Measurement of cutaneous vibrotactile thresholds may be useful for assessment of the functional integrity of the somatosensory system. To validate a rapid method of determining vibrotactile thresholds that uses a commercially available electromechanical device, vibrotactile thresholds were compared with standardized physical examination findings of sensory function and electrophysiological parameters in 79 patients referred to the Mount Sinai Hospital Neurophysiology Laboratory for clinical electrophysiological evaluation. A statistically significant monotonic association between graded physical examination of vibration perception and vibrotactile threshold was observed for all digits tested in the upper and lower extremities. Statistically significant associations were also observed between vibrotactile thresholds and a variety of electrophysiological measures of the median, ulnar, tibial, peroneal, and sural nerves. The strongest associations were observed between great toe vibrotactile thresholds and late response latencies measured in nerves in the lower extremities. Determination of vibrotactile thresholds may be useful in settings where quantitative measures of large fiber nerve function are desirable and electrophysiological study is not feasible.
Key words: vibrotactile threshold • physical examination • nerve conduction velocity • late response • validation study

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COMPARISON OF VIBROTACTILE THRESHOLDS WITH PHYSICAL EXAMINATION AND ELECTROPHYSIOLOGICAL ASSESSMENT

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Determination of vibrotactile thresholds has been proposed as a technique useful for the detection of peripheral nervous system disease or dysfunction.[2,3,4,12,13] This nonaversive method allows for rapid, reliable, and quantitative assessment of the integrity of the somatosensory pathways that transmit information induced by cutaneous vibratory stimuli. Although these characteristics render them as useful measures of somatosensory function, their acceptance has been limited. Factors that have contributed to the slow acceptance of these methods include a lack of standardization of testing protocols, use of poorly defined units for reporting thresholds, limited normative data for comparison purposes, and insufficient demonstration of associations between vibrotactile thresholds and accepted methods of assessing peripheral nervous system function, particularly physical examination and electrophysiological evaluation, in diverse groups of patients.

Vibrotactile thresholds have certain advantages over conventional techniques currently in widespread use for the detection of dysfunction of the peripheral nervous system. In comparison with physical examination, the measurement of vibrotactile threshold is quantitative, of known reliability, and results in an outcome that can be adjusted for age and other potential confounding variables such as height. In comparison with electrophysio-

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logical testing, which is considered the "gold-standard" method for evaluation of peripheral nerve function, determination of vibrotactile thresholds is nonaversive, does not require costly equipment, and can be performed rapidly by an examiner with relatively little training.

The measurement of vibrotactile thresholds is especially useful in settings where groups of subjects are to be studied, or when a known pathological process is to be followed over time with repeated measurements. For example, studies of neuropathy in renal dialysis patients,[16] diabetics,[5] cancer patients receiving chemotherapy,[12] and workers exposed to neurotoxicants,[10] have utilized vibrotactile thresholds as measures of disease severity. Many of the individuals in such settings are free of neuropathic symptoms and may, therefore, be unwilling to undergo potentially noxious electrophysiological evaluation. In addition, these nonaversive methods are of even greater utility in situations where repeated testing is useful, such as when evaluating the efficacy or toxicity of a new therapeutic agent or of reduction of workplace exposures to neurotoxicants.

Few studies have been performed to quantify the association between vibrotactile thresholds and electrophysiological measures. Typically, they have been performed on either diabetic[5,9,15] or dialysis[1,16] patients. No study comparing these methods in an unselected group of patients referred for routine electrophysiological study is available. In addition, only one published study has compared vibrotactile thresholds with late responses.

The present study was conducted to determine the association between a rapid and reliable protocol for determining vibrotactile thresholds and the two commonly employed methods for assessing the integrity of the peripheral nervous system, physical examination, and electrophysiological testing. Studies of the reliability of this protocol in both normals and diabetics, as well as the determination of the effect of age and height on the measure, have been reported previously.[6,7]

METHODS

Subjects. Subjects receiving standard electrodiagnostic evaluation at the Mount Sinai Electromyography Laboratory were eligible for study. One hundred-twenty patients were solicited, of which 79 chose to participate. The most commonly stated reason for declining participation was lack of time. Electrodiagnostic evaluation was performed on all subjects for clinical purposes. Therefore, not all subjects had the same nerves studied electrophysiologically. Patients with myasthenia gravis were not included in this study. Informed consent was obtained from all participants according to institutional guidelines. Electrophysiological evaluation was performed first, followed by standardized physical examination and determination of vibrotactile thresholds.

Electrophysiological Studies. All electrophysiological tests were performed by a study neurologist (DS or JF) in the Mount Sinai Hospital Department of Clinical Neurophysiology. Nerve conduction studies were performed with standard techniques[8] on a TECA Mystro or TE-4. The median, ulnar, and radial motor and sensory nerves were studied in the upper extremity. The tibial and peroneal motor nerves and the sural sensory nerve were studied in the lower extremity. For motor nerves, proximal and distal latency and compound muscle action potential (CMAP) amplitude were recorded, and conduction velocity calculated. Sensory nerve action potential (SNAP) studies were performed orthodromically; latency, amplitude, and calculated conduction velocity were recorded. Motor nerve F-wave (minimum, maximum, and range of 10 responses) and tibial H-reflex latencies were recorded. The neurologist's electrophysiological diagnosis was recorded for all subjects. For the purposes of this study, subjects were diagnosed as having distal sensorimotor axonal polyneuropathy (distal axonopathy) if symmetrical abnormalities in sensory and motor nerves were found, including reduction in SNAP and CMAP amplitude and conduction velocity (60% to 100% normal) without evidence for focal conduction block, mild increase in late response latency ($\leq$120% upper limit of normal) or dispersed range, fibrillation potentials, and neuropathic motor unit recruitment patterns in distal muscles during electromyography.

Physical Examination. A standardized physical examination of sensory function was performed on all study participants by one examiner (FG). The examining physician was board-certified in Internal Medicine and had been trained to perform the examinations by the supervising neurologist (DS). The examination consisted of determination of vibration perception with a tuning fork, assessment of proprioception, and determination of pain perception with a pin. The sensory examination was performed on the index and little fin-

gers, bilaterally, as well as on the great toes, bilaterally. The results of all clinical tests were recorded as normal, equivocal, or abnormal. The examining physician was unaware of the results of the electrophysiological evaluation until after completion of the examination.

Vibrotactile Thresholds. The Vibratron II (Sensortek, Inc., Clifton, NJ), a vibrotactile threshold-testing instrument, was used for all measurements. The instrument and associated testing protocols have been described previously.[6] In brief, the device consists of a controller unit and 2 identical electromechanical stimulus delivery units or transducers. A 1.4-cm diameter plastic post protrudes from the transducer and delivers the stimulus. The stimulus frequency is fixed at 120 Hz. The amplitude of the stimulus is controlled by turning a knob on the controller unit and is displayed in "vibration units," ranging from 0 to 20.

The measured thresholds were converted from "vibration units," a measure of vibration intensity idiosyncratic to the Vibratron II, to log microns of stimulator displacement. Vibration units are related to microns of peak-to-peak displacement by the formula: microns = k * (vibration unit)**2. The value of k was determined empirically for the equipment used in this study by measuring the peak-to-peak displacement of the freely vibrating stimulator post with a calibrated accelerometer (model GY-125–10, Kulite Corp., Leonia, NY). Calibration was performed without finger contact on the post; thus vibration thresholds are reported in units equivalent to log microns of displacement of the freely vibrating post. These units are linearly related to age and height.[7]

A method of limits procedure (MOL), shown previously to be reliable and rapid,[6] was used for all measurements. Its administration and threshold calculation algorithm have been reported previously.[6,7] The investigator administering the vibrotactile threshold-testing protocol was unaware of the results of any other component of the patient's evaluation.

Statistical Analysis. Statistical analysis was performed using the PC-SAS statistical package.[14] Pearson product-moment correlation coefficients were calculated to assess the association between vibrotactile thresholds and the various corresponding electrophysiological measures. Analysis of variance was utilized to test for significant associations between vibrotactile thresholds and physical examination outcome categories. An index of association analogous to the correlation coeffecient was calculated from the analysis of variance tables.[11]

RESULTS

The study population consisted of 79 subjects. The mean age was 47 years (SD = 14.3). Forty-four subjects were male, and 35 were female. The mean level of education was 14 years (SD = 3.6). Sixty-one subjects were white, 14 were black, and 4 were Hispanic. The electrophysiological diagnoses of the study population are shown in Table 1. Electrophysiological findings were normal in 20 of the subjects. Some subjects had more than one abnormality, hence, the sum of abnormalities is slightly greater than 79.

Analyses were conducted separately for each anatomic site. To be included in the analyses comparing results from the three types of examinations, a subject had to have physical examination results, a vibrotactile threshold and at least one corresponding electrophysiological test result for that site. Because few electrophysiological studies were performed on the radial nerve in this population, statistical analyses of this nerve were not performed.

Comparison of Vibrotactile Thresholds with Physical Examination. To determine the association between vibrotactile threshold and standardized clinical examination of vibration perception, joint position, and perception of pain, vibration thresholds for each of the anatomic sites tested were subjected to analyses of variance with the physical examination categories (normal, equivocal, and abnormal) considered the independent variable. The strength of association between vibrotactile thresholds and physical examination results are presented in Table 2. The strongest asso-

Table 1. Electrophysiologic Diagnoses.

Diagnosis	*N*
Distal axonopathy	18
Radiculopathy	15
Carpal tunnel syndrome	11
Myopathy	8
Entrapment neuropathy (not CTS)	5
Motor neuron disease	3
Brachial plexopathy	1
No electrophysiologic abnormality	20

Note: Some subjects had more than one electrophysiologic diagnosis; hence, the sum of diagnoses is greater than the number of subjects.

Table 2. Correlations between vibrotactile thresholds and physical examination results.

	Tuning fork	Joint position	Pin prick
Index finger:			
Vibration threshold	0.66‡ (49)	0.46† (49)	0.33* (47)
Fifth finger:			
Vibration threshold	0.63‡ (64)	0.43‡ (64)	0.34† (63)
Great toe:			
Vibration threshold	0.70‡ (59)	0.43† (59)	0.10 (59)

*$P < 0.05$;
†$P < 0.01$;
‡$P < 0.001$; ( ) number of observations in the comparison.

ciations were found between vibrotactile threshold and clinical examination with a tuning fork. Moderate associations were observed between vibrotactile thresholds and proprioception, and the weakest associations were found between vibrotactile threshold and perception of pin prick.

The relationships between physical examination results and vibrotactile thresholds are illustrated in Figure 1. A monotonic relationship was found in which thresholds increased with increasing grade of clinical abnormality. This relationship was found for all three sites tested and is similar to, although somewhat stronger than, the relationship between vibrotactile thresholds and physical examination results for proprioception and pain perception.

Comparison of Vibrotactile Thresholds with Electrophysiological Test Results. To evaluate the strength of associations between vibration threshold and various electrophysiological parameters, Pearson product-moment correlation coefficients were calculated for vibration threshold and corresponding electrophysiological parameters. Subjects for whom data were not obtained or for whom electrophysiological measures were unobtainable (because of technical difficulties or disease) were not included in these analyses. The correlations between digit 2 vibrotactile thresholds and median nerve motor conduction velocities and amplitudes, median nerve sensory conduction velocities and amplitudes, and late responses are presented in Table 3. In all cases, the correlations indicated poorer electrophysiological results in subjects with higher vibrotactile thresholds. The associations with the greatest magnitude were be-

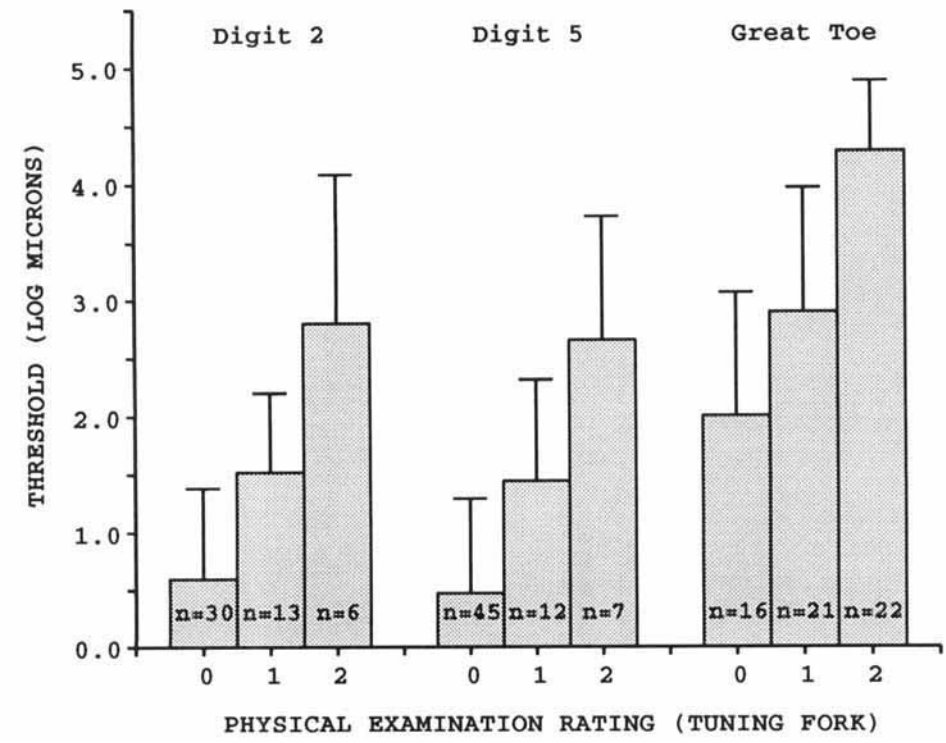

FIGURE 1. Comparison of physical examination rating (tuning fork) and vibrotactile threshold.

Table 3. Correlations between electrophysiologic parameters and their corresponding vibration thresholds.

	Motor		Sensory		F-wave	
	Amp.	Vel.	Amp.	Vel.	Min.	Max.
Median nerve:						
Vibration threshold of digit 2	−0.37* (49)	−0.19 (48)	−0.43† (39)	−0.40* (39)	0.30* (47)	0.38† (47)
Ulnar nerve:						
Vibration threshold of digit 5	−0.24 (64)	−0.31* (64)	−0.28* (58)	−0.35† (58)	0.35† (60)	0.34† (60)
Peroneal nerve:						
Vibration threshold of great toe	−0.29 (33)	−0.55‡ (34)	— —	— —	0.56† (30)	0.58‡ 30)
Sural nerve:						
Vibration threshold of great toe	— —	— —	−0.29 (41)	−0.28 (43)	— —	— —
			H-reflex			
Tibial nerve:						
Vibration threshold of great toe	−0.53‡ (49)	−0.42† (49)	0.61‡ (28)		0.62‡ (47)	0.68‡ (47)

*P < 0.05; †P < 0.01; ‡P < 0.001; ( ) number of observations in the comparison.

tween the index finger vibrotactile threshold and the median nerve sensory amplitude ($r = -0.43$, $P < 0.01$) as well as between digit 2 vibrotactile threshold and the median nerve maximum F-wave latency ($r = -0.38$, $P < 0.01$).

Correlations between digit 5 vibrotactile thresholds and ulnar nerve sensory and motor conduction velocities and amplitudes, as well as late responses, are also presented in Table 3. The correlations were similar to those obtained for the median nerve. Specifically, the correlations indicated that subjects with higher thresholds tended to have poorer electrophysiological test results. The associations with the greatest magnitude were between digit 5 vibrotactile threshold and ulnar sensory velocity ($r = -0.35$, $P < 0.01$), as well as between digit 5 vibrotactile threshold and the F-wave latencies (minimum latency: $r = -0.35$, $P < 0.01$; maximum latency: $r = -0.34$, $P < 0.01$).

Analyses analogous to the ones described above were performed for the vibration thresholds obtained from the great toe and corresponding electrophysiological parameters. Correlations between the great toe vibrotactile threshold and peroneal nerve motor conduction velocity and amplitude, tibial nerve motor conduction velocity and amplitude, and sural nerve sensory conduction velocity and amplitude are also presented in Table 3. In addition, the correlations between the vibrotactile threshold and peroneal and tibial late responses are presented in Table 3.

In general, the correlations between vibrotactile thresholds and corresponding electrophysiological parameters were greater in the lower extremities than in the upper extremities. The highest correlations were observed between the vibrotactile thresholds and the lower extremity late responses. Specifically, they ranged between 0.56 ($P < 0.01$) and 0.68 ($P < 0.001$) for the association between great toe vibrotactile thresholds and lower extremity late responses. The relationship between the tibial nerve F-wave latency (maximum) and the great toe vibrotactile threshold is illustrated in Figure 2.

Sensitivity of Vibrotactile Thresholds for the Detection of Distal Axonopathy. Of interest was the sensitivity of the vibrotactile threshold for detection of distal axonopathy, the most common pathologic consequence of toxic insult to the peripheral nervous system, and the largest subgroup of electrophysiological diagnoses in this study population. On the basis of electrophysiological study, 18 subjects were determined to have generalized distal sensory or sensory-motor axonopathy. Thresholds were standardized for age and height according to a method described previously.[7] Those subjects whose great toe vibration thresholds exceeded the

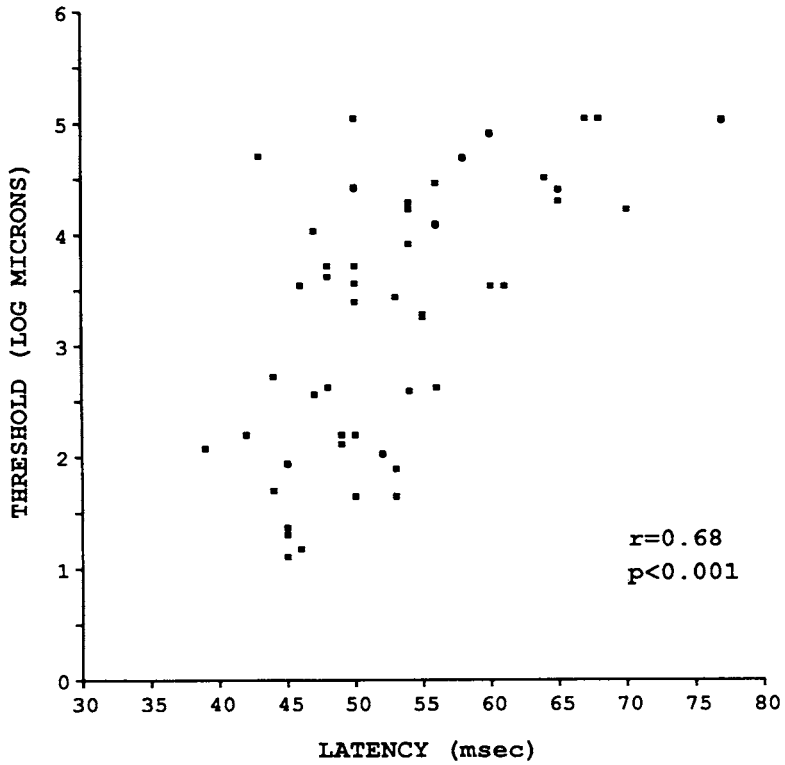

FIGURE 2. Tibial nerve F-wave latency (maximum) vs. great toe vibrotactile threshold.

estimated 95th and 90th percentiles for age and height were identified. Subjects over age 70 (n = 3) were excluded from the analysis because the upper 95th percentile vibration threshold for such individuals exceeds the maximum deliverable stimulus intensity for the Vibratron II. Of the 15 remaining patients with distal axonopathy, 10 and 12 exceeded the 95 and 90 percentile values, respectively. Therefore, with specificities of 95% and 90%, the corresponding sensitivities of vibrotactile thresholds for the identification of distal axonopathy were 71% and 86%, respectively.

DISCUSSION

Vibrotactile thresholds correlated well with physical examination of vibration perception. In addition, significant but weaker associations were found between vibrotactile thresholds and physical examination of both proprioception and perception of pain. Using a more complex physical assessment of neurologic function, Dyck et al.[5] compared neurologic examination findings with vibrotactile thresholds determined with another protocol in a group of 180 diabetics. They observed associations of similar magnitude (r = 0.54) to those found in the current study.

Vibrotactile thresholds, determined with the method-of-limits protocol used in this study, correlated strongly with late responses in the lower extremities. Correlation coefficients ranged from 0.56 to 0.68 for these associations, depending upon the nerve studies. In addition, a trend of increasing vibrotactile threshold with both decreasing conduction velocity and amplitude of the evoked response was observed in all nerves tested. The associations were stronger in the lower extremities. These associations suggest that vibrotactile thresholds, as they were performed in the current study, most closely reflect the function of long segments of peripheral nerves rather than shorter segments.

The correlations between vibrotactile thresholds and electrophysiological parameters found in the current study are comparable to or of greater magnitude than those reported by other investigators utilizing a variety of methods. Bertelsmann et al.[1] found a lower correlation (r = 0.35) between vibrotactile threshold and the tibial nerve H-reflex latency in a group of 50 diabetics. Sosenko et al.[15] found correlations similar to those found in this

study between lower extremity vibrotactile thresholds and electrophysiological measurements of the peroneal (conduction velocity: $r = -0.55$; motor amplitude: $r = -0.49$) and tibial (conduction velocity: $r = -0.45$; motor amplitude: $r = -0.51$) nerves in a group of 50 diabetics. Tegner and Lindholm[16] found similar correlations between peroneal nerve conduction velocity and lower extremity vibrotactile thresholds ($r = -0.54$) in a group of 46 patients with renal failure. Dyck et al.[5] found correlations comparable to those reported in this study between both peroneal nerve motor velocity ($r = -0.48$) and amplitude ($r = -0.46$) and lower extremity vibrotactile thresholds in a group of 180 diabetics. They found slightly greater correlations between lower extremity vibrotactile thresholds and both the sural nerve sensory conduction velocity ($r = -0.37$) and sensory amplitude ($r = -0.54$) than were found in the current study. It is not clear why the correlations between vibrotactile thresholds and electrophysiological measures of the sural nerve observed in the current study were poorer than (1) those observed by Dyck et al.,[5] and (2) those observed for the peroneal and tibial nerves in the current study.

Analysis of the subgroup of patients in the current study diagnosed electrophysiologically as having distal axonopathy demonstrated sensitivity and specificity comparable to the observations of 73% sensitivity and 93% specificity reported for the detection of diabetic neuropathy by Sosenko et al.[15] The results of both studies suggest that these methods are sensitive for the detection of generalized neuropathy and should perform well in screening studies of neuropathy such as in the case of evaluating workers exposed to potential neurotoxicants such as heavy metals, hexacarbon solvents, or organophosphate pesticides.

Another potential use of vibrotactile thresholds is assessment of nerve function in patients in whom nerve conduction parameters are unobtainable because of disease severity. Of the 15 sural nerves evaluated in the current study for which no sensory potential could be evoked, great toe vibrotactile thresholds could be determined in 9 (64%) ipsilateral great toes. Serial determinations of sensory thresholds for evaluation of disease progression in such patents may be useful and should be studied further.

The magnitude of the correlation coefficients presented in this article should be considered lower-bound estimates of the true correlations between these methods. Although a correlation of 1.0 is theoretically possible, in practice it is not obtainable between methods that each have measurement error. The correlations presented here were not corrected for attenuation due to measurement error and, therefore, underestimate the true agreement between the measures themselves. In addition, rather than assigning an arbitrarily low value (i.e., 20 m/s) for conduction velocity when no potential could be obtained from a nerve, the corresponding thresholds were removed from the correlation analyses. Such assignment would have only strengthened the observed relationships between vibrotactile threshold and nerve conduction velocity.

Several factors may contribute to variability in the relationship between vibrotactile thresholds and electrophysiological parameters. Sensory thresholds reflect the performance of the entire somatosensory pathway; nerve conduction velocities and amplitudes are measured over shorter, well-defined nerve segments. Receptor pathology, extremely distal nerve damage, and other pathological processes may affect one measure to a greater degree than the other. In addition, determination of sensory thresholds requires active patient participation. Those who are not cooperative, do not understand the instructions, or wish to falsify results deliberately will add to the variability of the relationship between conduction parameters and vibrotactile thresholds.

In summary, vibrotactile thresholds determined with the method of limits procedure have been shown in this study to correlate with both physical examination and electrophysiological evaluation in unselected patients referred for electrodiagnostic tests.

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