

Original article

Determination of reference intervals for vibratory perception thresholds of the lower extremities in normal subjects

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Abstract The assessment of vibratory perception thresholds (VPTs) is important for evaluating human somatosensory functions and provides new aspects in clinical practice and research. However, there has been little information concerning determinants of the VPT in normal individuals, and there has been no investigation to determine the reference intervals for the lower extremities by vibrometers using appropriate statistical analysis. We determined reference intervals for the VPT in lower extremities of 377 healthy subjects (241 males, 136 females; ages 11–74 years) using Suzuki-Matsuoka vibrometer-5 according to the National Committee for Clinical Laboratory Standards guidelines. The VPT was measured at 12 points: ulnar styloids, patellae, medial and lateral malleoli and the tip of the great toes, dorsal aspect of the distal phalanx of the fifth toes. The effects of age, sex, height, weight, alcohol consumption, and smoking on the VPTs were also investigated. The VPTs of normal subjects increased significantly with age. The difference between the two sides was negligible for determining reference intervals of the VPT. The average VPT was higher in men than in women at the lateral malleolus, the great toe, the patella, and the ulnar styloid but not significantly different at the fifth toe or the medial malleolus. There were no significant differences in the VPTs among the four sites of the foot. The reference interval for the VPT of the lower extremity is less than $13 \times 10^{-2}G$. The influence of body mass index, smoking, and alcohol consumption on the VPT was not significant. We provide the reference interval for the VPT of lower extremities in normal subjects. This information can serve as a basis for future clinical applications of VPT measurements.

Introduction

Quantitative assessment of somatosensory deficit and motor dysfunction is of considerable clinical significance for the diagnosis and treatment of spinal disorder.

However, clinical evaluation for sensory perception has mostly been carried out qualitatively owing to technical limitations as well as time constraints.

In recent years, vibratory perception threshold (VPT) testing has been used to detect peripheral neuropathy in terms of amplitude.^{1,2} It has been shown that the psychophysical responses to vibration are determined by activation of the Meissner and Pacinian corpuscles, which are rapidly adapting receptors.³ It is, therefore, important to determine the VPT in terms of acceleration, as these mechanoreceptors respond to acceleration of stimulation.⁴ The development of biothesiometers — simple, hand-held measuring devices for VPT — has enabled quantitative measurement of peripheral, sensory nerve function. The Suzuki-Matsuoka vibrometer-5 (SMV-5; Medience, Tokyo, Japan) (Fig. 1), which is one of such biothesiometers, was developed for the diagnosis of diabetic neuropathy. It is a fine instrument that can measure responses to acceleration of vibratory stimulation.

In Japan, the SMV-5 has gradually been used for several clinical studies.^{5,6} Ohnishi et al. made a comparative study of the three vibrometers (SMV-5, Vibratron II, TM-31A) and reported that SMV-5 was the most reliable.⁷ When diagnosing peripheral neuropathy based on measurement of the VPT, the determination of reference intervals for VPT data is epidemiologically and clinically important. However, there has been little information concerning determinants of the VPT in normal individuals, and there has been no investigation to determine the reference intervals for the lower extremities by the vibrometers using appropriate statistical analysis. In 1995 the National Committee for Clinical Laboratory Standards (NCCLS) proposed a guideline for terminology and procedures for determining reference intervals (C28-A).⁸

The purpose of the present study was to establish reference intervals for the VPT in the lower extremity of healthy Japanese subjects according to the NCCLS

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guidelines. The effects of age, sex, height, weight, alcohol consumption, and smoking on the VPT were also investigated.

Materials and methods

Subjects

The VPT was examined in 377 healthy Japanese volunteers (241 males, aged 11–74, mean 34 ± 11 years; and 136 females, aged 11–74, mean 31 ± 13 years). Subjects participated voluntarily, with informed consent obtained before testing. The age distribution and demographics of the subjects are presented in Tables 1 and 2, respectively.

A brief questionnaire that included information on smoking habits, alcohol consumption, and hand domi-

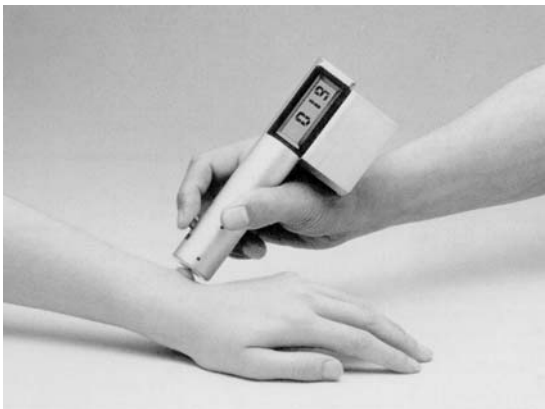


Fig. 1. Vibrometer used in present study: SMV-5 (Suzuki-Matsuoka vibrometer; Medience, Tokyo, Japan)

nance was completed by each subject. Subjects who had a history of neurological diseases or medical conditions that might predispose the person to sensory abnormalities (e.g., diabetes mellitus, malignancy, alcohol abuse, neck or back disorders, kidney failure) and those who had undergone surgery within a year were excluded. Subjects who were taking medications that may cause peripheral neuropathy were also excluded. The body mass index (BMI) was calculated as by dividing the weight in kilograms by the height in meters squared ($BMI = \text{weight}/\text{height}^2$).

Stimulation and measurement procedures

Instrument

The VPT was determined by applying a stimulus from the electromagnetic vibrator, SMV-5, which is a hand-held instrument producing sine-wave vibration at a frequency of 220 Hz with an accelerometer recording the actual movements of a vibrating probe (between 0 and 150×10^{-2} G) by automatically controlling stimulatory strength. The probe is 15 mm in diameter with a flat contacting surface in a firm plastic cylinder. The real vibratory acceleration could be monitored directly on a digital display. The principle of the device action has been described by Suzuki et al.^{9,10} Previous studies have already confirmed the validity and reliability of the VPT measurements by this equipment.⁷ The coefficients of variation for the intra- and interobserver of the VPT measurements by the SMV-5 have been reported to be 15.2% and 18.5%, respectively.⁵

Testing procedure

The measurements were obtained in a silent, closed room with ambient temperature control (20° – 24° C).

Table 1. Age distribution of subjects

Subjects	No. of patients, by decades of age						Total
	11–19	20–29	30–39	40–49	50–59	60–74	
Males	5	105	73	29	16	13	241
Females	10	74	22	14	13	3	136

Table 2. Demographics of subjects

Characteristic	Males ($M = 241$)	Females ($M = 136$)
Age	33.8 ± 11.2 (11–74)	30.8 ± 12.9 (11–74)
Height (cm)	171.6 ± 5.8 (151.0–185.0)	157.8 ± 6.0 (135.0–171.5)
Weight (kg)	68.0 ± 9.4 (41.5–110.0)	52.0 ± 7.4 (30.0–80.0)
BMI (kg/m^2)	23.1 ± 2.8 (15.9–34.7)	20.9 ± 2.7 (16.4–32.2)
Hand dominance	R:183, L:12, A:8, U:38	R:100, L:5, A:2, U:29
Skin temperature ($^{\circ}$ C)	32.0 ± 1.6 (28.0–35.2)	31.7 ± 1.5 (28.7–35.3)

Results are means \pm SD (range)

R, right dominance; L, left dominance; A, ambidextrous; U, unknown; BMI, body mass index

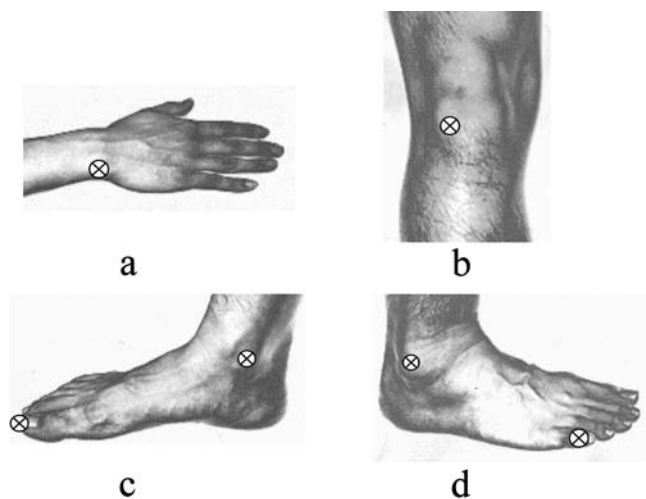


Fig. 2. Regions examined by SMV-5. **a** Ulnar styloid. **b** Patella. **c** Tip of great toe and medial malleolus of tibia. **d** Lateral malleolus of fibula and dorsal aspect of distal phalanx of fifth toe

The subject was in a supine or sitting position to provide optimal relaxation and concentration. The probe was placed at a right angle to the bare skin with gentle pressure to ensure full contact. The VPT was measured at 12 points (Fig. 2): the ulnar styloids, the patellae, the medial malleoli and tip of the great toes, the dorsal aspect of the distal phalanx of the fifth toes, and the lateral malleoli. The stimulus was gradually increased from zero; and when the subject first perceived the stimulus, the value on the display was recorded. The measurements were repeated five times, and the median of five measurements was used to represent the VPT for each site. After completing the measurements, the peripheral temperature at the bilateral dorsal foot of each subject was measured by surface thermometer (Nihonkoden, Tokyo, Japan). Total time for the interview, trials, and actual measurements using SMV-5 was 20–25 min for each subject. The same apparatus was used throughout the whole study, and all measurements were carried out by the principal investigator.

To examine the effect of leg positions during measurements, the VPT values were compared between two age- and sex-matched groups of 76 subjects each who were tested with their knees bent or extended. To investigate the effect of the dominant side of the hand on the VPT value, the subjects were divided into groups based on their dominant hand. The differences in VPT values were assessed for all the combinations of dominant/nondominant hand and the measurement sites. To examine the effect of obesity, the VPT values at the six measurement sites were compared between 59 subjects with a BMI of 25 or more and 315 subjects with a BMI of less than 25. The subjects were also divided by the

amount of alcohol consumed (i.e., those with none and intake of less than twice per week and those with intake of more than twice per week), and the VPT between the two groups were compared. The VPTs of the nonsmokers and habitual smokers were also compared. Heavy smokers who consume more than two packs per day and occasional smokers were excluded for this study.

Data analysis

In subjects who had a higher than maximum intensity of vibration ($>150 \times 10^{-2}G$), $150 \times 10^{-2}G$ was used as the VPT value. Although the VPT of the whole sample group (377 subjects) did not show a normal distribution, normality could be demonstrated by the Smirnov-Kolgomonov test when VPT values underwent logarithmic transformation (\log_{10}). However, because VPTs in each of the stratified groups did not show a normal distribution, nonparametric tests were used to compare VPTs among groups. Wilcoxon tests were used to determine statistically significant differences in VPTs between left and right sides of the body. The Mann-Whitney U-test was used to compare the results in different sex and age groups. The Wilcoxon signed rank test was used to assess differences among measured sites. The correlation between age and VPT measurements at each site was estimated by Spearman's rank correlation coefficients. $P < 0.05$ was considered significant. All statistical analyses were performed on a Macintosh computer (Apple, Cupertino, CA, USA) using Statview (version 5.0; SAS Institute, Cary, NC, USA).

Results

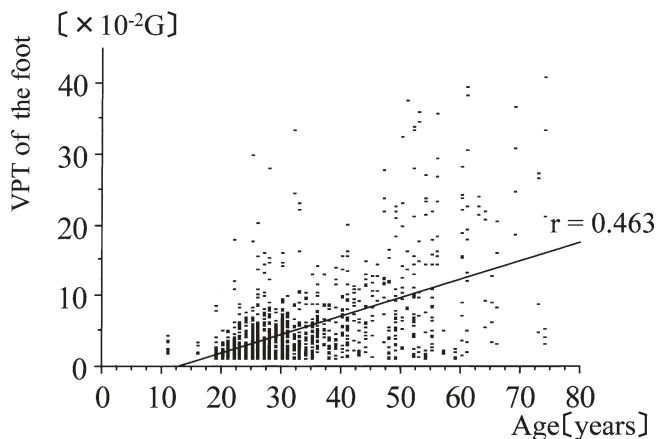
Males were significantly taller than females (171 ± 6 vs. 157 ± 6 cm, $P < 0.001$). The mean skin temperature of the dorsum of the foot in whole subjects was $31.9^{\circ}C \pm 1.6^{\circ}C$ (range 28.0° – $35.4^{\circ}C$). There were no significant differences in VPTs at any site between the two groups with measurements in different leg positions. Both the average and standard deviation of the VPTs showed a tendency to increase with age. There was a highly significant ($P < 0.001$) correlation between the age of the subjects and the VPT (Fig. 3), and the age-related increase in VPT was significant at all sites: The correlation between VPTs and age was strongest at the fifth toe ($r = 0.519$) followed by the great toe ($r = 0.443$), the lateral malleolus ($r = 0.391$), the medial malleolus ($r = 0.368$), the ulnar styloid ($r = 0.303$), and the patella ($r = 0.285$).

Table 3 shows means (\pm SD) of the vibratory perception thresholds at the six measurement sites for the left and right sides. Among all tested sites, the medial

Table 3. Vibration perception thresholds for tested sites

	Right	Left	<i>P</i>
Head of the ulna	1.8 ± 1.0	1.6 ± 0.7	0.044
Lateral malleolus	5.0 ± 5.3	5.0 ± 5.4	0.916
Fifth toe	5.1 ± 6.0	4.8 ± 5.1	0.916
Great toe	4.8 ± 5.7	5.1 ± 6.4	0.047
Medial malleolus	4.8 ± 5.1	4.1 ± 4.4	0.004
Foot	5.0 ± 5.0	4.9 ± 4.9	0.52
Patella	22.5 ± 40.1	25.0 ± 44.4	0.578

[×10⁻²G]

**Fig. 3.** Scatter-plots of vibration perception thresholds (VPT) of the foot in 377 normal individuals. Mean values of tested sides for two sides were plotted

malleolus, the great toe, and the ulnar styloid showed significant differences in VPT between the left and right sides. The VPT values were not significantly different between the dominant and nondominant sides.

Because it was not feasible to compare VPT values directly between males and females owing to uneven age distribution, the same number ($n = 96$) of subjects adjusted for age were chosen from both groups and compared. As a result, the average VPT was higher in men than in women at the lateral malleolus, the great toe, the patella, and the ulnar styloid but not significantly different at the fifth toe or the medial malleolus.

The VPT values for the lower extremities were higher than those for the upper extremities in all decades. There was no significant difference in VPTs among the four sites of the foot. The VPT values measured at the foot were significantly lower than that at the patella. Wide variations of VPT were observed for the patella, and in 50 subjects (16%) the VPT at the patella exceeded the upper limit of measurement (150×10^{-2} G).

There was no significant difference in VPTs with regard to different BMI groups at any measurement site. Similarly, no significant difference in VPT was observed at any site between 134 smokers and 229 nonsmokers. There were also no significant associations between the VPTs and alcohol consumption.

However, the difference in the VPT values between the two sides of the body was small ($<3 \times 10^{-2}$ G) and negligible enough to determine the reference intervals. There was also no significant difference in the VPTs among the four sites of the foot. These eight values, therefore, were averaged for each subject. The mean and standard deviation were calculated for each sex and decade. As suggested by document C-28P (NCCLS), it is probably advisable to consider 95% range of the value of reference population as the reference intervals; which could be obtained by calculating the mean value $\pm 1.96 \times$ standard deviations of VPTs in our subjects. The upper limit alone was specified, as the lower limit has no clinical meaning. The reference intervals of the VPT for the foot of normal Japanese were defined by decades for each sex in Table 4. The reference interval for the VPT of the lower extremity is less than 13×10^{-2} G for the total subjects.

Discussion

Although we cannot completely exclude abnormal values that may be obtained in normal subjects by chance, we set exclusion criteria (including metabolic disease, habitual drug use, and prior surgery) known to affect VPTs in the previous literature (a priori exclusion) when selecting the reference population. In addition, data obtained from these subjects (reference values) were subjected to rigorous statistical exclusion (a posteriori exclusion). As a result, the reference VPT values obtained in the present study from the population that included 377 subjects were confirmed to show a normal distribution by logarithmic transformation.

Several instruments have been developed to overcome lack of sensitivity and reproducibility in VPT

Table 4. Reference interval of VPT in the foot, by age group

Group	No.	Mean	SD	Minimum	Maximum	Reference interval
11–19 years						
Male	5	3.3	1.6	2.0	6.0	6.4
Female	10	2.0	1.2	1.0	5.0	4.4
20–29 years						
Male	105	3.3	2.1	1.0	12.0	7.4
Female	74	2.4	2.1	1.0	15.0	6.4
30–39 years						
Male	73	4.2	2.8	1.0	16.5	9.8
Female	22	3.9	2.4	1.0	10.0	8.7
40–49 years						
Male	29	6.8	4.8	2.0	21.0	16.1
Female	14	7.2	6.1	1.0	20.5	19.1
50–59 years						
Male	16	10.8	7.3	1.0	26.0	25.2
Female	13	4.9	5.2	1.0	20.0	15.1
60–74 years						
Male	13	13.3	10.1	3.0	32.0	33.1
Female	3	10.8	3.2	8.5	13.0	17.0
Totes						
Male	241	4.9	4.7	1.0	32.0	14.1
Female	136	3.5	3.6	1.0	20.5	10.5
All	377	4.4	4.4	1.0	32.0	12.9

[$\times 10^{-2}$ G]

VPT, vibration perception threshold

measurements.^{10–13} The reliability of VPT measurements seems to be dependent on the type of vibrometer used and on the observers who perform the procedure. Because of its high precision,⁵ the SMV-5 vibrometer is sensitive enough to detect sensory impairment that cannot be detected by conventional neurological examinations.⁹ In many studies, the VPT has been tested in normal subjects.^{1,14–18} Hilz et al. reported the reference values for VPT in 530 healthy subjects using the Vibrometer. They presented the VPT in terms of amplitude, and only one site was studied in the lower extremity.¹ The Vibrometer requires a control unit in addition to the stimulating probe. The advantages of the SMV-5 vibrometer are that it is noninvasive, time-efficient, and easy to apply at various test sites and angles as it is small and portable. We applied it to five sites in the lower extremity on both sides and compared the VPT values of different anatomical sites.

The VPTs of normal subjects increased significantly with age in both the upper and lower extremities, as in earlier reports. Pearson was the first (1928) to study a large series with respect to the influence of aging on VPTs.¹⁷ He found a slight decrease in vibratory sensitivity in different age groups, which became striking after age 50.¹⁷ The present study yielded similar results. Usually, the vibration sense diminishes in the legs and feet with advancing age.^{14,15,17,18} On the other hand, Laidlaw and Hamilton found no significant increase in VPTs in

the hands and fingers with aging,¹⁹ whereas a significant increase was obtained for the ulnar styloid in our study. The precise nature of the mechanism responsible for the age-related decrease in vibration sensitivity remains unknown. Among various hypotheses, one possibility is a diminution in the blood supply to the peripheral nerves,²⁰ as arteriosclerosis become prominent with aging.²¹ It is generally accepted that VPTs determined at high frequencies (80–400 Hz) are the result of neural activity in Pacinian corpuscles and that the changes in the structures of the Pacinian corpuscle occur between birth and 93 years of age.²² In addition to the changes in the structures, the population of Pacinian corpuscles decreases with age.²² These changes, therefore, could be associated with the loss of vibratory sensitivity at high frequencies.²³ Moreover, there is progressive fiber loss and demyelination in the peripheral nerve and the spinal nerve roots with aging.²⁴ Progressive changes such as loss of nerve cells also occur in the central nervous system, which may also contribute to the decreased vibration sense.²⁵ The spinal cord and spinal nerve roots may suffer significant compression in the elderly because of degenerative changes in the cervical and lumbar spine, even in the absence of symptoms and clinical findings. Indeed, we found a wide variation in the VPT values of elderly persons.

We found women to be more sensitive than age-matched men at several of the tested sites. The

difference between the sexes has been studied previously.^{2,15,18,26} It has been suggested that the vascular disorders of the heart and the lower limbs occur more frequently and earlier in men than in women.¹⁸ Therefore, separate reference intervals of VPT should be determined for each sex and decade.

Several authors have reported that sensitivity differs on the left and right sides of the body, with the limb on the left side reported to be more sensitive.²⁶ In the present study, the left side was more sensitive than the right side on the great toe, medial malleolus, and ulnar styloid. However, the difference in VPT values between the two sides of the body was small ($<3 \times 10^{-2}$ G) and negligible enough for determining the reference intervals.

The VPT of the ulnar styloid was lower than those in the lower extremities, which is in accordance with previous reports. As early as 1897, Treitel showed that the VPT is most sensitive in the upper limbs, and that it is finest in the distal parts of the limbs and poorer on the trunk. One explanation may be the difference in the size of the projection field in the central nervous system. The hands have wide projection areas in the cerebral cortex. The difference in the areas of perception may be due to the difference in receptor density.¹⁴

The knees are not very sensitive to vibratory stimuli.^{26,27} It was concluded that measuring the VPT at the patella with this instrument (SMV-5) is not feasible. No significant differences were found among the four foot regions (medial malleolus, lateral malleolus, great toe, fifth toe). Therefore, we provide average VPT values of the four sites as the reference interval of the foot.

The influence of BMI, smoking, and alcohol consumption on the VPT were not apparent in the present study. Previous studies have also revealed that neither habitual drinking nor smoking affected the VPT.

This study provides reference intervals of the VPT around the foot regions. The upper limit alone was specified, as the lower limit has no clinical meaning.

In the actual clinical applications there are several points to take into account. Measurements can be performed with the knees either bent (sitting position) or extended (supine position). Green²⁸ reported a U-shaped relation between skin temperature and the VPT in nondiabetic subjects, with 34°C being the nadir. He concluded that cooling might affect VPT by decreasing the sensitivity of Pacinian corpuscles; the reason for the decreased sensitivity due to warming is unclear. According to several other reports^{15,29} the VPT may be stable between 28°C and 36°C skin temperature. It would be preferable to measure the VPT at four sites of the foot bilaterally for comparison.

The VPT assessment can be used in diagnostic procedures, research, and follow-up studies to investigate the

course of the disease and the therapeutic effect. VPT measurements can be recommended as a complement to conventional neurological and neurophysiological evaluations. The present study is the first to define the reference interval of the VPT using a large population and taking into account the possible variables that may affect the measurement.

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