Cardiovascular Systemic Regulation by Plantar Surface Stimulation

Guruprasad Madhavan, MSc; Julian M. Stewart, MD, PhD; Kenneth J. McLeod, PhD

The decreased blood pressure and flow rates associated with orthostasis have been implicated in the etiology of numerous clinical conditions, including deep vein thrombosis, chronic fatigue syndrome, and more recently osteoporosis. Here, we investigate the potential of low-magnitude vibration, applied at the plantar surface, to inhibit the cardiovascular responses of adult women to the orthostatic stress associated with quiet sitting. ***Methods:*** *Thirty healthy women, aged 22–82 years, were exposed to a plantar-based vibration immediately after taking a seated position. Seven stimulus frequencies (0, 15, 22, 44, 60, 90, and 120 Hz, all at 0.2g) were tested on each subject, and cardiovascular responses were followed for 20 minutes. Each subject experienced only a single test frequency on any day. Pre- and poststimulus blood pressures and continuous electrocardiogram results were obtained, from which mean arterial pressure (MAP) and heart rate variability (HRV) were calculated.* ***Results:*** *In the per-protocol study population (n = 25), 20 minutes of quiet sitting was associated with an average depression of 8.95 mm Hg in systolic pressure and of 1.9 mm Hg in diastolic blood pressure, corresponding to an average decrease in MAP of 5.15 mm Hg. These orthostasis-based changes in blood pressure were significantly reduced by exposure to plantar vibration, in a frequency-dependent manner, with essentially complete suppression of the drop in MAP achieved with plantar stimulation at 44 Hz ($P \leq\leq .01$). In the orthostatically hypotensive subpopulation (n = 15), both the 9.3-mm Hg depression in MAP and the decline in HRV were eliminated by exposure to plantar vibrations in the 40- to 60-Hz range ($P = .01$ and $P = .03$, respectively). These results are consistent with the hypothesis that the plantar vibration may be stimulating type IIA muscle fiber activity in the leg, which is critical for effective skeletal muscle pumping in the absence of locomotion.* ***Conclusions:*** *Our findings lead us to suggest that noninvasive, low-level, plantar-based vibration in the regime of 30–60 Hz can significantly inhibit the effects of the orthostatic stress of quiet sitting on the cardiovascular system.*

(Biomedical Instrumentation & Technology 2006; 40:78–84).

The impact of orthostatic stress has been implicated in a variety of common clinical conditions, including syncope,[1] chronic fatigue syndrome,[2,3] deep venous thrombosis,[4] and more recently osteoporosis.[5] Orthostatic stress occurs during both upright sitting and standing and can result in significant sequestration of blood in the extremities in some individuals. Consequently, these individuals will experience a depression in both systolic and diastolic blood pressure due to the decreased venous blood return to the heart.[6] Although the cardiovascular response to orthostatic stress is usually measured in subjects moving from supine to upright standing, representing, for example, waking and rising from bed, the transition from walking/standing to sitting is a far more common daily activity. Despite its applicability to many activities of daily living, such as long-duration sitting in modern work environments or during long-distance travel, the impact of the orthostatic stress of quiet sitting on cardiovascular performance has been studied less than that experienced during upright stance. During upright stance, the skeletal muscle pump activity associated with postural swaying helps to maintain low tissue pressures and assists in both venous and lymphatic clearance. Conversely, sitting requires little postural muscle activity, resulting in increased opportu-

From the Departments of Orthopaedics and Biomedical Engineering, School of Medicine, Health Sciences Center, State University of New York, Stony Brook (GM); the Departments of Physiology and Pediatrics, Westchester Medical Center & New York Medical College, Valhalla, NY (JMS); and the Clinical Sciences Research Center, Department of Bioengineering, Thomas J. Watson School of Engineering and Applied Science, State University of New York, Binghamton (GM, KJM).

The authors declare that they do not have any competing commercial, financial interest. The vibration platforms utilized in this study were supplied by Juvent Corporation, New Jersey.

Address correspondence and reprint requests to Mr Madhavan, Clinical Sciences Research Center, Department of Bioengineering, Thomas J. Watson School of Engineering and Applied Science, State University of New York, PO Box 6000, Binghamton, NY 13902-6000 (e-mail: guru@binghamton.edu).

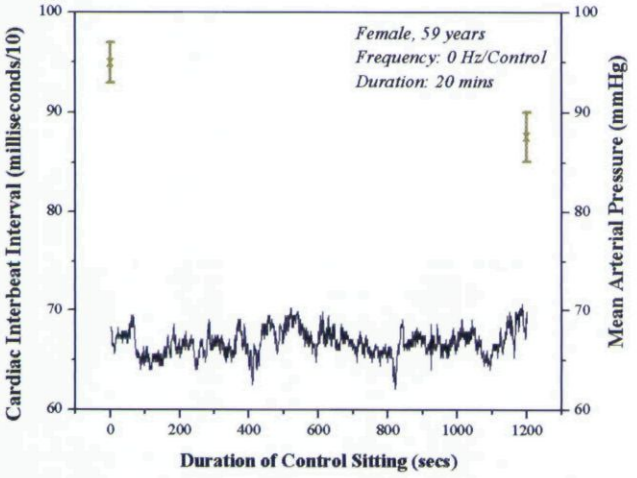

Figure 1. *Graphical illustration of the experimental protocol. Systolic and diastolic pressures were measured in duplicate, immediately preceding and following the 20 minutes of quiet sitting, from which the mean arterial pressure was determined. Electrocardiogram was used to monitor interbeat intervals throughout the test period, from which heart rate variability was determined.*

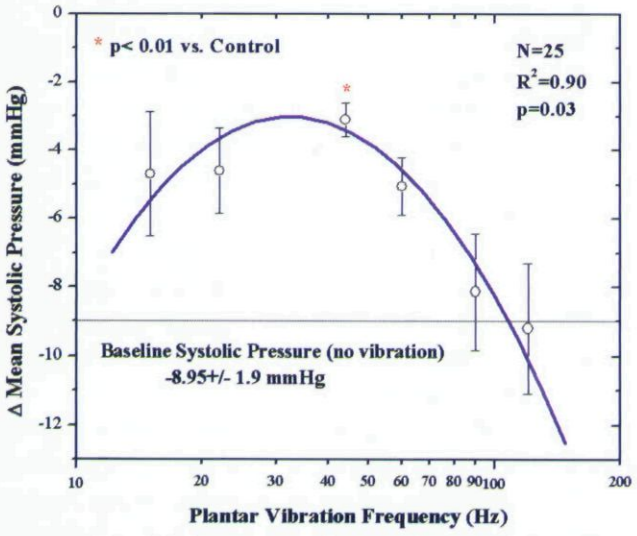

Figure 2. *Response of systolic blood pressure to orthostatic stress and plantar vibration in the per-protocol study population. An orthostatic stress consisting of 20 minutes of quiet sitting results in significant depression of systolic pressure (-8.95 mm Hg). A 44-Hz, 0.2g plantar vibration effectively mitigates this drop (P < .01).*

nity for both venous and interstitial pooling, with a correspondingly greater depression in mean arterial blood pressure (MAP). In addition, it would be expected that this decreased MAP would be associated with a corresponding decrease in heart rate variability (HRV). These cardiovascular responses may have profound effects on health, as reduced venous flow, particularly in the lower extremities, is the major cause of pulmonary emboli, the primary cause of death in as many as 200,000 individuals each year in the United States.[7]

As a means of circumventing these detrimental effects of orthostatic stress, we proposed that stimulation of the type IIA muscle fibers in the lower extremities, which are responsible for much of the skeletal muscle pumping activity in the lower extremities,[8] may be sufficient to inhibit the depression of MAP and HRV during quiet sitting. To address this hypothesis, we investigated the impact of quiet sitting, from an upright stance, on both blood pressure and heart rate, both in the absence of, and with, plantar vibration designed to stimulate type IIA muscle fiber activity in the lower leg.

Methods

This investigation conformed with the principles outlined in the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board's Committee on Research Involving Human Subjects of Stony Brook University School of Medicine and was carried out in the University Health Sciences Center at Long Island, NY, during the months of March through early August 2002.

Subjects and Study Design

The entrance criteria for this clinical study were healthy adult women with no current fractures, peripheral vascular disease, or systemic illness. From an initial upright stance, each subject sat down in a relaxed position, with spine against a chair back, with knees at an approximately 90 angle, and feet (shoeless) on a vibration platform that was raised approximately 8 cm above floor level. The vibration platform allowed the subjects to be exposed to plantar vibration at any one of six frequencies at a time, 15 Hz, 22 Hz, 44 Hz, 60 Hz, 90 Hz, and 120 Hz, this frequency range being selected so as to be centered around the normal range of firing activity of type IIA muscle fibers.[9] Peak-to-peak accelerations of ~0.2g (g = 9.8 m/s^2) were utilized, corresponding to a peak displacement of approximately 120 m at the lowest frequency utilized (15 Hz). Each subject also completed a 0-Hz (no vibration) control exposure. The study subjects returned once each week for testing, with the seven tests being randomized and conducted with one exposure frequency each week. To ensure that variations in

biorhythmic dynamics did not influence the results, the tests were carried out on each respective subject at approximately the same time of day.

All recording periods were 20 minutes in duration. Heart rate was continuously monitored by electrocardiogram using wrist electrodes (Heart Rhythm Scanner Software, Version 2.0, Biocom Technologies, WA). Blood pressure values were measured from the arm using a semiautomatic digital blood pressure monitor (Model HEM 741C, Omron Health Care, Inc, IL). In order to minimize the perturbations of the subjects during the therapy, blood pressures were obtained, in duplicate, only at the beginning and end of the 20-minute treatment duration. The first set of previbration measurements was acquired within 1 minute after the subject sat from the standing position and removed her footwear. A graphical illustration of the recording protocol is presented in Figure 1.

Analysis

The duplicate systolic and diastolic blood pressure values were averaged, and the respective variations over the treatment duration were plotted as a function of stimulation frequency. The MAP was derived as (diastolic pressure + [1/3 Pulse pressure]),[10] and the change in MAP over the 20-minute exposure period was determined. The HRV was characterized using the standard deviation of cardiac cycle length (SDNN),[11,12] which was calculated from each 2-minute interval of the acquired real-time, beat-to-beat interval data using custom software code in Matlab V 6.5 (Math Works, Inc, MA). Time-dependent changes in SDNN (HRV) were then evaluated by linear regression. Changes in the mean pre- and postexposure values of MAP were analyzed by polynomial (quadratic) regression against vibration frequency. Similarly, HRV values were regressed against vibration frequency to model the frequency dependence of the response. Regression analyses were carried out utilizing Origin Version 7.0 (Origin Lab, Inc, MA), and statistical analyses were confirmed with Sigma Stat Version 10.0 for Windows (SPSS, Inc, IL). Within-group multiple comparisons were carried out using analysis of variance. Data are expressed as mean ± SEM. Statistical significance was accepted at $P < .05$.

Results

Thirty adult female volunteers aged 22–82 years (mean age ± SD, 54.3 ± 15.3 years) were recruited for the study and scheduled for testing at each of the seven vibration frequencies over a period of 7 to 10 weeks. Twenty-five women completed the experimental protocol, having undergone four or more treatment sessions, and these represented the per-protocol population in subsequent analyses. Of the possible 175 trials for these 25 volunteers for the seven frequencies, a total of 133 trials were accomplished because of missed sessions by some volunteers. Randomization resulted in the highest participation for the 22-Hz test frequency (n = 23) and the lowest participation at the test frequency of 120 Hz (n = 13).

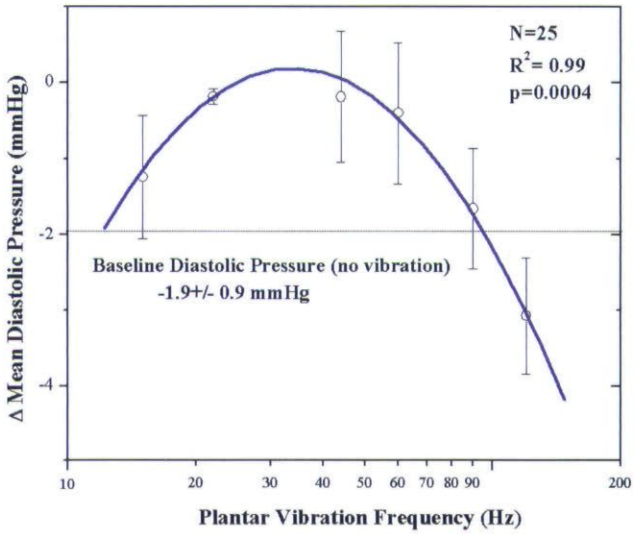

Figure 3. *Diastolic blood pressure response to orthostatic stress and plantar vibration in the per-protocol study population. The depression in diastolic pressure (-1.9 mm Hg) due to the orthostatic stress of sitting can be inhibited by plantar vibration, in a frequency-dependent manner (P = .0004).*

During quiet sitting, and in absence of any plantar vibration, a significant decrease in the systolic pressure of 8.95 ± 1.9 mm Hg ($P < .01$) was observed for the 25 women completing the study. Similarly, in the absence of any plantar stimulation, a drop in diastolic pressure of 1.9 ± 0.9 mm Hg was observed during the seated period ($P = .2$). Consistent with the average decrease in both systolic and diastolic pressures, 20 minutes of sitting resulted in a significant drop in MAP (–5.15 ± 0.81 mm Hg; $P < .01$) in the absence of any plantar vibration. Because these blood pressure responses demonstrated no age dependence, we elected to pool the estimates of MAP and HRV of all individuals in the subsequent investigation of the influence of plantar vibration exposure.

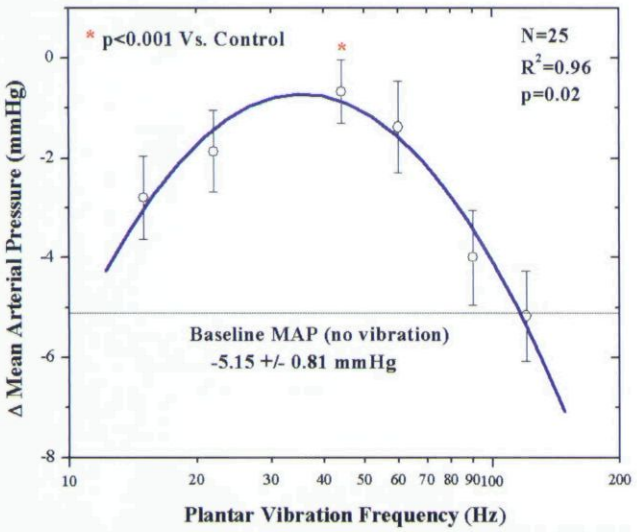

Figure 4. *Response of mean arterial pressure (MAP) to orthostatic stress and plantar vibration in the per-protocol study population. Twenty minutes of quiet sitting resulted in a significant depression in MAP (-5.15 mm Hg), whereas plantar vibration significantly inhibited this depression in a frequency-dependent pattern (P = .02). Plantar vibration at 44-Hz frequency, 0.2g, significantly eliminated this effect of orthostasis (P < .001).*

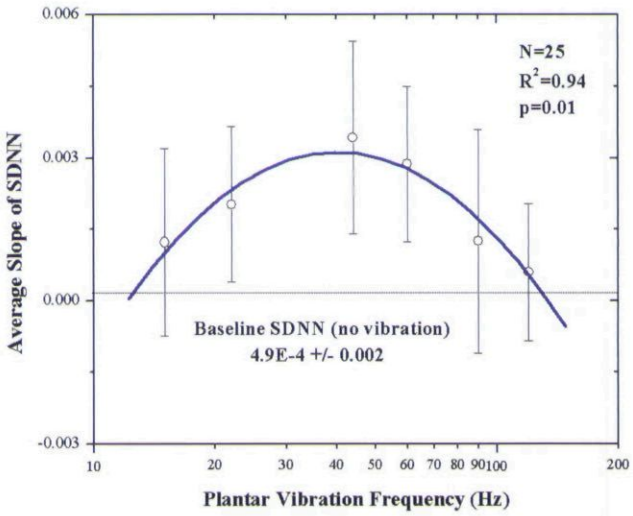

Figure 5. *Heart rate variability (HRV) response to orthostatic stress and plantar vibration in the per-protocol study population. In the per-protocol population, 20 minutes of quiet sitting had no effect on the average HRV. However, plantar vibration was able to elevate the HRV in a frequency-dependent manner that was found to be significant (P = .01). Peak efficacy was observed in the stimulus domain of 30–60 Hz.*

Upon application of plantar vibration, the drop in systolic pressure was observed to be mostly eliminated by the 44-Hz vibration frequency ($P < .01$). A second-order polynomial fit suggests that the efficacy of the plantar stimulation is strongly frequency dependent, with peak efficacy in the 40- to 60-Hz regime ($R^2 = 0.90$, $P = .03$; Figure 2). Similarly, stimulation of plantar surface in the frequency range of 40–60 Hz was also observed to mitigate the depression in diastolic pressure ($R^2 = 0.99$, $P = .0004$; Figure 3).

Analysis of variance of the MAP data showed a significant effect of treatment (stimulus frequency), and subsequent *t* tests identified 44 Hz as being associated with a significant inhibition of the drop in MAP with respect to the control exposures ($P < .001$; Figure 4). Again, a quadratic regression analysis of MAP against stimulus frequency resulted in excellent correlation ($R^2 = 0.96$; $P = .02$), suggesting a relatively broad band of efficacy of the vibration extending over the range of approximately 30–60 Hz.

Unlike that typically observed during the hypotensive response to upright stance, tachycardia was not evident in the per-protocol population, in fact, average heart rate dropped by approximately 2 ± 1 beats per minute, though this did not represent a significant decrease. The time rate of change of HRV, as represented by the sequence of 2-minute SDNNs, also was not altered in the per-protocol population by the orthostatic stress of quiet sitting. However, a significant effect of plantar vibration on HRV was observed in this population, resulting in an actual net increase in HRV for stimuli in the 40- to 60-Hz range ($R^2 = 0.94$, $P = .01$; Figure 5).

We isolated the subgroup (n = 15) of women who experienced a drop in their MAP during the 20 minutes of orthostatic stress in the absence of any plantar vibration, defining this group as orthostatically hypotensive. For this subpopulation, a much larger drop in mean MAP (–9.29 ± 1.29 mm Hg; $P < .001$) was observed in the absence of any plantar stimulation (Figure 6). A very distinct frequency-dependent response to plantar stimulation was observed in this population, confirming the maximal response observed at 44 Hz, where the depression in MAP was essentially eliminated ($P < .01$). Quadratic regression on the MAP response as a function of frequency also identified a peak response band in the 30- to 60-Hz domain.

This orthostatically hypotensive subpopulation also demonstrated a significant depression in HRV during

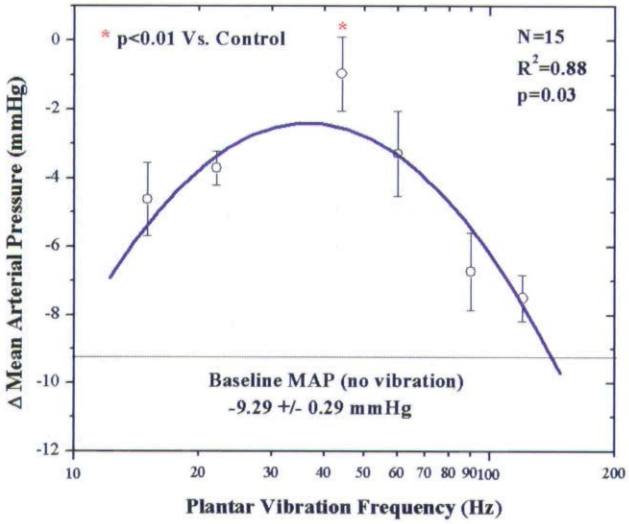

Figure 6. *Response of mean arterial pressure (MAP) to orthostatic stress and plantar vibration in the orthostatically hypotensive subpopulation. Among the subpopulation experiencing a drop in MAP during the 20 minutes of quiet sitting in the absence of any plantar stimulation, MAP decreased by 9.3 mm Hg. Plantar vibration inhibited this depression in a frequency-dependent manner (P = .03), with 44-Hz vibration at 0.2g largely eliminating this effect of orthostasis (P < .01).*

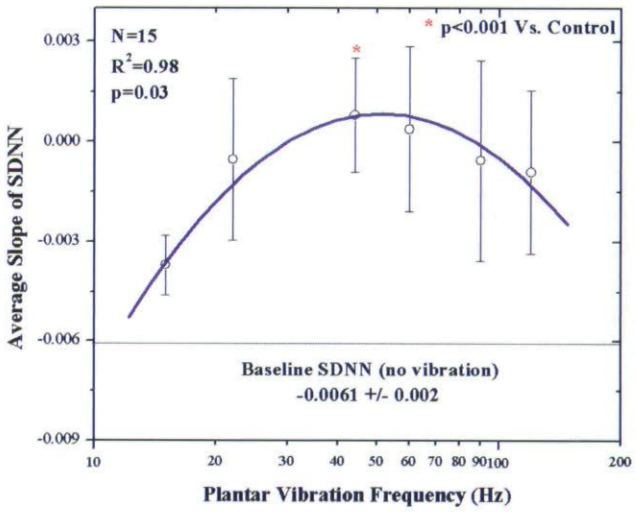

Figure 7. *Heart rate variability (HRV) response to orthostatic stress and plantar vibration in the orthostatically hypotensive subpopulation. Among the subpopulation experiencing a drop in mean arterial pressure during the 20 minutes of quiet sitting, a significant depression in HRV was also observed (P = .03). Plantar vibration resulted in a frequency-dependent inhibition of this response, with the 44-Hz stimulus effectively eliminating this depression (P < .001).*

the 20 minutes of quiet sitting ($P = .002$; Figure 7). Furthermore, a frequency-dependent response of the HRV to plantar stimulation was observed in this population, with the 44-Hz plantar stimulus significantly inhibiting the drop in HRV ($P < .001$). A quadratic regression fit to this dataset resulted in excellent correlation, indicating the frequency of peak response to be in the range of 40–60 Hz ($R^2 = 0.98$).

Discussion

The focus of this investigation was on characterizing the response of the cardiovascular system to the orthostatic stress of quiet sitting, and the ability of plantar vibration to influence this response. Orthostatic hypotension concomitant with the translocation of thoracic blood volume into the lower extremities appears to be a remarkably common response to the orthostatic stress of quiet sitting, even for this group of otherwise healthy adult women. Indeed, 15 of the 25 women completing our study were not able to maintain their MAP during 20 minutes of quiet sitting. In fact, the average decline in MAP that we observed came close to meeting the clinical definition of orthostatic intolerance, which is usually accepted as being a drop in diastolic pressure during standing of >10 mm Hg or a drop in systolic pressure of >20 mm Hg. This high rate of orthostatic hypotension may, therefore, be important clinically because of the long durations over which many individuals sit quietly during the course of the day, carrying out activities of daily living or those associated with their occupation. Of the various causes of orthostatic intolerance that have been identified—increased venous capacitance, depressed autonomic function, decreased cardiac function, declined baroreceptor activity, and reduced skeletal muscle tone—the latter tends to predominate.[13] In the absence of sufficient tonic skeletal muscle pump activity, there is insufficient interstitial and venous return back to the heart to sustain systolic blood pressure. Correspondingly, various approaches to chronic muscle stimulation might be expected to have beneficial effects under these circumstances. Consistent with this hypothesis, we have found that plantar vibration appears to be capable of stimulating sufficient skeletal muscle pump activity to significantly enhance venous return, and therefore cardiovascular performance, as reflected in the inhibition of the drop in both MAP and HRV that was observed during the control sitting.

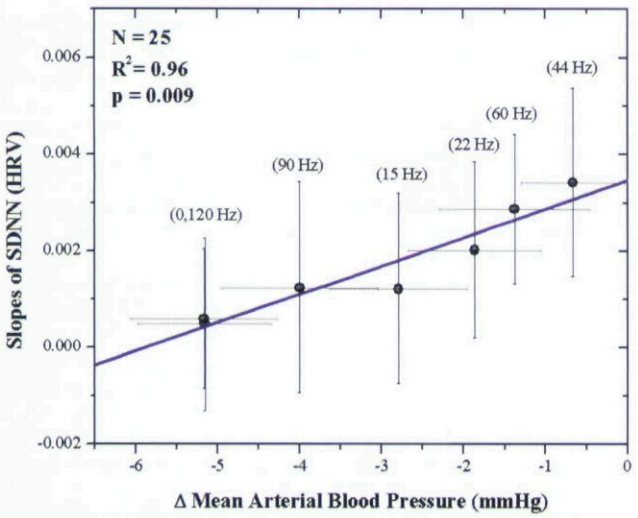

Figure 8. *Variation of heart rate variability (HRV) with respect to the mean arterial pressure (MAP) as a function of plantar vibration frequency. The HRV demonstrates a significant (P = .009), uniform, positive correlation with the change in MAP, over the range of MAP changes observed in this study.*

That the effects of plantar vibration appeared to be maximal for the 44-Hz stimulus frequency is consistent with our hypothesis that stimulation of type IIA muscle fibers would be an effective means of enhancing skeletal muscle pump activity in the absence of locomotion or significant postural muscle activity. However, because the mechanism of coupling of the plantar vibration to the cardiovascular system remains unknown, whether we actually were coupling to type IIA fiber activity is unclear. Recent work, for example, has shown that receptor activity in glabrous skin, specifically Meissner corpuscles, has a peak sensitivity in the range of 30–60 Hz, with detection thresholds well within the range utilized in this study.[14] The effect we are observing, therefore, could well be mediated by these cutaneous receptors, confounding our ability to extrapolate to any effect at the muscle level. Nonetheless, primary muscle spindle endings show a distinct increase in sensitivity near 30 Hz, with thresholds well below the displacements utilized in this study.[15] Because we utilized a constant peak acceleration as a function of frequency, the decreased responsiveness at increasing frequencies may be a result of the decreasing amplitude of the stimulus at higher frequency. In this scenario, our results would be consistent with a more direct effect on the musculature of the lower leg.

Because the frequency responses of both HRV and MAP to plantar stimulation appear quite similar, it is only natural to consider the relationship between these two responses (Figure 8). Linear regression analysis of SDNN *vs* MAP shows, in fact, a clear linear relationship between these two parameters. This observation on subjects with normal and hypotensive blood pressures during orthostasis confirms the work of others[16] who have shown strong correlations between MAP and HRV in hypertensive individuals. Given the ease with which heart rate data can be collected during the course of the day and the difficulty in obtaining continuous blood pressure measurements, this observation may lead to techniques for following or identifying individuals at risk of orthostatic intolerance.

Although the results are encouraging with respect to the potential benefits of plantar vibration on cardiovascular regulation, certain aspects of the experimental design limit the interpretation of these results. Specifically, only pre- and postvibration blood pressures were obtained, spanning an interval of 20 minutes between the measurements. Continuous blood pressure measurements would provide both increased accuracy as well as providing insight into the dynamics of the systemic response to the vibration. Similarly, continuing recordings beyond 20 minutes would provide knowledge of the ability of plantar vibration to maintain blood pressure in response to a sustained orthostatic stress such as encountered during long-distance travel and occupations requiring extended sitting. Additionally, it would be useful to know whether the plantar stimulation is effective in reversing the effects of orthostatic stress or is capable only of inhibiting the development of these effects. Finally, it is not clear from these initial observations the extent to which the plantar vibration altered venous or lymphatic return or leg blood flow. Continued studies, to include direct measurements of fluid distribution and flow in the legs, with and without plantar vibration, will be required to address these issues.

Nonetheless, we suggest that these initial findings may have important implications for development of vibration-based therapeutic modalities for the prevention of orthostatically induced conditions such as deep venous thrombosis, chronic fatigue syndrome, and osteoporosis. ■

We express our gratitude for the contributions of the volunteer subjects and the financial support of the Whitaker Foundation, Smith & Nephew, Inc, and Juvent Corporation.

References

1. **Lagi A, Cipriani M, Buccheri AM, et al.** Heart rate and blood pressure variability in orthostatic syncope. *Clin Sci (Lond).* 1996;91(suppl):62–64.
2. **Schondorf R, Benoit J, Wein T, et al.** Orthostatic intolerance in the chronic fatigue syndrome. *J Auton Nerv Syst.* 1995;75:192–201.
3. **Rowe PC.** Orthostatic intolerance and chronic fatigue syndrome: new light on an old problem. *J Pediatr.* 2002;140: 387–389.
4. **Hirsh J, Hoak J, for the Council on Thrombosis (in consultation with the Council on Cardiovascular Radiology), American Heart Association.** Management of deep vein thrombosis and pulmonary embolism. a statement for healthcare professionals. *Circulation* 1996;93:2212–2245.
5. **Vogt MT, Cauley JA, Kuller LH, et al.** Bone mineral density and blood flow to the lower extremities: the study of osteoporotic fractures. *J Bone Miner Res.* 1997;12:283–289.
6. **Rowell LB.** *Human Cardiovascular Control.* Oxford University Press; 1993.
7. **Garmon RG.** Pulmonary embolism: incidence, diagnosis, prevention, and treatment. *J Am Osteopath Assoc.* 1985;85: 176–185.
8. **Mackie BG, Terjung RL.** Blood flow to different skeletal muscle fiber types during contraction. *Am J Physiol.* 1983;245:H265–H275.
9. **Bellemare F, Woods JJ, Johansson R, et al.** Motor-unit discharge rates in maximal voluntary contractions of three human muscles. *J Neurophysiol.* 1983;50:1380–1392.
10. **Smith J, et al.** *Essentials of Circulatory Physiology.* 3rd ed. Lippincott, Williams & Wilkins; 1990.
11. **Robinson BF.** Relation of heart rate and systolic blood pressure to the onset of pain in angina pectoris. *Circulation.* 1967;35:1073–1083.
12. **Huikuri HV, Kessler KM, et al.** Reproducibility and circadian rhythm of heart rate variability in healthy subjects. *Am J Cardiol.* 1990;65:391–393.
13. **Blomqvist CG, Stone HL.** Cardiovascular adjustments to gravitational stress. In Shepherd JT, Abboud FM, Geiger SR, eds. *Handbook of Physiology: The Cardiovascular System: Peripheral Circulation and Organ Blood Flow.* Sect. 2, Vol. 3, Part 2. Bethesda, Md: American Physiological Society; 1983:1025–1063.
14. **Kennedy PM, Inglis JT.** Distribution and behavior of glabrous cutaneous receptors in the human foot sole. *J Physiol.* 2002;538:995–1002.
15. **Mathews PBC.** Muscle spindles: their messages and their fusimotor supply. In: Darian-Smith I, ed. *The Handbook of Sensory Physiology: Sensory Processes.* Vol. 3. Bethesda, Md: American Physiological Society; 1984:189–228.
16. **Parati G, DiRienzo M, Groppelli A, et al.** Heart rate and blood pressure variability and their interaction in hypertension. In: Malik M, Camm AJ, eds. *Heart Rate Variability.* Armonk, NY: Futura Publishing Company; 1995.