Noise-Enhanced Balance Control in Patients with Diabetes and Patients with Stroke

Attila A. Priplata, PhD,[1] Benjamin L. Patritti, PhD,[1] James B. Niemi, MS,[2] Richard Hughes, PT, NCS,[3] Denise C. Gravelle, MS,[1] Lewis A. Lipsitz, MD,[4–6] Aristidis Veves, MD,[7] Joel Stein, MD,[3] Paolo Bonato, PhD,[3,8] and James J. Collins, PhD[1]

Objective: Somatosensory function declines with diabetic neuropathy and often with stroke, resulting in diminished motor performance. Recently, it has been shown that input noise can enhance human sensorimotor function. The goal of this study was to investigate whether subsensory mechanical noise applied to the soles of the feet via vibrating insoles can be used to improve quiet-standing balance control in 15 patients with diabetic neuropathy and 15 patients with stroke. Sway data of 12 healthy elderly subjects from a previous study on vibrating insoles were added for comparison. **Methods:** Five traditional sway parameters and three sway parameters from random-walk analysis were computed for each trial (no noise or noise). **Results:** Application of noise resulted in a statistically significant reduction in each of the eight sway parameters in the subjects with diabetic neuropathy, the subjects with stroke, and the elderly subjects. We also found that higher levels of baseline postural sway in sensory-impaired individuals was correlated with greater improvements in balance control with input noise. **Interpretation:** This work indicates that noise-based devices could ameliorate diabetic and stroke impairments in balance control.

Ann Neurol 2006;59:4–12

The human balance control system relies on feedback from the somatosensory, vestibular, and visual systems. Diminished somatosensation is associated with increased postural instability during quiet standing with eyes closed, which is clinically referred to as sensory ataxia and is assessed via the Romberg test.[1] Somatosensory loss is a characteristic of patients with diabetic neuropathy and is also observed in approximately 50% of patients with stroke.[2] In patients with diabetic neuropathy, somatosensory deficits are associated with increased sensory thresholds of mechanoreceptors and changes in the characteristics of the afferent fibers.[3–6] In contrast, the sensory deficits of patients with stroke stem from an inability to interpret afferent traffic from the periphery.[7–9]

Postural sway during quiet standing is typically increased in patients with diabetic neuropathy compared with healthy control subjects,[10–13] and some work suggests that the loss of sensitivity in the soles of the feet in patients with diabetic neuropathy leads to postural instability.[13] Studies have also shown that patients with stroke exhibit greater postural sway than healthy control subjects,[14] and this increased sway has been associated with the inability to integrate peripheral somatosensory information.[7,8,15,16] Although the loss of balance control can be attributed to many factors including diminished vision, muscle weakness, vestibular disorders, bone integrity, spinal injury, and somatosensory deficits, the amelioration of any one of these factors (eg, somatosensory deficits) may have a significant impact on the improvement of balance.[17] Somatosensory stimulation may thus prove to be an effective way to improve balance control in these patients.

It has been shown that noise can enhance the detection and transmission of weak signals in sensory systems, via a mechanism known as stochastic resonance (SR).[18–20] The phenomenon of SR, which is counterintuitive given that noise has traditionally been viewed as a detriment to signal detection and system performance, 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. SR was

From the [1]Center for BioDynamics and Department of Biomedical Engineering, Boston University, Boston, MA; [2]Afferent Corporation, Providence, RI; [3]Department of Physical Medicine and Rehabilitation, Harvard Medical School, Spaulding Rehabilitation Hospital; [4]Hebrew Rehabilitation Center for Aged Research and Training Institute; [5]Beth Israel Deaconess Medical Center, Gerontology Division; [6]Harvard Medical School, Division of Aging; [7]Department of Surgery, Joslin-Beth Israel Deaconess Foot Center and Microcirculation Laboratory, Beth Israel Deaconess Medical Center, Boston; and [8]Harvard-Massachusetts Institute of Technology Division of Health Sciences and Technology, Cambridge, MA.

Received Jun 21, 2005, and in revised form Aug 12. Accepted for publication Aug 17, 2005.

Published online Nov 14, 2005 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/ana.20670

Address correspondence to Dr Collins, Department of Biomedical Engineering, Boston University, 44 Cummington St., Boston, MA 02215. E-mail: jcollins@bu.edu

originally proposed in the context of global climate modeling.[21,22] Since then, SR-type dynamics have been demonstrated in a variety of neurophysiological and perceptual systems,[23–48] including human muscle spindles[27] and cutaneous receptors.[24–26,28,31,36,38,44,48] We have shown previously that subsensory mechanical noise applied to the fingertip or foot, or both, can improve touch sensitivity of patients with diabetic neuropathy[36,38] and patients with stroke,[38] respectively. More recently, we have shown that subsensory mechanical noise applied to the soles of the feet via vibrating insoles can enhance balance control in healthy young and elderly individuals.[42]

In this study, we assessed the effects of noise input to the somatosensory system on posture control in patients with diabetic neuropathy and patients with stroke. We postulated that the postural sway of patients with diabetic neuropathy and patients with stroke during quiet standing could be significantly reduced by applying mechanical noise to the soles of the feet via vibrating insoles. We further examined whether sensory impairments in patients with diabetic neuropathy and patients with stroke lead to an increase in baseline postural sway. We also tested the hypothesis that higher levels of baseline postural sway in sensory-impaired individuals are correlated with greater improvements in balance control with input noise.

Subjects and Methods

Fifteen subjects with diabetic neuropathy (9 female and 6 male subjects; 3 with type 1 diabetes and 12 with type 2 diabetes; age range, 38–81 years; mean age, 60 ± 11 years [mean ± standard deviation]) and 15 subjects at least 10 months after experiencing unilateral stroke (10 female and 5 male subjects; 8 with left hemiparesis and 7 with right hemiparesis; age range, 31–90 years; mean age, 61 ± 17 years) were tested. The mean time after stroke was 5.5 ± 3.3 years. Sway data of 12 healthy elderly subjects (8 female and 4 male subjects; age range, 68–78 years; mean age, 73 ± 3 years) from a previous study on vibrating insoles[42] were added for comparison. This study was approved by the Institutional Review Boards of Boston University, Spaulding Rehabilitation Hospital, and Beth Israel Deaconess Medical Center, and informed consent was obtained from each subject before their participation.

Subjects with diabetes (types 1 or 2) participated in a clinical evaluation for the presence of moderate peripheral neuropathy using a vibration perception threshold (VPT) test. The VPT was tested using a biothesiometer. A VPT score in the range of 20 to 40V identified subjects with diabetes with moderate peripheral neuropathy, defined according to the American Diabetes Association Expert Committee. The level of 20 to 40V was chosen in an effort to exclude patients with severe neuropathy who would have functional loss of peripheral nerve function. Previous studies have shown that patients with similar VPT scores have mild histopathological changes in sural nerve biopsies and moderately reduced nerve conduction velocities.[49] Furthermore, we chose the VPT score as our main selection criterion because it tests the function of large $\alpha\beta$ fibers, the same fibers that are involved in sensory ataxia.[50] The mean VPT score for subjects with diabetes was 28 ± 13V on the left foot and 27 ± 5V on the right foot. Subjects with diabetes were excluded if they had foot ulcerations, custom orthotics, stroke, a history of a neuropathic condition other than diabetes mellitus, or a positive Romberg test, as indicated by an inability to maintain standing with eyes closed for 30 seconds.

Subjects with stroke were interviewed to exclude those with a history of diabetes or peripheral neuropathy, unexplained falls, and the use of medications known to impair balance. All subjects reported ambulating independently in their home environments. Those who demonstrated severe aphasia or hemispatial neglect, or a history or signs of neurological pathology other than stroke were also excluded. All subjects scored at least 23 of 30 on the Mini-Mental Status Examination. Clinical tests of sensation and balance were administered to the subjects in the stroke group. Subjects were excluded for a positive Romberg test, as indicated by an inability to maintain standing with eyes closed for 30 seconds. All subjects demonstrated plantar touch-pressure sensitivity to Semmes–Weinstein monofilaments of at least 5.07. The mean monofilament score was 3.95 ± 0.62. Proprioceptive sensitivity of the great toes and ankles, respectively, was assessed by asking subjects to repeatedly discriminate "up or down" segment positions; the same joints were tested for vibration sensitivity with a 256Hz tuning fork. Five presentations were given for each clinical test and a score between 0 and 5 was then awarded for their ability to detect the stimulus. The mean proprioceptive score for subjects with stroke at both the great toe and ankle was 4.75 ± 0.50. The mean score for the vibration test with a tuning fork at both the great toe and ankle was 4.87 ± 0.57. In addition, all subjects were able to detect the highest amplitude of vibration produced by the experimental vibrating insoles.

Two insoles[42] were molded with a viscoelastic silicone gel. Three vibrating elements, called "tactors" (C-2; Engineering Acoustics, Winter Park, FL), were embedded in each insole (two under the forefoot and one under the heel) to propagate vibrations to the plantar foot surface. Each insole received the same noise signal, the amplitude of which was set independently using potentiometers for each foot, from a small portable control box. The noise generator consisted of a single-chip record/playback device, in which a digitized white noise signal, low-pass filtered to 100Hz and distributed uniformly in amplitude, was stored.

During the experiments, subjects were asked to stand quietly on the insoles (position fixed with heels separated by approximately 8 cm, feet abducted by 40 degrees) with their hands at their sides (Fig 1). The subjects were also asked to close their eyes to remove visual cues; this enabled us to focus on the effects of somatosensation on balance control. Also, tests with eyes closed are known to be more "provocative" than tests performed with eyes open. This observation is clear when performing a Romberg test: the eyes-closed condition typically leads to larger sway than the eyes-open tests. A potentially stronger effect size of the subsensory stimulation is thus expected for eyes-closed tests compared with eyes-open tests, which could be particularly important for a small sample size such as that used in this study.

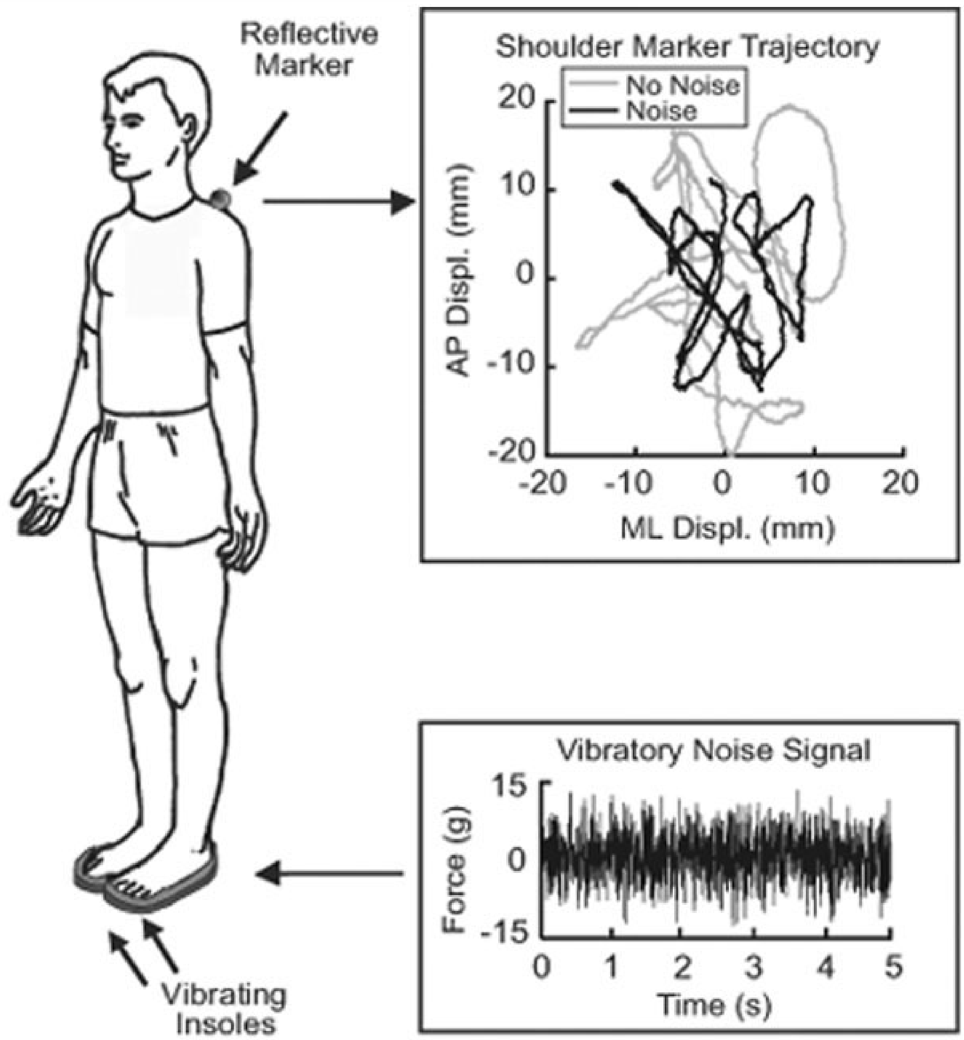

Fig 1. The experimental setup with sample input noise and sample shoulder-marker stabilograms comparing the control and noise conditions. AP = anteroposterior; ML = mediolateral.

At the beginning of the testing session, investigators used separate potentiometers on a control box to adjust the amplitude of the noise applied by the insoles to the soles of the feet until the stimulation could just be felt by the subject. The stimulation level for the experiments was then set to 90% of this sensory threshold level for each foot. Thus, the noise signals were subsensory, and subjects were blinded to the stimulus condition, that is, no noise (control) or noise.

A reflective marker was attached to the right shoulder of each subject to assess postural sway. A camera-based motion analysis system (Vicon 512; Oxford Metrics, Oxford, United Kingdom) was used to record the displacement of this marker during each 30-second stance trial. This system and associated protocol described earlier are well suited for quantifying the small fluctuations observed during quiet standing and can be viewed as an electronic version of the Romberg test. In a previous study in our laboratory,[51] we found that displacement data obtained from markers attached to various single points on the body (including the shoulder) were highly correlated with foot center-of-pressure displacement data (eg, the average cross-correlation coefficient between shoulder and center-of-pressure data was 0.91) and accurately quantify quiet-standing postural sway. Ten trials were performed on each subject: five with mechanical noise and five without noise. The presentation sequence, noise or control, was pairwise randomized. All subjects took a 2-minute seated break midway through the experiment.

A plot of the anteroposterior (AP) and mediolateral (ML) shoulder displacement, called a stabilogram, was analyzed for each trial. To characterize balance during quiet standing, we used both traditional stabilogram analyses and random-walk analyses. Five traditional sway parameters were computed: the mean stabilogram radius (measured in millimeters), the area swept by the stabilogram over time (mm^2), the maximum radius of sway (mm), and the range of the AP and ML excursions (mm), respectively.[42,43] We hypothesized that with the application of mechanical noise to the feet, there would be a reduction in postural sway, as indicated by decreases in these traditional measures.

We also considered three random-walk sway parameters[52,53]: the critical mean square displacement $\langle \Delta r^2 \rangle_c$ (measured in square millimeters), the effective long-term diffusion coefficient D_{rl} (mm^2/sec), and the long-term scaling exponent H_{rl}. In earlier studies on healthy young and elderly subjects,[52,53] we found that over short-term intervals during undisturbed stance, the body sways as a positively correlated random walk, that is, it tends to move or drift away from a relative equilibrium point; conversely, over long-term time intervals, it resembles a negatively correlated random walk, that is, it tends to return to a relative equilibrium point. We interpreted this finding as an indication that during quiet standing the postural control system uses open-loop and closed-loop control schemes over short-term and long-term intervals, respectively. An open-loop control system is one that operates without sensory feedback, and in the case of the human postural control system, it may correspond to descending commands that set the steady-state activity levels of the postural muscles. A closed-loop control system, in contrast, operates with sensory feedback, and in the case of the human postural control system, it corresponds to the visual, vestibular, and somatosensory systems.[52,53] Within this modeling framework, the critical mean square displacement $\langle \Delta r^2 \rangle_c$ characterizes the threshold at which feedback mechanisms are called into play by the postural control system, whereas D_{rl} and H_{rl} characterize the stochastic activity and antidrift-like dynamics, respectively, of these feedback mechanisms.[52,53] Notably, a reduction in $\langle \Delta r^2 \rangle_c$ indicates a tendency to switch from open-loop postural control strategies to closed-loop postural control strategies at smaller excursions. A reduction in D_{rl} indicates a decreased tendency for random walking around a relative equilibrium point. Also, a reduction in H_{rl} indicates an increased tendency to return to a relative equilibrium point after a perturbation, and thus corresponds to a more stable control system. In this study, we hypothesized that the addition of mechanical noise to the feet would lead to a reduction in the feedback threshold (as indicated by a decrease in $\langle \Delta r^2 \rangle_c$) and a more tightly regulated control system (as indicated by decreases in D_{rl} and H_{rl}).

Mean radius, maximum radius, range AP, and range ML for each subject were normalized by dividing by the height ($\times 10^{-3}$) of the reflective marker for each subject. Swept area, $\langle \Delta r^2 \rangle_c$, and D_{rl} were normalized by dividing by the height squared ($\times 10^{-6}$) of the reflective marker.

For each parameter, we calculated the mean value for the control and noise trials, respectively, for each subject. Mean values of the sway parameters from published data on 12 healthy elderly subjects using the vibrating insoles were added for comparison.[42] Two-way repeated-measures analysis of variance (ANOVA) was used to assess the main effects of stimulation (control vs noise) and subject group (subjects with diabetic neuropathy vs subjects with stroke vs elderly subjects) on postural sway and whether interactions were present between stimulation and subject group ($p \leq 0.05$). Interactions were also explored using an approach originally proposed by Zellner[54] and further developed by Clogg and colleagues[55]; this approach is commonly referred to as "estimation of seemingly unrelated regression models." It allows one to consider together subsets of parameters, thus gaining power over traditional ANOVA tests performed on individual variables.

Finally, to determine the factors across the three populations that contribute to the amount of sway during the control condition (ie, baseline, no noise) and the amount of reduction in sway from baseline when noise is applied, we developed two linear regression models. The first model was designed to determine whether age, height, and/or sensory threshold of each subject had an effect on the amount of the baseline sway, as described by each sway parameter. We hypothesized that increases in these independent variables would lead to an increase in the dependent variable, baseline sway, as indicated by positive coefficient estimates for each sway parameter ($p \leq 0.05$). The second model was designed to determine whether age, height, sensory threshold, and/or baseline sway of each subject had an effect on the difference measure for each sway parameter (difference measure = mean value of control condition − mean value of noise condition). We hypothesized that increases in these independent variables would lead to an increase in the dependent variable (the difference measure of the sway parameter), as indicated by positive coefficient estimates for each sway parameter ($p \leq 0.05$).

Results

Figure 2 shows that *all* of the sway parameters among the subjects with diabetic neuropathy, subjects with stroke, and healthy elderly subjects decreased with the application of noise. Notably, reductions in the sway parameters range from 2.9% in $\langle \Delta r^2 \rangle_c$ to 53.8% in D_{rl}.

The main effects of stimulation and subject group were assessed via two-way repeated-measures ANOVA tests, as described earlier. Table 1 presents the statistical results for the main effect of stimulation and subject group on traditional and random-walk sway parameters. Table 1 shows that the decreases observed when comparing control versus noise conditions were statistically significant in *all* of the sway parameters. There was no statistically significant difference for the main effect of subject group, that is, among individuals with diabetic neuropathy, subjects with stroke, and healthy elderly subjects.

Table 1 also shows the results of the tests to assess significant interactions between stimulation condition and subject group. Results of the ANOVA show that no significant interactions were found between stimulation and subject group in any of the sway parameters. This observation suggests that there were no differential effects of mechanical noise in the subjects with diabetic neuropathy, subjects with stroke, and healthy elderly subjects.

Additional analyses were performed to assess potential interactions between stimulation and subject group for the set of traditional sway parameters versus the set of random-walk sway parameters. The analyses via estimation of seemingly unrelated regression models did not show any significant interactions ($p = 0.942$) for

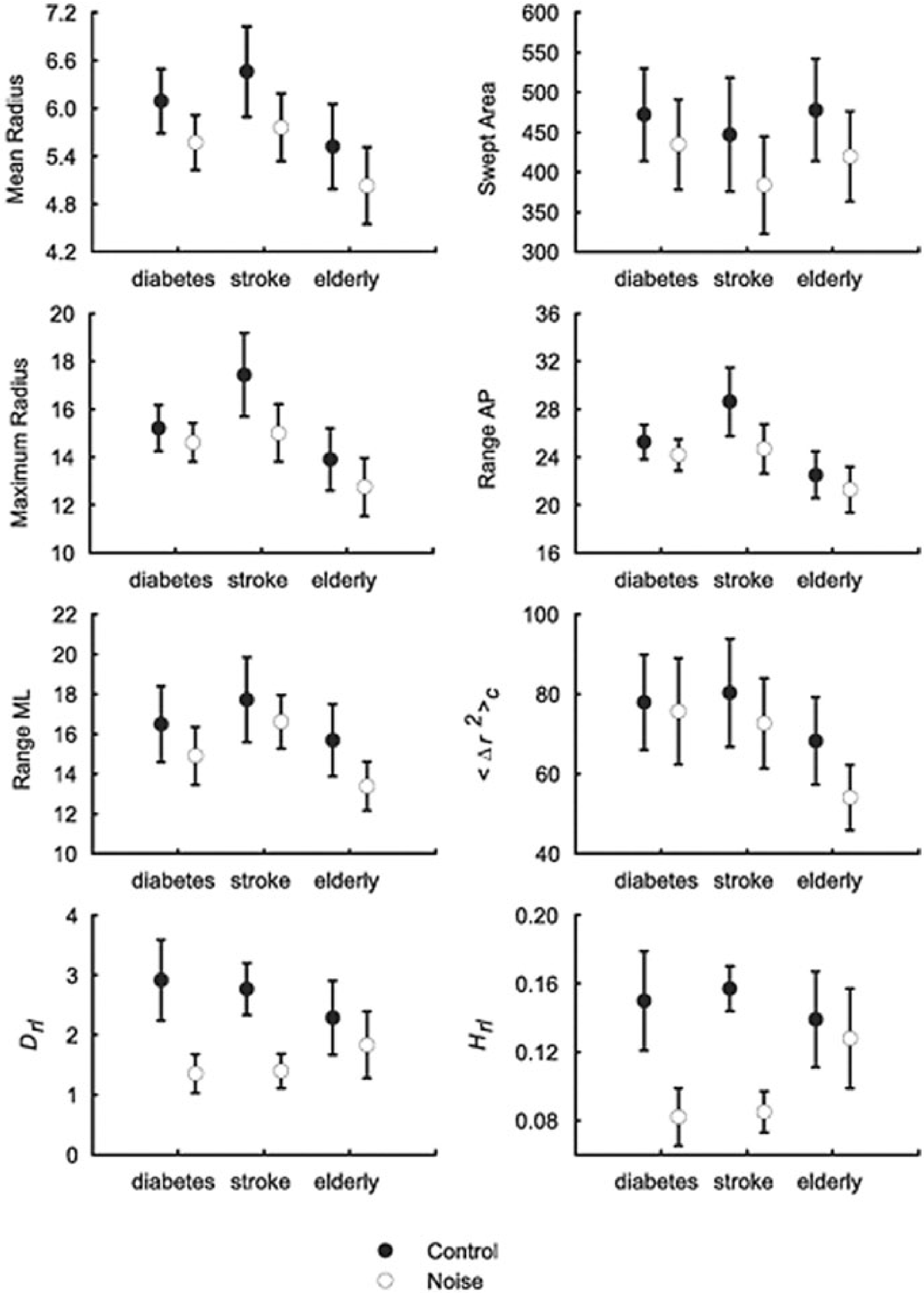

Fig 2. Dimensionless values of the traditional and random-walk sway parameters for the control and noise trials for 15 subjects with diabetic neuropathy, 15 subjects with stroke, and 12 elderly subjects. The group mean and standard error for the control and noise trials, respectively, are shown. $\langle \Delta r^2 \rangle_c$ *= critical mean square displacement; AP = anteroposterior;* D_{rl} *= long-term diffusion coefficient;* H_{rl} *= long-term scaling exponent; ML = mediolateral.*

Table 1. p *Values from a Two-Way Repeated-Measures Analysis of Variance for the Main Effects of Stimulation (Control vs Noise) and Subject Group (Subjects with Diabetic Neuropathy vs Subjects with Stroke vs Healthy Elderly Subjects) and the Interaction between Stimulation and Subject Group*

Parameters	Subject Group (p)	Stimulation (p)	Interaction (p)
Mean radius	0.439	<0.001[a]	0.705
Swept area	0.886	<0.001[a]	0.707
Max radius	0.260	0.001[a]	0.152
Range AP	0.247	0.002[a]	0.127
Range ML	0.535	0.005[a]	0.691
$\langle \Delta r^2 \rangle_c$	0.591	0.005[a]	0.232
D_{rl} (s^{-1})	0.992	<0.001[a]	0.249
H_{rl}	0.784	0.001[a]	0.203

[a] $p < 0.05$ is statistically significant.

AP = anteroposterior; ML = mediolateral; $\langle \Delta r^2 \rangle_c$ = critical mean square displacement; D_{rl} = long-term diffusion coefficient; H_{rl} = long-term scaling exponent.

the five traditional stabilogram parameters (ie, the mean stabilogram radius, the area swept by the stabilogram over time, the maximum radius of sway, and the range of the AP and ML excursions). In addition, no significant interactions ($p = 0.229$) were found for the set of the three random-walk parameters (ie, critical mean square displacement, long-term diffusion coefficient, and long-term scaling exponent). However, a significant interaction ($p < 0.001$) was found when considering the overall effect of all the parameters including the five traditional sway parameters and the three random-walk sway parameters. The differences observed between the ANOVA tests and the analyses via estimation of seemingly unrelated regression models for interactions between stimulation and subject group are most likely due to the limited sample size and the higher power of the analyses via estimation of seemingly unrelated regression models. Overall, these results suggest differences in the response observed for stimulation conditions (control vs noise) across the subject groups, but marked by limited effect size.

Differences were observed in sensory thresholds (identified using the input noise signal) across the three groups considered in the study. The mean sensory threshold of subjects with diabetic neuropathy (16.2 ± 9.9gm) and subjects with stroke (15.4 ± 10.2gm) was significantly greater ($p = 0.030$) than that of the elderly subjects (8.73 ± 3.16gm). These results are consistent with the somatosensory impairment observed in the subjects with diabetic neuropathy via clinical examination and suggest that similar levels of sensory impairment may have been present in the subjects with stroke.

The regression model designed to determine whether age, height, and/or sensory threshold of each subject had an effect on the amount of the baseline sway demonstrated no relations among age, height, and sensory threshold versus the mean baseline value of all the sway parameters except the critical mean square displacement $\langle \Delta r^2 \rangle_c$. The coefficient estimate for sensory threshold versus the mean baseline value of $\langle \Delta r^2 \rangle_c$ was statistically significant (1.9 ± 0.8; $p = 0.029$). The critical mean square displacement $\langle \Delta r^2 \rangle_c$ did not show any statistically significant relations with age or height.

In the second regression model, all coefficient estimates for the mean baseline value of each sway parameter versus the difference measure of each sway parameter, respectively, were statistically significant (Table 2). Note, six of the eight parameters are significant at p less than 0.001. Coefficient estimates for age, height, and sensory threshold for each subject versus the difference measure for each sway parameter, respectively, were not statistically significant; therefore, these independent variables were removed from the model.

Discussion

This study shows that subsensory mechanical noise applied via vibrating insoles to the feet of subjects with diabetic neuropathy and subjects with stroke leads to reduced postural sway. These results are consistent with our earlier findings in healthy young and elderly subjects.[42] This work also shows that noise-based devices can provide benefit to patients with sensorimotor deficits that are of a peripheral origin (diabetic neuropathy), as well as patients with deficits that are of a central origin (stroke).

One possible explanation for our findings is that subsensory noise can enhance the detection of pressure changes on the soles of the feet, leading to improved balance control. A possible neuronal mechanism underlying such an effect involves mechanical noise producing small changes in strain on the receptor membrane that translate to small fluctuations in receptor transmembrane potentials through changes in ion permeability. As the membrane partially depolarizes, the po-

Table 2. Coefficient Estimates ± Standard Errors of the Traditional and Random-Walk Sway Parameters from the Linear Regression Model of Baseline Postural Sway versus the Difference Measure for Each Sway Parameter

Parameters	Coefficient Estimates	p
Mean radius	0.2 ± 0.1	<0.001
Swept area	0.2 ± 0.1	0.004
Max radius	0.3 ± 0.1	<0.001
Range AP	0.3 ± 0.1	<0.001
Range ML	0.4 ± 0.1	<0.001
$\langle \Delta r^2 \rangle_c$	0.1 ± 0.1	0.034
D_{rl} (s^{-1})	0.6 ± 0.1	<0.001
H_{rl}	0.4 ± 0.1	<0.001

AP = anteroposterior; ML = mediolateral; $\langle \Delta r^2 \rangle_c$ = critical mean square displacement; D_{rl} = long-term diffusion coefficient; H_{rl} = long-term scaling exponent.

tential of the neuron is brought closer to the threshold for firing an action potential in the presence of a weak signal. It effectively becomes predisposed to fire or sensitized to additional mechanical stimulation or input. Therefore, a mechanism is provided by which normally subthreshold mechanical stimuli (eg, slight pressure changes on the soles of the feet) become detectable in the presence of mechanical noise. Along these lines, it is interesting that *in vitro* studies[24,31,56] have shown that the sensitivity of cutaneous afferents to weak stimuli can be enhanced by the introduction of mechanical noise.

Alternate explanations are also plausible and deserve further study. For example, it is possible that the reported effects are of a central origin. Studies have shown that noisy stimulation of peripheral receptors can lead to stochastic-resonance–type effects in the central nervous system.[34,39] Identifying and studying patients with precisely localized lesions in the nervous system who do not benefit from the vibrating insoles could help to identify the mechanisms and sites of action of the noise-mediated improvements in balance control. This study justifies such further work with more detailed screening procedures.

Previous studies have linked sensory impairment in the soles of the feet to an increase in baseline postural sway and poor balance control.[57–60] We demonstrate that reduction of postural sway during the application of noise to the soles of the feet is greater in individuals with larger baseline postural sway. As a result, it may be possible to predict the magnitude of the stimulation effect by measuring the baseline performance of the individual. We also found that the sensory threshold of the feet is significantly correlated with the critical mean square displacement $\langle \Delta r^2 \rangle_c$. This provides support for our open-loop/closed-loop posture control model,[52,53] and also suggests that sensory impairments of the feet may lead to increased feedback thresholds in the balance control system.

There are limitations that exist in the design of this pilot study. For example, results for the amount of reduction of postural sway during the application of noise to the soles of the feet in quiet-standing individuals may not indicate that vibrating insoles will have a clinical impact on everyday balance activities (eg, walking and ascending/descending stairs). Moreover, because this study focused on eyes-closed conditions, work is needed to explore whether the vibrating insoles are effective in improving balance control under eyes-open conditions. In addition, the small number of subjects tested may limit the observation of differences in performance of vibrating insoles among the patients with diabetic neuropathy, patients with stroke, and the comparison group of older adults, as we discuss in more detail later.

The analyses presented in this article identified statistically significant differences in balance parameters observed in the control versus noise conditions. No statistically significant differences were observed via two-way repeated-measures ANOVA for the three groups for which balance data were considered in the study. Also, no significant interactions were found; that is, when individual balance parameters were analyzed, the response across the considered subject groups was assessed to be identical. To explore whether this result was caused by the limited power of the analysis likely due to the small sample size, we performed additional analyses via estimation of seemingly unrelated regression models. We obtained results indicating a statistically significant interaction, that is, differences across the three groups, when considering all of the balance parameters. We hypothesize that this result is an indication that differences exist in the responses to subsensory stimulation of the soles of the feet in elderly individuals, patients with stroke, and patients with diabetic neuropathy. Further work involving a larger sample of subjects is needed to test this hypothesis.

There is also a need for more extensive clinical assessment and classification of patients to determine the extent to which different patient populations can benefit from this technology. For example, stroke patients have a variety of characteristic lesions that could alter the effects of input noise in this population. It would be interesting, for example, to study whether input noise has differential effects on balance control in patients with right versus left hemisphere lesions due to reported differences in balance control between these two groups.[14,61] In addition, because the parietoinsular vestibular cortex has been hypothesized to be involved in the processing and integration of sensory information for balance control,[62] it would be interesting to study the effect of input noise on patients with stroke lesions in this area. Moreover, patients with cerebellar strokes would be interesting to study because the cerebellum is implicated in the control of movement and recently has been suggested to be involved in the planning of movements.[63] Future studies considering lesions affecting pathways involved in sensory gating mechanisms may also be worthwhile. For instance, evidence indicates that thalamic stroke disrupts sensory gating, which affects cortical sensory input, leading to potential effects on balance control.[64]

This study constitutes the first steps toward assessing the clinical significance of using vibrating insoles to improve balance control in patients with sensory deficits. It will be interesting to examine whether such devices are applicable to other patient populations, such as patients with multiple sclerosis[65] or Parkinson's disease,[66] that exhibit disease-related sensory loss. Future studies are also needed to determine whether noise-based devices,[67] such as randomly vibrating shoe insoles, are effective in enhancing performance of dynamic balance activities (eg, walking) and reducing incidence of falls. The former could benefit from field-based monitoring involving wearable technologies,[68,69] whereas the latter will require extensive prospective studies. The current insoles were not designed for in-shoe use (subjects simply stood on them; see Fig 1), and thus we were limited in the types of studies that could be conducted. We have now designed and constructed insoles for in-shoe use and are currently planning to use these in studies investigating locomotion and other activities.

This work was supported by the NIH (National Institute of Child Health and Human Development, HD37880, J.J.C.; National Institute of Aging, AG08812, L.A.L., National Institute of Diabetes and Digestive and Kidney Diseases, DK60295, J.B.N.; National Institute on Disability and Rehabilitation, H133P990003, J.J.C.) and the Irving and Edyth S. Usen and Family Chair in Geriatric Medicine (L.A.L.).

We thank L. Khaodhiar, C. Lima, J. Lelas, D. Sherrill, and S. Midwood for their guidance and assistance in the recruitment of patients. We also thank R. Goldstein for his help in the design of the statistical analyses.

References

1. Lanska DJ, Goetz CG. Romberg's sign: development, adoption, and adaptation in the 19th century. Neurology 2000;55:1201–1206.
2. Carey LM, Matyas TA, Oke LE. Sensory loss in stroke patients: effective training of tactile and proprioceptive discrimination. Arch Phys Med Rehabil 1993;74:602–611.
3. Nardone A, Schieppati M. Group II spindle fibers and afferent control of stance. Clues from diabetic neuropathy. Clin Neurophysiol 2004;115:779–789.
4. Simoneau GG, Derr JA, Ulbrecht JS, et al. Diabetic sensory neuropathy effect on ankle joint movement perception. Arch Phys Med Rehabil 1996;77:453–460.
5. van Deursen RWM, Sanchez MM, Ulbrecht JS, Cavanagh PR. The role of muscle spindles in ankle movement perception in human subject with diabetic neuropathy. Exp Brain Res 1998;120:1–8.
6. Mizobuchi K, Kuwabara S, Toma S, et al. Properties of human skin mechanoreceptors in peripheral neuropathy. Clin Neurophysiol 2002;113:310–315.
7. Di Fabio RP, Badke MB. Stance duration under sensory conflict conditions in patients with hemiplegia. Arch Phys Med Rehabil 1991;72:292–295.
8. Perennou DA, Leblond C, Amblard B, et al. The polymodal sensory cortex is crucial for controlling lateral postural stability: evidence from stroke patients. Brain Res Bull 2000;53:359–365.
9. Perennou DA, Leblond BA, Amblard B, et al. Transcutaneous electric nerve stimulation reduces neglect-related postural instability after stroke. Arch Phys Med Rehabil 2001;82:440–448.
10. Cavanagh PR, Simoneau GG, Ulbrecht JS. Ulceration, unsteadiness, and uncertainty: the biomechanical consequences of diabetes mellitus. J Biomech 1993;26:23–40.
11. Simoneau GG, Ulbrecht JS, Derr JA, et al. Postural instability in patients with diabetic sensory neuropathy. Diabetes Care 1994;17:1411–1421.
12. Uccioli L, Giacomini PG, Pasqualetti P, et al. Contribution of central neuropathy to postural instability in IDDM patients with peripheral neuropathy. Diabetes Care 1997;20:929–934.
13. Horak FB, Dickstein R, Peterka RJ. Diabetic neuropathy and surface sway-referencing disrupt somatosensory information for postural stability in stance. Somatosens Mot Res 2002;19:316–326.
14. Rode G, Tiliket C, Boisson D. Predominance of postural imbalance in the left hemiparetic patients. Scand J Rehabil Med 1997;29:11–16.
15. Miyai I, Mauricio RL, Reding MJ. Parietal-insular strokes are associated with impaired standing balance as assessed by computerized dynamic posturography. J Neurol Rehabil 1997;11:35–40.
16. Marigold DS, Eng JJ, Tokuno CD, Donnelly CA. Contribution of muscle strength and integration of afferent input to postural instability in persons with stroke. Neurorehabil Neural Repair 2004;18:222–229.
17. Lipsitz LA, Jonsson PV, Kelley MM, Koestner JS. Causes and correlates of recurrent falls in ambulatory frail elderly. J Gerontol 1991;46:M114–M122.
18. Hänggi P. Stochastic resonance in biology: how noise can enhance detection of weak signals and help improve biological information processing. Chemphyschem 2002;3:285–290.
19. Moss F, Ward LM, Sannita WG. Stochastic resonance and sensory information processing: a tutorial and review of application. Clin Neurophys 2004;27:677–682.
20. Wiesenfeld K, Moss F. Stochastic resonance and the benefits of noise: from ice ages to crayfish and SQUIDs. Nature 1995;373:33–36.
21. Benzi R, Parisi G, Sutera A, Vulpiani. Stochastic resonance in climatic change. Tellus 1982;34:10–16.
22. Nicolis C. Stochastic aspects of climatic transitions: response to a periodic forcing. Tellus 1982;34:1–9.
23. Bahar S, Moss F. Stochastic resonance and synchronization in the crayfish caudal photoreceptor. Math Biosci 2004;188:81–97.
24. Collins JJ, Imhoff TT, Grigg P. Noise-enhanced information transmission in rat SA1 cutaneous mechanoreceptors via aperiodic stochastic resonance. J Neurophysiol 1996;76:642–645.
25. Collins JJ, Imhoff TT, Grigg P. Noise-enhanced tactile sensation. Nature 1996;383:770.
26. Collins JJ, Imhoff TT, Grigg P. Noise-mediated enhancements and decrements in human tactile sensation. Phys Rev E 1997;56:923–926.
27. Cordo P, Inglis JT, Verschueren S, et al. Noise in human muscle spindles. Nature 1996;383:769–770.
28. Dhruv NT, Niemi JB, Harry JD, et al. Enhancing tactile sensation in older adults with electrical noise stimulation. Neuroreport 2002;13:597–600.
29. Douglass JK, Wilkens L, Pantazelou E, Moss F. Noise enhancement of information transfer in crayfish mechanoreceptors by stochastic resonance. Nature 1993;365:337–340.
30. Fallon JB, Carr RW, Morgan DL. Stochastic resonance in muscle receptors. J Neurophysiol 2004;91:2429–2436.
31. Fallon JB, Morgan DL. Fully tuneable stochastic resonance in cutaneous receptors. J Neurophysiol 2005;94:928–933.
32. Gluckman BJ, Netoff TI, Neel EJ, et al. Stochastic resonance in a neuronal network from mammalian brain. Phys Rev Lett 1996;77:4098–4101.
33. Gravelle DC, Laughton CA, Dhruv NT, et al. Noise-enhanced balance control in older adults. Neuroreport 2002;13:1853–1856.
34. Hidaka I, Nozaki D, Yamamoto Y. Functional stochastic resonance in the human brain: noise induced sensitization of baroreflex system. Phys Rev Lett 2000;85:3740–3743.
35. Jaramillo F, Wiesenfeld K. Mechanoelectrical transduction assisted by Brownian motion: a role for noise in the auditory system. Nat Neurosci 1998;1:384–388.

36. Khaodhiar L, Niemi JB, Earnest R, et al. Enhancing sensation in diabetic neuropathic foot with mechanical noise. Diabetes Care 2003;26:3280–3283.
37. Kitajo K, Nozaki D, Ward LM, Yamamoto Y. Behavioral stochastic resonance within the human brain. Phys Rev Lett 2003;90:218103.
38. Liu W, Lipsitz LA, Montero-Odasso M, et al. Noise-enhanced vibrotactile sensitivity in older adults, patients with stroke, and patients with diabetic neuropathy. Arch Phys Med Rehabil 2002;83:171–176.
39. Manjarrez E, Rojas-Piloni G, Mendez I, Flores A. Stochastic resonance within the somatosensory system: effects of noise on evoked field potentials elicited by tactile stimuli. J Neurosci 2003;23:1997–2001.
40. Morse RP, Evans EF. Enhancement of vowel coding for cochlear implants by addition of noise. Nat Med 1996;2:928–932.
41. Moss F, Milton JG. Medical technology: balancing the unbalanced. Nature 2003;425:911–912.
42. Priplata AA, Niemi JB, Harry JD, et al. Vibrating insoles and balance control in elderly people. Lancet 2003;362:1123–1124.
43. Priplata A, Niemi J, Salen M, et al. Noise-enhanced human balance control. Phys Rev Lett 2002;89:238101.
44. Richardson KA, Imhoff TT, Grigg P, Collins JJ. Using electrical noise to enhance the ability of humans to detect subthreshold mechanical cutaneous stimuli. CHAOS 1998;8:599–603.
45. Simonotto E, Riani M, Seife C, et al. Visual perception of stochastic resonance. Phys Rev Lett 1997;78:1186–1189.
46. Stacey WC, Durand DM. Stochastic resonance improves signal detection in hippocampal CA1 neurons. J Neurophysiol 2000;83:1394–1402.
47. Suki B, Alencar AM, Sujeer MK, et al. Life-support system benefits from noise. Nature 1998;393:127–128.
48. Wells C, Ward LM, Chua R, Inglis JT. Touch noise increases vibrotactile sensitivity in old and young. Psychol Sci 2005;16:411–417.
49. Veves A, Malik RA, Lye RH, et al. Correlations between sural nerve histology and electrophysiology and quantitative sensory tests in mild diabetic neuropathy. Diabet Med 1991;8:917–921.
50. Bloom S, Till S, Sonksen P, Smith S. Use of a biothesiometer to measure individual vibration thresholds and their variation in 519 non-diabetic subjects. Br Med J 1984;288:1783–1785.
51. Greenhalgh BL. A measurement methodology for multisegmental posturography. Master's thesis. Boston University, Boston, 1996.
52. Collins JJ, De Luca CJ. Open-loop and closed-loop control of posture: a random-walk analysis of center-of-pressure trajectories. Exp Brain Res 1993;95:308–318.
53. Collins JJ, De Luca CJ, Burrows A, Lipsitz LA. Age-related changes in open-loop and closed-loop postural control mechanisms. Exp Brain Res 1995;104:480–492.
54. Zellner A. An efficient method of estimating seemingly unrelated regressions and tests of aggregation bias. J Am Stat Assoc 1962;57:348–368.
55. Clogg CC, Petkova E, Haritou A. Statistical methods for comparing regression coefficients between models. Am J Sociol 1995;100:1271–1293.
56. Ivey C, Apkarian AV, Chialvo DR. Noise-induced tuning curve changes in mechanoreceptors. J Neurophysiol 1998;79:1879–1890.
57. Lord SR, Clark RD, Webster IW. Physiological factors associated with falls in an elderly population. J Am Geriatr Soc 1991;39:1194–1200.
58. Simoneau GG, Ulbrecht JS, Derr JA, et al. Postural instability in patients with diabetic sensory neuropathy. Diabetes Care 1994;17:1411–1421.
59. van Deursen RW, Simoneau GG. Foot and ankle sensory neuropathy, proprioception, and postural stability. J Orthop Sports Phys Ther 1999;29:718–726.
60. Kusoffsky A, Wadell I, Nilsson BY. The relationship between sensory impairment and motor recovery in patients with hemiplegia. Scand J Rehabil Med 1982;14:27–32.
61. Perennou DA, Amblard B, Leblond C, Pelissier J. Biased postural vertical in humans with hemispheric cerebral lesions. Neurosci Lett 1998;252:75–78.
62. Bonan IV, Colle FM, Guichard JP, et al. Reliance on visual information after stroke. Part I: balance on dynamic posturography. Arch Phys Med Rehabil 2004;85:268–273.
63. Gonzales B, Rodriguez M, Ramirez C, Sabate M. Disturbance of motor imagery after cerebellar stroke. Behav Neurosci 2005;119:622–626.
64. Staines WR, Black SE, Graham SJ, McIlroy E. Somatosensory gating and recovery from stroke involving the thalamus. Stroke 2002;33:2642–2651.
65. Merchut MP, Gruener G. Quantitative sensory threshold testing in patients with multiple sclerosis. Electromyogr Clin Neurophysiol 1993;33:119–124.
66. Prätorius B, Kimmeskamp S, Milani TL. The sensitivity of the sole of the foot in patients with Morbus Parkinson. Neurosci Lett 2003;346:173–176.
67. Milton JG. Noise as therapy: a prelude to computationally-based neurology? Ann Neurol 2005;58:173–174.
68. Bonato P. Wearable sensors/systems and their impact on biomedical engineering. IEEE Eng Med Biol Mag 2003;22:18–20.
69. Bonato P. Advances in wearable technology and applications in physical medicine and rehabilitation. J Neuroengineering Rehabil 2005;2:2.