stimulus. Before data acquisition, the subject's detection threshold for the mechanical noise signal was determined by using the method of levels.[34] The noise intensity level applied during testing was set at 90% of this threshold; therefore, the applied mechanical noise signals were subthreshold and thus not detectable by the subjects.

Subjects were tested under 2 conditions, presented in random sequence, during each trial: a no-noise condition (the vibration stimulus only), and a noise condition (the vibration stimulus plus the mechanical noise signal). Each trial consisted of 50 presentations: 25 for the no-noise condition (20 vibration stimuli, 5 null stimuli) and 25 for the noise condition (20 vibration stimuli plus mechanical noise, 5 null stimuli plus mechanical noise; see fig 3). The subject and examiner were blinded to the presence or absence of a vibration stimulus during each trial. The subject's detection thresholds for the vibration stimulus with and without mechanical noise were

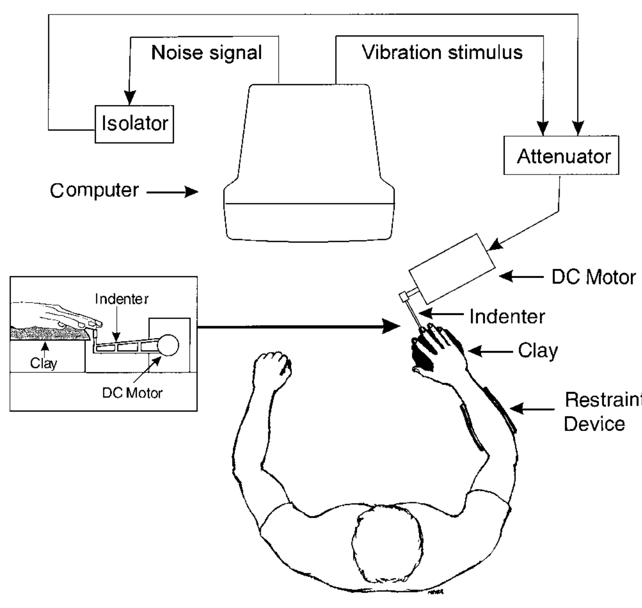

Fig 1. A schematic representation of the experimental set-up.

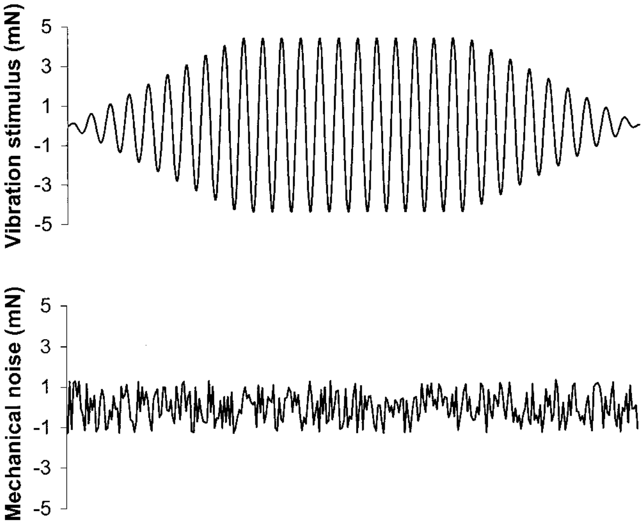

Fig 2. Representative samples of the 30-Hz vibration stimulus (upper trace) and the mechanical noise signal (lower trace).

determined by using a 4, 2, and 1 stepping algorithm.[35] Each trial lasted approximately 4 minutes. Nine trials were conducted with the healthy elderly subjects and the stroke patients. Rest periods of 2 minutes followed each trial; during the rest period, subjects were free to move their hand and fingers. Each testing session lasted approximately 60 minutes.

Five fingertip trials were conducted on each diabetic patient. In addition, 5 trials were conducted on their feet. During the foot tests, each subject was seated in front of the computer screen, with their feet placed on a wooden table. The same device used for the fingertip tests was used for the foot tests. The 2-mm flat cylindric probe protruded through a hole in the table to make contact with the skin of the left foot at the first metatarsal head. The probe was fixed on an arm that was driven by the force-controlled DC motor. The testing procedure was the same as that for the fingertip tests.

For each subject, a paired Student *t* test was used to compare the detection thresholds at the fingertip for the vibration stimulus with and without mechanical noise. For each patient with diabetes, a paired Student *t* test was also used to compare the detection thresholds at the foot for the vibration stimulus with and without mechanical noise. A representative detection threshold for each subject under each test condition was obtained by averaging the thresholds over the 9 trials for the fingertip (for the elderly subjects and stroke patients), or the 5 trials for the foot and fingertip, respectively, for the diabetic patients. A paired Student *t* test was used to compare the representative detection thresholds for the vibration stimulus with and without mechanical noise across the respective subject populations. It is difficult to verify normal distributions of measured sensory threshold within each subject and each group because of the limited number of trials for each subject, and the limited number of subjects for each group. A nonparametric test, the Wilcoxon signed-rank test, which does not depend heavily on the distribution assumptions, was therefore conducted for each analysis to confirm the results obtained by using the paired Student *t* test.

RESULTS

The detection threshold at the fingertip for the vibration stimulus with mechanical noise was lower than that for the vibration stimulus without mechanical noise in all 9 trials for all 12 elderly subjects. This effect for a representative elderly subject is shown in figure 4A. Results for a patient with stroke and a patient with diabetic neuropathy are shown in figures 4B and 4C, respectively. The noise-mediated decrease in the vibrotactile detection threshold measured in 9 trials was statistically significant ($P < .05$) for each of the elderly subjects (fig 5). The group mean of the representative detection thresholds reduced by 30%, from 4.4 ± 3.1mN to 3.1 ± 2.0mN, with the input noise. Moreover, the differences in the representative detection thresholds under the 2 conditions (with and without mechanical noise) for the elderly subjects were found to be statistically significant ($P < .01$), with a confidence interval (CI) of 0.5 to 2.0mN.

The vibrotactile detection threshold at the fingertip in 4 of the 5 stroke patients was significantly reduced ($P < .05$) by application of mechanical noise (fig 6). Moreover, the group mean of the representative detection thresholds was reduced by 16%, from 20.1 ± 12.5mN to 16.9 ± 12.1mN, with the input noise. The differences in the representative detection thresholds for the vibration stimulus with and without mechanical noise were statistically significant ($P < .01$), with a CI of 1.1 to 5.1mN.

For each of the 8 patients with diabetic neuropathy, mechanical noise significantly reduced ($P < .05$) the vibrotactile detection threshold at both the fingertip (fig 7A) and the foot (fig 7B). The group mean of the representative detection thresholds was reduced by 34% at the fingertip, from 3.2 ± 0.9mN to 2.1 ± 0.6mN, and by 31% at the foot, from 64.3 ± 25.8mN to 44.5 ± 22.1mN, with the input noise. The noise-mediated decreases in the representative detection thresholds were statistically significant ($P < .01$), with a CI of 0.7 to 1.4mN and 9.8 to 29.7mN for the fingertip and foot, respectively.

The magnitude of the noise-mediated reduction in a subject's detection threshold varied on a trial-by-trial basis (fig 4), but, in general, the stochastic resonance–type effect was not attenuated over the course of the trials (fig 8). Thus, there were no apparent learning or adaptation effects to the protocol, the repeated vibration stimuli, or the mechanical noise signals.

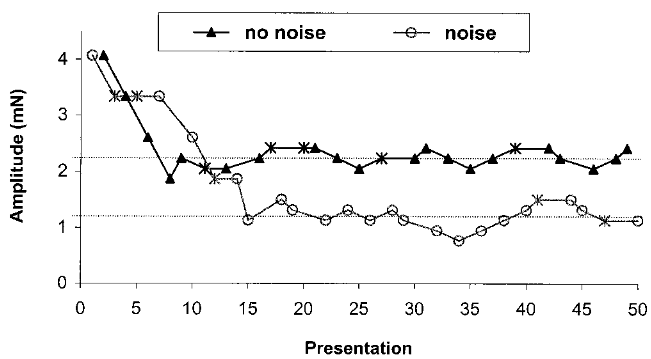

Fig 3. Representative results—vibration stimulus amplitude versus presentation number—from 1 trial for 1 elderly subject. Each trial consisted of 50 presentations at the fingertip: 25 for the no-noise condition, consisting of 20 vibration stimuli (solid triangles) and 5 null stimuli (*), and 25 for the noise condition, consisting of 20 vibration stimuli plus mechanical noise (open circles) and 5 null stimuli plus mechanical noise (*). The upper dashed line corresponds to the subject's determined detection threshold for the vibration stimulus without noise; the lower dashed line corresponds to the subject's determined detection threshold for the vibration stimulus with noise.

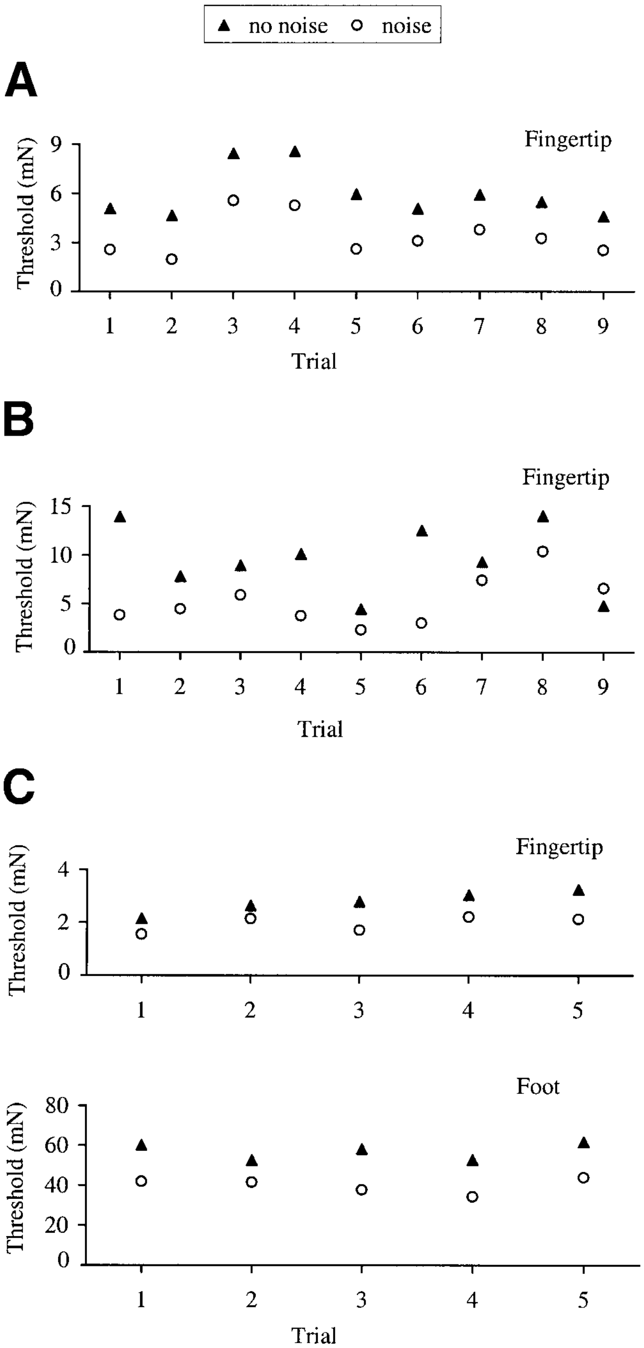

Fig 4. Detection thresholds for the vibration stimulus without and with mechanical noise for 3 representative subjects. Shown are results from (A) the 9 fingertip trials for an elderly subject, (B) the 9 fingertip trials for a patient with stroke, and (C) the 5 fingertip trials and 5 foot trials for a patient with diabetic neuropathy.

DISCUSSION

The results of the present study show that vibrotactile detection thresholds in older adults, patients with stroke, and patients with diabetic neuropathy can be significantly reduced by adding mechanical noise to the site of application of the vibratory stimuli. These novel findings suggest that age- and disease-related sensory loss may be reversible by exploiting

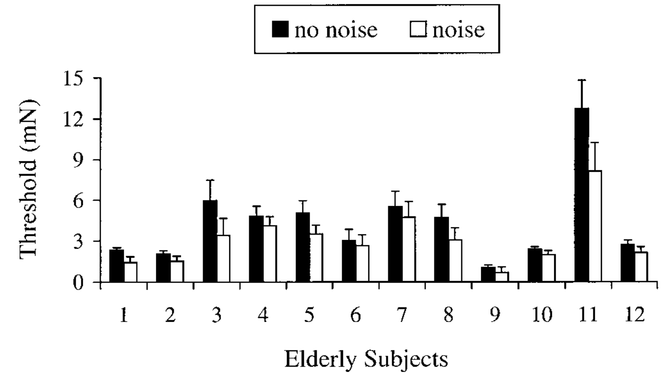

Fig 5. Means and standard deviations (SDs) of the detection thresholds at the fingertip for the vibration stimulus without and with mechanical noise over the 9 trials for each of the elderly subjects. Paired Student *t* tests showed that for each subject the detection threshold for the vibration stimulus with noise was significantly lower ($P < .05$) than that for the vibration stimulus without noise.

stochastic resonance–type effects. The experiment's design reduced the possibility of subject bias because subjects were unaware of the sequence of presentations and null stimuli were presented in a blinded fashion. This is supported by the fact that repeated trials showed similar results and there was no evidence of decay in the response.

Negative masking is a psychophysical phenomenon in which the detectability of a weak stimulus is enhanced by the presence of another signal. This phenomenon has been observed in vibrotactile sensation for cases wherein the test stimulus and the masker (or pedestal) are sinusoidal signals of the same frequency and phase.[36-38] In this study, we showed that noise, which is usually viewed as a detriment to signal detection, can be used as a suitable pedestal for enhancing detection of a subthreshold vibrotactile stimulus. This is important from a practical standpoint because noise can be used to enhance vibrotactile sensation without knowing a priori the characteristics of the external stimuli, which is in contrast with previous work with sinusoidal pedestals.

Many studies[1-7] have documented that vibrotactile sensitivity declines with age. Moreover, reduced cutaneous sensation

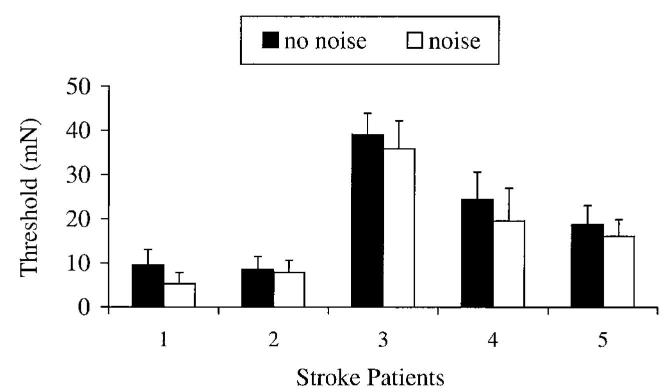

Fig 6. Means and SDs of the detection thresholds at the fingertip for the vibration stimulus without and with mechanical noise over the 9 trials for each of the patients with stroke. Paired Student *t* tests showed that for each patient (except patient 3) the detection threshold for the vibration stimulus with noise was significantly lower ($P < .05$) than that for the vibration stimulus without noise.

in the elderly is associated with diminished motor performance.[39-41] Reduction in density and sensitivity of dermal mechanoreceptors, rigidity and inelasticity of the surrounding dermal tissue, and peripheral nerve degeneration may all contribute to age-related decreases in cutaneous sensitivity.[42] However, as we have shown, the superposition of mechanical noise onto a weak cutaneous stimulus appears to enhance afferent sensory input, making the stimulus perceptible at a lower amplitude. It is not known whether the input noise overcomes structural changes in surrounding cutaneous tissues that may dampen signal transmission, or whether it has a direct effect on receptor sensitivity.

Impaired touch and discriminative and vibration sensation are common in patients with stroke, regardless of lesion location.[10,11] Sensory impairment is among the predictors for motor recovery of patients with stroke,[8,9] and sensory stimulation has been used in the neurofacilitation approach to improve movement of stroke patients.[43,44] A 1994 randomized study by Magnusson et al[45] found a significantly better functional recovery in terms of balance, mobility, and activities of daily living in stroke patients who received additional sensory stimulation when compared with control patients. Our study showed a significant improvement in vibrotactile sensory thresholds in stroke patients that was achieved with the application of subthreshold mechanical noise. The concept of noise-enhanced sensation may be further developed into techniques and devices to help stroke patients in both their rehabilitation and their functional activities.

Patients with diabetic neuropathy may also benefit from noise-enhanced technology. Impaired touch and vibrotactile sensation in patients with diabetes has been studied extensively with quantitative sensory testing.[12-18] Diminished sensitivity to touch, vibration, and pinprick was found to be worse at the foot than at the hand in diabetic patients.[13] We have shown here that significant noise-mediated sensory improvement in patients with diabetes was at the same level as that of healthy elderly people, and similar results were obtained at the fingertip and foot. The finding that the elderly subjects and patients with diabetic neuropathy had large improvements, compared with patients with stroke, suggests that the noise-enhanced effect is at the peripheral nerve level. Stroke patients, who presumably have central nervous system impairments in sensory integration, may not benefit to the same extent from boosting afferent sensory information with the application of noise. Nevertheless, the relatively small improvement they do achieve may have significant functional benefits.

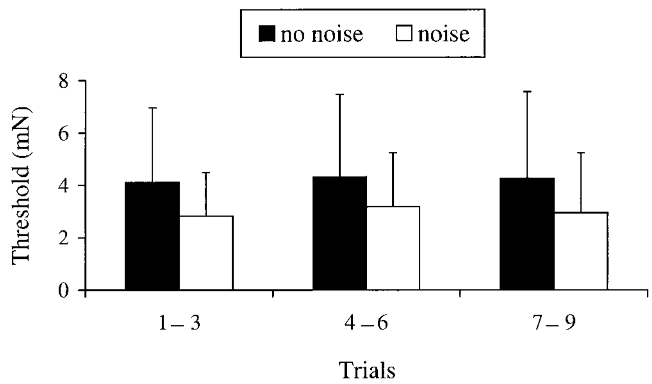

Fig 8. Group means and SDs of the elderly subjects' detection thresholds for the vibration stimulus without and with mechanical noise for trials 1 to 3, 4 to 6, and 7 to 9. Note that the results for the respective detection thresholds do not change considerably across the trials. Similar results were obtained for patients with stroke and patients with diabetic neuropathy.

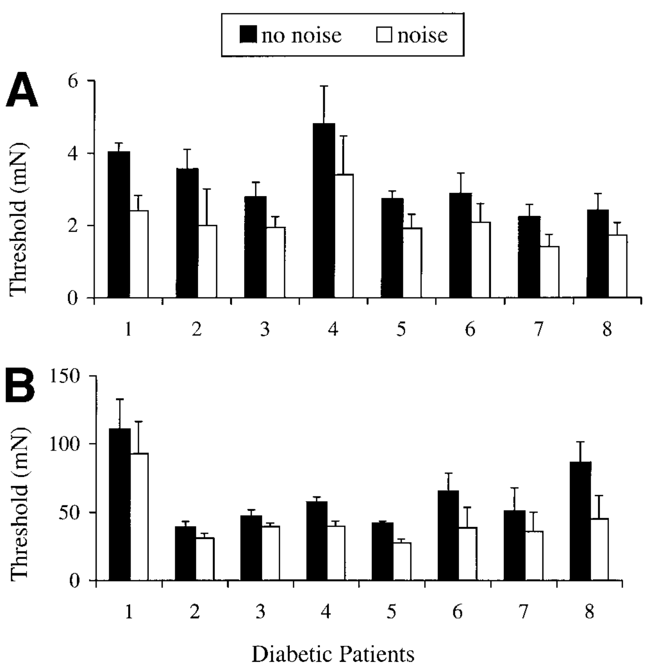

Fig 7. Means and SDs of the detection thresholds at (A) the fingertip and (B) the foot for the vibration stimulus without and with mechanical noise over the 5 trials for each of the patients with diabetic neuropathy. Paired Student *t* tests showed that for each patient the detection threshold for the vibration stimulus with noise was significantly lower ($P < .05$) than that for the vibration stimulus without noise.

CONCLUSION

This study showed that input noise can enhance sensory detection in healthy elderly people as well as in patients with central or peripheral nerve damage from stroke or diabetes. These findings are potentially important, insofar as impaired sensation leads not only to serious secondary medical complications, but also to impaired dexterity and coordination. Because sensation is an integral component of motor function, impaired sensation significantly hinders an individual's ability to perform everyday tasks and their ability to function independently. For instance, impaired lower-extremity proprioception significantly limits an individual's ability to walk safely and efficiently. In the future, noise-based techniques and devices may enable people to overcome functional difficulties resulting from age- or disease-related sensory loss. It may be possible, for example, to build a special shoe insert with a minishaker that can vibrate randomly or to develop wearable glove or stocking electrodes that continuously apply noise during specific activities or throughout the day. We hope our study will stimulate collaborations between clinicians and biomedical engineers to develop new methods to improve sensation and to reduce the morbidity associated with sensory loss in elderly and disabled people.

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Suppliers

a. 300B lever system; Cambridge Technology, 109 Smith Pl, Cambridge, MA 02138.

b. Measurement Computing Corp, 16 Commerce Blvd, Middleboro, MA 02346.