Somatosensory Loss Increases Vestibulospinal Sensitivity

F. B. HORAK1 AND F. HLAVACKA2
1Neurological Sciences Institute of Oregon Health Sciences University, Beaverton, Oregon 97006; and
2Institute of Normal and Pathological Physiology SAS, 81371 Bratislava, Slovakia

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Horak, F. B. and F. Hlavacka. Somatosensory loss increases vestibulospinal sensitivity. J Neurophysiol 86: 575–585, 2001. To determine whether subjects with somatosensory loss show a compensatory increase in sensitivity to vestibular stimulation, we compared the amplitude of postural lean in response to four different intensities of bipolar galvanic stimulation in subjects with diabetic peripheral neuropathy (PNP) and age-matched control subjects. To determine whether healthy and neuropathic subjects show similar increases in sensitivity to galvanic vestibular stimulation when standing on unstable surfaces, both groups were exposed to galvanic stimulation while standing on a compliant foam surface. In these experiments, a 3-s pulse of galvanic current was administered to subjects standing with eyes closed and their heads turned toward one shoulder (anodal current on the forward mastoid). Anterior body tilt, as measured by center of foot pressure (CoP), increased proportionately with increasing galvanic vestibular stimulation intensity for all subjects. Subjects with peripheral neuropathy showed larger forward CoP displacement in response to galvanic stimulation than control subjects. The largest differences between neuropathy and control subjects were at the highest galvanic intensities, indicating an increased sensitivity to vestibular stimulation. Neuropathy subjects showed a larger increase in sensitivity to vestibular stimulation when standing on compliant foam than control subjects. The effect of galvanic stimulation was larger on the movement of the trunk segment in space than on the body’s center of mass (CoM) angle, suggesting that the vestibular system acts to control trunk orientation rather than to control whole body posture. This study provides evidence for an increase in the sensitivity of the postural control system to vestibular stimulation when somatosensory information from the surface is disrupted either by peripheral neuropathy or by standing on an unstable surface. Simulations from a simple model of postural orientation incorporating feedback from the vestibular and somatosensory systems suggest that the increase in body lean in response to galvanic current in subjects with neuropathy could be reproduced only if central vestibular gain was increased when peripheral somatosensory gain was decreased. The larger effects of galvanic vestibular stimulation on the trunk than on the body’s CoM suggest that the vestibular system may act to control postural orientation via control of the trunk in space.

INTRODUCTION

Do the close interactions between the vestibular and somatosensory systems for postural orientation permit increased sensitivity of one sensory system to compensate for loss of information from the other system? Complex interactions such as sensory substitutions are likely because the vestibular and somatosensory systems do not operate independent sensory channels in the nervous system for control of posture. Rather these two sensory systems converge anatomically, physiologically, and functionally in the vestibular nuclei, cerebellum, cortex, thalamus, brain stem, and spinal cord, allowing opportunities for many types of interactions (Aiello et al. 1983; Rubin et al. 1979; Wilson 1991; Wilson et al. 1995). For example, animal studies show that the activity of neurons in the vestibular nuclei are affected by changes in somatosensory information such as deafferentation, spinal cord injury, body movements, and the conditions of support (Kasper et al. 1985; Orlovsky 1972; Orlovsky and Pavlova 1972).

In humans, studies of the effects of galvanic vestibular stimulation on postural sway have produced some of the most convincing evidence of vestibular-somatosensory interaction (Britton et al. 1993; Day et al. 1997; Fitzpatrick et al. 1994; Inglis et al. 1995). Studies have shown that the same vestibular stimulus results in different postural responses depending on the state of the somatosensory system (Lund and Broberg 1983; Nashner and Wolfson 1974). Bipolar galvanic stimulation induces an asymmetry of vestibular activity in humans with relative inhibition of the eighth nerve on the side of the anode and relative excitation on the side of the cathode (Goldberg et al. 1984; Nissim et al. 1995), resulting in directionally specific postural sway toward the side with the anode (Coats and Stoltz 1969). The sway is toward the anode regardless of the position of the head relative to the feet, suggesting that somatosensory information from the entire body is taken into account in shaping a functionally relevant positioning of the head relative to the support surface during vestibular stimulation (Lund and Broberg 1983; Nashner and Wolfson 1974).

Recent studies suggest that changes in somatosensory information from the support surface can change the magnitude of responses to galvanic vestibulospinal signals. For example, normal subjects standing on a translating surface showed increased responses to galvanic vestibular stimulation (Inglis et al. 1995). When subjects are sitting or when their trunks are stabilized by a support, galvanic stimulation does not produce electromyographic (EMG) responses in the legs. In contrast, when subjects stand on an unstable, spring-loaded surface, EMG responses to galvanic stimulation increase by 1.5 times (Fitzpatrick et al. 1994). Postural responses to galvanic current are also larger when subjects simultaneously make voluntary movements (Day et al. 1997; Gurfinkel et al. 1988). These effects are not limited to vestibular stimulation arising from

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galvanic current; ankle muscle responses to head perturbations increase when subjects stand on a compliant (sway-referenced) surface (Horak et al. 1994). Thus responsiveness to vestibular signals appears to go up whenever somatosensory information from surface contact regarding body orientation in space is absent or uncertain.

An increase in postural sway in response to vestibular stimulation in subjects with somatosensory loss does not necessarily mean that the gain or sensitivity of the vestibular response has increased. Placing subjects with normal somatosensory function on an unstable surface also results in increased postural instability, even without galvanic stimulation, implying that controlling sway without somatosensory information is more difficult. It would, therefore, not be surprising if loss of surface somatosensory information combined with galvanic stimulation of the vestibular system resulted in more postural instability than galvanic stimulation alone. However, in addition to an increase in postural instability in subjects with somatosensory loss, we hypothesize a compensatory increase in vestibular sensitivity as a sensory substitute.

Studies of compensation for sensory loss in animals have shown that vestibular-somatosensory substitution can take place when one sense is lost; for example, several studies in animals have demonstrated increased sensitivity to somatosensory inputs in the vestibular nuclei following peripheral vestibular lesions (Dieringer 1997; Dieringer et al. 1984; Pfaltz 1983; Putkonen et al. 1977). In humans, vestibular loss results in stronger drive for somatosensory information from the feet and neck (cervico-ocular) on compensatory eye movements to rotations in space (Bles et al. 1984). While it is also widely believed that a similar increase in vestibular sensitivity results from somatosensory loss in humans, few studies have systematically tested this hypothesis (Horak and Shupert 1994; Inglis et al. 1995).

An observation of increased sensitivity to galvanic stimulation in subjects with neuropathy alone cannot reveal the underlying source of the increase. If healthy subjects show similar increases in galvanic sensitivity when standing on unstable surfaces, it is likely that the change in sensitivity observed in subjects with chronic somatosensory loss is related to a similar adaptive change in “weighting” of sensory information for postural control (Horak and Maclpherson 1996; Nasher et al. 1982) rather than to long-term plasticity of underlying neuroanatomical structures.

In fact, Mergner has a model of vestibular-somatosensory interaction that predicts that healthy subjects primarily rely on somatosensory information for postural orientation. However, it is also possible that subjects with somatosensory loss show a compensatory increase in vestibulospinal sensitivity when standing on unstable surfaces because of addition of the two somatosensory deficits. However, it is also possible that subjects with somatosensory loss may not be as affected by unstable surfaces as healthy subjects. Their loss of sensation may prevent them from either detecting the changed surface characteristics or from implementing an altered sensorimotor strategy.

To test our hypothesis that subjects with chronic somatosensory loss show a compensatory increase in vestibulospinal sensitivity, we compared changes in extent of postural lean in response to four different intensities of bipolar galvanic vestibular stimulation in subjects with diabetic peripheral neuropathy and age-matched control subjects. To determine whether this increased sensitivity to vestibular stimulation occurs immediately as a sensory reweighting when standing on unstable surfaces, healthy subjects and patients with somatosensory loss stood on compliant foam surface during galvanic stimulation. If the vestibular system acts primarily to control the position of the trunk rather than controlling whole body posture, we predict larger motions of the trunk than the body CoM induced by galvanic stimulation, especially when somatosensory information for postural orientation to the support surface is disrupted.

A linear feedback control model is used to determine whether the sensitivity to vestibular stimulation in subjects with somatosensory loss simply reflects a decrease in somatosensory feedback or whether an increase in central vestibular gain is likely. Parts of this material were presented earlier as abstracts (Hlavacka et al. 1999a; Shupert et al. 1998).

**Methods**

**Subjects**

Eight subjects (6 males and 2 females) with diabetic peripheral neuropathy (mean age 57.9 ± 11 yr, range 38–70 yr) and eight age-matched healthy volunteers (6 males and 2 females; mean age 58.6 ± 12 yr, range 38–72 yr), gave informed consent to participate in these studies. Mean duration of diagnosis with diabetes mellitus was 16 ± 9 years with three subjects on oral insulin and five on intramuscular insulin. One potential control subject (EH) was found to have a previously undiagnosed loss of sensation in the feet (see Fig. 1), and this subject’s data were analyzed separately. Later, electrophysiological testing indicated absent sural nerve conduction.

Subjects with diabetic peripheral neuropathy were identified according to San Antonio Consensus Conference guidelines; the presence of both signs and symptoms of peripheral neuropathy and patho-
logical results of nerve conduction velocity (American Diabetes Association 1995). Before testing, each subject underwent a history and physical examination that excluded subjects with signs of CNS or vestibular dysfunction. All subjects were community ambulators without assistive devices.

The severity of peripheral neuropathy in the subjects with diabetes was established by a clinical sensory assessment index for proprioception and vibration, superficial plantar pressure sensation (Semmes-Weinstein monofilaments), and sensory and motor nerve conduction velocity tests. Results of the clinical and electrodiagnostic tests of each of the subjects with neuropathy compared with control subjects and laboratory norms are summarized in Table 1. Subjects in this table with mild somatosensory loss have present, but delayed, sural nerve conduction and moderate vibration/proprioception and plantar Semmes-Weinstein clinical test results. Patients with severe somatosensory loss have absent sensory nerve conduction (NR) and very abnormal vibration/proprioception and plantar Semmes-Weinstein clinical test results. The clinical vibration/proprioception index assigned a value of 2 = absent, 1 = diminished, and 0 = normal for ankle and great toe vibration and interphalangeal joint proprioception (passive joint motion) summed for both feet. This vibration/proprioception index was higher in the subjects with diabetes mellitus than in the healthy control subjects (Fig. 1). Mann Whitney test, P < 0.05).

The Semmes-Weinstein monofilament test followed the “yes-no” method in which the patient needed to respond “yes” to at least 80% of the trials to be graded at that site (Mueller 1996). The largest filament was 7 applied to foot zones that were unresponsive to the largest filament. Semonofilament test results were averaged for two plantar foot zones (1st hallux and head of the 5th metatarsal) which are supplied by two separate cutaneous branches and averaged for both feet because no significant asymmetries were evident. Superficial sensation in each of the plantar sites were significantly reduced in the patients compared with the control subjects (P < 0.05). Note the poor sensation scores for the control subject whose data were analyzed separately (hatched area). Motor nerve conduction velocities were slightly affected in all neuropathy subjects, and clinical scores for muscle strength at the ankles, knees and hips were between 4 and 5 (good to excellent) in all subjects. Sensory nerve amplitude was absent in all plantar nerves and in the sural nerves of five of the eight subjects with diabetes. Normal vestibular function (within 1 SD of normative values) was verified in all subjects with horizontal vestibuloocular reflex rotation testing using previously published protocols (Peterka and Black 1990a,b; Peterka et al. 1990a,b).

**Protocol**

Subjects stood on two computer-controlled force platforms with their eyes closed and their head turned toward their right shoulder so that galvanic stimulation would produce mainly anterior sway (Nashner and Wolfson 1974). Their arms were folded and each foot placed on a force plate with stance width self-selected (approximately 10–20 cm intermalleolar distance). Subjects were instructed to maintain balance without stepping during each trial.

| TABLE 1. Subject characteristics

<table>
<thead>
<tr>
<th>ID</th>
<th>Duration Diabetes, yrs</th>
<th>Age</th>
<th>Vibration/Proprio. Index*</th>
<th>Plantar Semmes. Score†</th>
<th>Sensory Nerve Conduction</th>
<th>Motor Nerve Conduction</th>
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<tr>
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<td>Tibial Nerve</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td>V CV, m/s Amp, mV</td>
<td>V CV, m/s Amp, mV</td>
</tr>
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<td>Mild Somatosensory Loss</td>
<td>P1</td>
<td>66</td>
<td>10</td>
<td>3.0</td>
<td>4.7</td>
<td>R/L</td>
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<td></td>
<td>P2</td>
<td>64</td>
<td>4</td>
<td>3.5</td>
<td>5.2</td>
<td>R/L</td>
</tr>
<tr>
<td></td>
<td>P3</td>
<td>49</td>
<td>13</td>
<td>2.0</td>
<td>4.9</td>
<td>R/L</td>
</tr>
<tr>
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<td>50</td>
<td>7</td>
<td>4.0</td>
<td>5.0</td>
<td>biop</td>
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<td>15</td>
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</table>

* Average of great toe and ankle proprioception and vibration scores across both feet (0 = normal, 1 = diminished, 2 = absent responses × 4 sites). † Average of Semmes-Weinstein Monofilament scores for two plantar sites across both feet. A score of 7.0 indicates no response to the largest filament (279.4 gm). § Means ± SD for control subjects (n = 7). R/L, right and left legs; NR, no response; NT, not tolerated.
For galvanic trials, a constant current isolation unit (A-M Systems Model 2200) was used to pass ramp-and-hold current impulses (50-ms ramp and 3-s hold) to 9-cm² pieces of carbon rubber placed over the subjects’ mastoid processes. In this bipolar, binaural stimulation, four current intensities for each subject were used (0.25, 0.5, 0.75, and 1 mA). In half the trials for each subject, the head was turned toward the right shoulder with the anode on left ear and in half the trials the head was turned toward the left shoulder with the anode on right ear so anterior sway only was obtained from galvanic stimulation. Head turning and associated direction of stimulation was randomized for each trial to minimize alteration of galvanic effect due to changes in perception of head position during prolonged head turns (Gurfinkel et al. 1988).

The experiment consisted of 6-s trials in five different conditions, including four galvanic intensities and one control condition of quiet stance without galvanic stimulation. The five different conditions were randomized to control for prediction, habituation, and fatigue and repeated three times each for a total of 15 trials per subject on the hard surface. In addition, the control subjects repeated the entire randomized series while standing on 5-cm and then on 10-cm, compliant, Temper foam (Sunmate, medium density with damping) and the neuropathy subjects repeated the series study on the 5-cm foam. The neuropathy subjects were not stable enough on the 10-cm foam to test in this condition. In all trials with galvanic stimulation, current was applied after a 100-ms baseline period and lasted for the duration of the 6-s trial.

The center of pressure (CoP) under each foot was sampled at 250 Hz and low-pass filtered at 20 Hz. The whole body CoP in the sagittal plane was calculated from the sum of the CoP from the two force plates normalized by the proportion of weight over each plate (Henry et al. 1998). Anterior/posterior (A/P) and lateral CoP was monitored on-line to ensure that all subjects realigned CoP to their initial positions prior to each trial, and these initial CoP positions were assigned to a value of 0. No significant lateral CoP was observed so analysis was limited to A/P CoP. The CoP was averaged for three like-trials for each subject, and figures show group averages across all subjects. The center of body mass (CoM) position in the sagittal plane was calculated from the weighted summation of individual CoM locations at the foot, shank, thigh, and trunk segments calculated from 32 morphologic measures from each subject (Koozekanani et al. 1983; Runge et al. 1999). For each trial, the maximum change in CoM angle in space (from the ankle axis) was compared with the maximum change in trunk segment in space by comparing change from the initial angle during the baseline period. Sagittal plane kinematic measures were derived with a motion-analysis system from reflective markers placed at the following bony landmarks on the right side of the body: the head of the fifth metatarsal (toe), the lateral malleolus (ankle), the lateral femoral condyle (knee), the greater trochanter (hip), and the seventh cervical vertebra (upper trunk). Head tilt could not be examined because of biomechanical constraints in the head turned position.

Data analysis

The average amplitude of the displacement of CoP, CoM, and trunk segment orientation was computed for each trial 1.5–2.5 s after galvanic stimulation onset while the effect of vestibular stimulation was relatively constant. Figure 2A shows an example of the CoP responses to galvanic stimulation of four different intensities in a subject with PNP. The sensitivity (gain) of vestibulospinal response was estimated for each subject and condition using the slope of the linear regressions between the CoP, CoM, or trunk final position response as a function of stimulus intensity. The values of the first points for regression were assigned to a value of 0.0 to quantify the change in those parameters as a function of galvanic stimulation. Figure 2B illustrates the measure of vestibulospinal sensitivity from the slope of the CoP/galvanic intensity linear regression in one PNP subject. Although the change in CoP for change in galvanic intensity was largest between 0.50 and 0.75 mA of current, the change in CoP per change in galvanic stimulus intensity fit a linear regression model for each subject (P < 0.05). ANOVA (4 × 2) was used to determine significance of four intensities of galvanic stimulation and two groups on CoP, CoM, or trunk segment amplitudes or slopes. ANOVA was also used to compare the effects of firm surface and foam on the sensitivity of the vestibulospinal response (slope of COP lean for galvanic intensities). Posthoc analysis used Newman-Keuls tests. Occasionally, paired t-tests were also used to determine the effects of conditions within a group.

Results

Healthy subjects increased anterior postural tilt with increasing intensity of galvanic vestibular stimulation

Figure 3A shows the CoP responses to four intensities of galvanic stimulation and no stimulation averaged across the control subjects. Initial dorsiflexor activation (Inglis et al. 1995) in response to the stimulation initially resulted in backward CoP (−1 cm), followed by sustained forward body lean resulting in forward CoP positions of 0.44 ± 0.29, 0.58 ± 0.22, 1.17 ± 0.21, and 1.15 ± 0.29 (SE) cm responses in response to 0.25, 0.50, 0.75, and 1.0 mA of galvanic stimulation, respectively.

Neuropathy increased vestibulospinal sensitivity

Subjects with peripheral neuropathy showed larger than normal forward CoP lean in response to galvanic stimulation, and the largest differences between subjects with neuropathy and control subjects were at the highest galvanic intensities. Figure 3B shows the CoP responses at each intensity of galvanic stimulation averaged across all the subjects with peripheral neuropathy. Figure 4A compares the control and neuropathy subjects’ mean ± SE of CoP responses to the four intensities of galvanic stimulation averaged across all subjects.

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On average over the 1.5–2.5 s period, the neuropathy subjects’ lean in forward CoP position was 0.80 ± 0.31, 1.12 ± 0.30, 1.70 ± 0.29, and 2.48 ± 0.42 cm across the four galvanic intensities. It means that neuropathy subjects leaned farther forward than normal subjects by 0.36, 0.54, 0.53, and 1.33 cm, for the 0.25-, 0.5-, 0.75-, and 1.0-mA galvanic stimulation, respectively. ANOVA (2 groups × 4 intensities) comparison of these CoP means shows a borderline significant effect of group (F = 4.1; P = 0.05) and a very significant effect of intensity (F = 27.3; P = 0.000) and a significant interaction effect with posthoc testing showing significant differences between groups (P < 0.001) only at 0.75 and 1.0 mA.

Figure 4B compares the slopes of the CoP/galvanic intensity relations for each neuropathy subject (5 with severe neuropathy in dotted lines and 3 with mild neuropathy in dashed lines) with the average slope (thick, solid line) and range (gray area) for the age-matched control subjects. The slopes of the relationship between the galvanic stimulus and the postural response for all subjects fit a linear regression model with \( r^2 \) ranging from 0.56 to 0.97. The slopes of the relations between CoP responses and galvanic stimulus intensity were significantly larger in subjects with peripheral neuropathy (2.3 ± 0.98) than in the age-matched control subjects (1.2 ± 0.21; P = 0.03). The subjects with severe neuropathy had a mean slope of 2.9 ± 0.25, which was very different from control subjects (P = 0.0007). Results from the one control subject who was considered separately because of his newly discovered neuropathy (Fig. 1) is shown as a thin, solid line in Fig. 4B. Note that the slope for this subject lies within the range of severe neuropathy, and nerve-conduction testing confirmed significant neuropathy in this potential control subject.

Thus the three neuropathy subjects with mild neuropathy in Table 1 showed similar responses to galvanic stimulation as the control subjects. When only the five severe neuropathy subjects are considered, ANOVA of mean CoP responses (2 groups × 4 intensities) shows a very significant difference between control and neuropathy subjects (F = 10.5; P = 0.008) and of intensity (F = 48.9, P = 0.000) as well as a significant interaction (F = 8.2; P = 0.000) with the largest differences between groups at the largest galvanic intensities. Post hoc tests show significant differences between groups (P < 0.001) at 0.75, and 1.0 mA.

**Standing on foam increased vestibulospinal sensitivity**

Control subjects showed increased slopes of linear regressions of CoP responses to galvanic stimulation when they stood on 5-cm compliant foam (P = 0.04), with larger slopes while standing on 10-cm than on 5-cm foam (P = 0.02). Figure 5A compares the CoP responses to four galvanic stimulation intensities when the control subjects stood on a firm surface, on 5-cm foam, and on 10-cm foam. The increase in CoP response when standing on foam were largest at the largest stimulus intensities, reflecting a significant increase in slope of CoP response to galvanic stimulus intensities when standing on foam. The average slopes increased from 1.3 ± 0.6 cm/mA on a firm surface to 3.2 ± 1.1 cm/mA on 5-cm foam to 57.5 ± 1.8 cm/mA on 10-cm foam.

Neuropathy subjects increased CoP responses to galvanic stimulation even more than control subjects when standing on
5-cm foam. Figure 5 compares the effect of standing on a firm and 5-cm foam surface for the control group (A) and the neuropathy group (B). The slopes for neuropathy subjects were significantly different on the firm and 5-cm foam surface (paired t = 7.8; P = 0.004). The average slope increased in the neuropathy group from 2.2 ± 0.98 on the firm surface to 6.6 ± 1.5 cm/mA on the 5-cm foam. The subjects with neuropathy were not able to maintain stable stance on the 10-cm foam.

Trunk is more affected than the CoM by galvanic vestibular stimulation

To determine whether the galvanic stimulation moved the body as an inverted pendulum with similar motion at the CoM and trunk as in an “ankle strategy” or primarily moved the trunk as in a “hip strategy” (Horak et al. 1990), the effect of galvanic stimulation on the CoM was compared with the effect on the trunk. Figure 6 compares forward motion of the CoM with forward motion of the trunk segment in space in response to four different galvanic intensities for control subjects (left) and neuropathy subjects (right). The trunk and CoM angles measured are illustrated at the top right of the figure. Stick figures show the final change of trunk, thigh and leg segment positions in space in response to three trials at each galvanic intensity in a representative control and neuropathy subject. Notice that the final kinematic position at each stimulus intensity was quite repeatable across the three trials as the stick figures are overlapped.

The slope of the relation between trunk segment angle and galvanic intensity is twice as large as the slope of the relation between CoM angle and galvanic intensity for both groups on the flat surface (Fig. 6A) and on the 5-cm foam surface (Fig. 6B). ANOVA analysis (group × trunk × CoM × surface) shows significant effect of trunk versus CoM (F = 17; P = 0.001) and a significant effect of the surface (F = 20; P = 0.000). Despite the fact that CoP responses to galvanic stimulation were larger in neuropathy than control subjects, there was no significant difference in trunk or CoM slopes between groups (F = 17; P = 0.41). When somatosensory information was altered by compliant foam, even more trunk motion relative to CoM motion occurs in both groups. In general, the larger the body forward lean, the larger the difference between the trunk and CoM responses such that the body bends forward at the hips to accommodate farther trunk inclination when forward CoM motion is limited.

**Fig. 6.** Larger trunk than CoM responses to galvanic stimulation on a normal surface (A) and 5-cm-thick foam surface (B). Group average (and SE) of forward movement of trunk segment-in-space and CoM angle in response to galvanic stimulation of 4 intensities in control subjects (left) and neuropathy subjects (right). Stick figures show maximum trunk, leg, and CoM (x) forward motion for a representative control and neuropathy subject for 3 trials at each galvanic intensity.
DISCUSSION

The present study provides evidence for an increase in the sensitivity of the vestibular-evoked postural responses from galvanic stimulation when somatosensory information from the surface is altered, either by neuropathy or by standing on a compliant surface. These results are consistent with previous studies showing increases in ankle EMG and CoP sway responses to galvanic stimulation when healthy subjects stood on moving surfaces or during voluntary movement and decreases in responses when subjects are supported or sitting (Britton et al. 1993; Fitzpatrick et al. 1994; Inglis et al. 1995; Smetanin et al. 1988; Storper and Honrubia 1992). However, this study goes further by demonstrating that this increase in responsiveness to galvanic stimulation represents a change in sensitivity of the vestibulospinal response rather than a generalized increase in postural instability. These results suggest that vestibulospinal responsiveness increases in subjects with pathological neuropathy to allow functional sensory substitution and that this increase in sensitivity can occur immediately when somatosensory information from the postural support surface is disrupted.

Effects of diabetic peripheral neuropathy on loss of somatosensory information

Although aging, alone, can result in some neuropathy, the loss of somatosensory information due to diabetic peripheral neuropathy is much more severe in the diabetic subjects in our study than in the elderly, control subjects. Neuropathy related to chronic diabetes is due to primary axonal degeneration with secondary demyelination and may be further modified by vascular lesions of the nerves. This type of neuropathy usually affects both small (pain and temperature and light touch) as well as large afferents (proprioceptive) to affect all modalities and reflexes in a glove-and-stocking distribution in both the feet and hands (Brown and Asbury 1984; Dyck et al. 1987).

The extreme severity of loss in the neuropathy subjects was reflected in their insensitivity to vibration, joint position, and light touch on the plantar surface of the feet as well as absent sural and plantar nerve amplitudes to electrical stimulation. Such psychophysiological testing of the threshold for appreciating sensory stimuli can be reliable clinical tools for detecting unmyelinated fiber function and electric potentials are best for detecting intactness of myelinated fibers (American Diabetes Assn. 1995; Feldman 1994). Nevertheless, joint position, vibration, and light touch at the knees, hips, and trunk were intact and could be used for postural orientation in our neuropathic subjects. The increased sensitivity to galvanic stimulation was a true marker for peripheral neuropathy and not for diabetes or age because only the one potential control subject who had a significant neuropathy (cancerigenic autoimmune response) showed a large response to galvanic current. Other studies have shown that diabetic patients with significant neuropathy, and not those with diabetes without neuropathy, increased postural sway in stance (Simmons et al. 1997).

Eventually, subjects with severe neuropathy also get damage to motor nerves that could compromise muscle strength and thus postural stability. The loss of larger diameter motor axons and sparing of smaller, slower-conducting axons is consistent with mild to moderate slowing of motor conduction velocities. Our subjects, however, all had much less involvement of the motor, than sensory, nerves. Although the plantar sensory nerves were totally unresponsive in all eight subjects and the sural sensory nerve was unresponsive in five of the eight subjects, all but one diabetic subject showed significant responses in both the peroneal and tibial motor nerves with nerve conduction velocities near clinical normative values. Furthermore, clinical strength testing showed good to excellent ankle, knee, and toe strength with sustained ability to support the body on toes or heels. Thus an increase in postural response to galvanic stimulation cannot be accounted for by postural instability derived from significant muscle weakness. Motor nerve involvement is also unlikely responsible for our findings because the effect of galvanic current was a significant forward lean and it takes more strength, not less, to maintain the farther forward leans in the subjects with somatosensory loss. Although ankle plantarflexion weakness could theoretically account for the increase in trunk flexion during forward leans, it is unlikely that this accounts for the differences between patients and control subjects because healthy control subjects also showed such trunk flexion when leaning exaggerated by standing on compliant foam.

Stance on unstable surfaces and neuropathy show similar increases in vestibulospinal sensitivity

It is unlikely that the change in sensitivity to galvanic responses in subjects with somatosensory loss is due to long-term synaptic plasticity and sprouting of vestibular connections as has been seen for increased somatosensory connections in the frog vestibular nucleus following vestibular deafferentation (Dieringer et al. 1984). Long-term adaptive plasticity is not necessary to explain our results because healthy control subjects show similar increases in sensitivity of galvanic responses instantaneously when standing on foam in this study or a translating surface in our previous study (Inglis et al. 1995). In fact, even subjects with severe neuropathy showed a further increase in galvanic sensitivity when they stood on foam. This additive effect of neuropathy and surface compliance suggests that the diabetic subjects had enough somatosensory information remaining to interpret the support surface as unstable and adaptively increase sensitivity to vestibular error signals.

We hypothesize that vestibular information normally only becomes critical for control of postural orientation and equilibrium in stance when somatosensory information from the support surfaces is inadequate. Mergner’s model of vestibular-somatosensory interaction for spatial orientation suggests that the nervous system normally compares a bottom-up control from somatosensory information with a top-down control from vestibular information (Mergner and Rosemeier 1998). If this comparison suggests that the surface is stable, somatosensory information is used for postural control, but if the comparison suggests that the surface is unstable, vestibular influence becomes more apparent. Mergner’s model assumes the vestibular loop interprets whether the support is actually stable and horizontal by creating an internal representation of the orientation of the foot and, hence, the support surface with respect to space. This internal representation of foot in space can be obtained by subtracting the orientation of the body with respect to the foot from orientation of the body-in-space. Thus although both somatosensory and vestibular information are available and compared, if they agree that the surface is rela-
able as an orientation reference, somatosensory information dominates, whereas if the convergence of these two senses agrees that surface information is unavailable or unreliable, vestibular information becomes more critical for control. Other studies have shown that somatosensory information becomes inadequate for control of postural orientation and equilibrium when healthy subjects stand on a sway-referenced surface (Horak et al. 1994; Nashner et al. 1982; Shupert et al. 1999), on a spring-loaded surface (Fitzpatrick and McCluskey 1994), on a narrow beam (Horak et al. 1990), on compliant foam (Shumway-Cook and Horak 1986), on a teeter-totter (Fitzpatrick et al. 1994), in water (Dietz et al. 1989), in outer space (Clement et al. 1985; Massion et al. 1998), or when the body is not in contact with support surfaces, such as when jumping, running, or diving (Berthoz and Pozzo 1988). Our results are consistent with the hypothesis that the CNS interprets the altered and/or reduced somatosensory information associated with peripheral neuropathy as an unstable support surface.

There is growing consensus that somatosensory information, including proprioceptive, joint, and cutaneous, is the primary sense responsible for postural orientation and equilibrium in quiet stance, at least when subjects stand on hard fixed surfaces (Horak and Macpherson 1996 for a review). Evidence for the dominance of somatosensory information for posture is the significant increase in sway excursion, sway velocity, and sway variance when somatosensory information from the feet is reduced by ischemia or cooling (Diener et al. 1984; Horak et al. 1990; Magnnsson 1990). Sway in stance on a hard surface is also larger than normal in subjects with somatosensory loss due to diabetic peripheral neuropathy (Boucher et al. 1995; Giacomini 1996; Simmons et al. 1997; Simonneau et al. 1994, 1995; Ucciolli et al. 1995). In addition, our previous studies showed that diabetic patients with loss of somatosensory information due to peripheral neuropathy have significantly delayed latencies of postural responses to surface displacements (Inglis et al. 1994). In fact, subjects with peripheral neuropathy have an approximately 23 times higher risk of falling than do healthy control subjects (Richardson and Hurvitz 1995; Richardson et al. 1992). A unique subject with profound, total body somatosensory loss, but intact vestibular function, showed extremely large postural sway in stance, inability to stand at all with eyes closed, and completely absent automatic postural responses to surface displacements (Horak et al. 1996). In contrast to the effects of somatosensory loss on postural control, loss of vestibular function often allows normal postural sway in quiet stance, even with eyes closed, as well as normal latencies of postural responses to surface displacements (Black et al. 1978; Horak et al. 1990, 1994; Nashner et al. 1982).

Eliminating vision also does not necessarily increase postural sway in quiet stance, nor does it result in longer latencies to postural perturbations, suggesting that it is not as critical as somatosensory information for postural control (Black et al. 1978; Horak and Macpherson 1996; Nashner et al. 1982). Nevertheless vision can be an important substitute for loss of somatosensory or vestibular function (Nashner et al. 1982; Putkonen et al. 1977). In this study, vision was eliminated by eye closure because vision can suppress the effects of galvanic stimulation on postural sway (Lund and Broberg 1983).

Vestibular control of the trunk in space

Galvanic vestibular stimulation caused greater tilts of the trunk segment angle in space than of the total body CoM angle. The differences in forward motion between the trunk and CoM became larger as the lean became larger, associated with larger galvanic current intensities. These results are consistent with the hypothesis that vestibular signals control body posture primarily by controlling the trunk in space (Horak and Macpherson 1996; Mergner and Rosemeier 1998). It is possible that vestibular information is used to create an internal representation of the trunk in space because the trunk represents the natural platform for the head and because subjects generally relate to their trunks when asked to describe their orientation and movement in space (Mergner et al. 1997). The large effect of vestibular stimulation on the trunk can also be seen in the frontal plane during galvanic stimulation with the head facing straight ahead (Day et al. 1997). These authors attribute lateral trunk bending from galvanic stimulation to a movement strategy that compensates for perceived tilt of the surface, whereas we attribute trunk tilt as alignment of the trunk with the perceived tilt of the gravito-inertial vector.

If galvanic stimulation was primarily driving total body sway and not the alignment of the trunk in space, then increasing the intensity of galvanic stimulation would have produced larger center of mass movements. Somatosensory information regarding limits of stability in stance, even in the neuropathy subjects, appears to have enabled reconfiguration of body alignment in space to accommodate vestibular drive signaling vertical realignment without compromising body equilibrium since no one fell in response to galvanic stimulation. If body CoM and the trunk tilted the same amount, then subjects would be swaying as an inverted pendulum, or so-called “ankle strategy” (Horak et al. 1990). In this study, the trunk continued to tilt long after the CoM tilt saturated suggesting that subjects used a so-called “hip strategy” to control equilibrium. The use of a hip strategy in this task is consistent with our previous study showing that loss of somatosensory information from the feet due to ischemia results in use of a hip strategy and that vestibular information is required for use of a hip strategy (Horak et al. 1990). However, standing on a compliant foam surface changes not only the availability of somatosensory information, it also alters the mechanical characteristics of the support surface by reducing the effectiveness of ankle torque for postural stabilization. This change in surface characteristics could also increase the use of a hip strategy for postural equilibrium.

It is likely that normal subjects are using somatosensory feedback during galvanic stimulation to limit the size of their tilt since normal subjects do not fall, even to very large galvanic currents (Britton et al. 1993; Day et al. 1997). Loss of somatosensory feedback due to neuropathy partly eliminates this constraint on body sway resulting in increased amplitude of sway. In fact, several responses to 1-mA galvanic current in neuropathy subjects resulted in an aborted trial because the patient stepped. A step could occur either because the sway was actually too large to allow independent equilibrium or because the subject perceived excessive sway and a potential fall. However, subjects may have stepped because their veloc-
ity of forward lean in response to the galvanic vestibular stimulation was too fast to control an in-place postural recovery (McIlroy and Maki 1995).

We favor the hypothesis that galvanic stimulation asymmetrically activates otolith signals, which alters the internal perception of vertical orientation to which the body responds by changing trunk alignment in space to match the actual with the perceived internal reference for vertical (Hlavacka et al. 1995, 1996; Inglis et al. 1995; Smetanin et al. 1988). The perception of subjects during galvanic stimulation that an external force is pulling them in the direction of vestibular-induced sway may represent the perception of the orientation “error signal” between the internally represented vestibular vertical goal and the actual body position coded by the somatosensory system. Subjects with loss of somatosensory information to signal actual body position lean their trunks farther than normals by aligning with the new vestibular vertical with weaker stabilizing effect from the somatosensory feedback loops.

Subjects with neuropathy may also be more sensitive than normal to vestibular error signals because they interpret the surface as “unstable” and thus reweight sensory orientation away from surface somatosensory signals that may be unreliable and toward space sensors, particularly vestibular sensory information, when the eyes are closed.

**Mechanisms for alteration in vestibulospinal sensitivity**

Does the increase in body lean in response to galvanic current truly represent an increased gain of vestibulospinal pathways in the CNS or could it be accounted for simply by a decreased somatosensory loop gain due to neuropathy and/or unstable surface? To address this question, we compared our results with results of a simulation of the effects of partial somatosensory loss using a simple feedback control model that includes parallel use of vestibular and somatosensory information to maintain body alignment in stance. A block diagram of the model is shown in Fig. 7.

The model is adapted from Hlavacka et al. (1996) with the addition of central processing of vestibular and proprioceptive information, neck sensory input to account for the directional effects of neck rotation on postural sway direction in response to galvanic stimulation (Lund and Broberg 1983; Nashner and Wolfson 1974), and the effects of standing on compliant foam to somatosensory feedback. The block of surface foam is represented by a nonlinear, saturation function that minimize ankle angle feedback during small amounts (<1°) of body sway. This model is based on the following assumptions: sensory interactions act on a stable, third-order musculoskeletal system representing a standing body with normal, background muscle activity; two parallel feedback loops, somatosensory and vestibular/otoliths, for supraspinal control of muscle activity are divided into a peripheral sensory block and a CNS block; the integration of somatosensory and vestibular feedback loops consist of simple addition; and linear transfer functions are used for deviations of the body in a small range around the center of equilibrium.

Based on measurements of postural responses to galvanic vestibular stimulation (Hlavacka et al. 1996), we assumed a transfer function \( C_v = (-0.4s + 1)(s + 1) \) for the central vestibular block. For the central proprioceptive block, we assumed ideal transfer characteristics \( C_p = 1 \). Transfer functions of body dynamics were estimated as third-order system \( B(AP) = 2/(0.004s^3 + 0.03s^2 + 0.6s + 1) \) for anteroposterior sway and \( B(LR) = 1.3/(0.004s^3 + 0.03s^2 + 0.6s + 1) \) for left-right direction of sway. When the head was rotated in the horizontal plane relative to the trunk by angle \( \alpha \), trunk to head

**FIG. 7.** Block diagram of control model of vestibular and somatosensory interaction for body orientation in stance. Vestibular loop including the influence of neck rotation is black and the somatosensory loop is gray. Stance on foam is simulated by a nonlinear saturation function. Galvanic stimulation sums with vestibular sensor output.
and head to trunk transformations were performed for both AP and LR directions as follows

\[
\text{Head}(AP) = \text{Trunk}(AP) \cdot \sin(\alpha) + \text{Trunk}(LR) \cdot \cos(\alpha)
\]

\[
\text{Head}(LR) = \text{Trunk}(AP) \cdot \cos(\alpha) - \text{Trunk}(LR) \cdot \sin(\alpha)
\]

and

\[
\text{Trunk}(AP) = \text{Head}(LR) \cdot \sin(\alpha) + \text{Head}(AP) \cdot \cos(\alpha)
\]

\[
\text{Trunk}(LR) = \text{Head}(LR) \cdot \cos(\alpha) - \text{Head}(AP) \cdot \sin(\alpha)
\]

The model simulation applied a similar pattern of galvanic stimulation to the vestibular loop as in our experiment and a somatosensory system gain of 1 for control subjects and a gain of 0.4 for subjects with severe somatosensory loss. Increased vestibular sensitivity was modeled as increasing gain in the transfer function \( CV = (-0.4s + 2)/(s + 1) \).

Model simulations showed that the experimental CoP data could be reproduced only if central vestibular gain was increased as well as peripheral somatosensory gain was decreased. Reduction of somatosensory gain, alone, resulted in a smaller than observed increase in amplitude of CoP forward compared with control subjects and did not change the initial rate of change of CoP as seen in the experimental data. Figure 8 shows a good match of the model simulation with the group averaged control and neuropathy CoP data when central vestibulospinal gain was increased and somatosensory gain was decreased (thick, dashed line) than when only somatosensory gain was decreased (dotted).

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