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Research paper

Psychophysical estimate of plantar vibration sensitivity brings additional information to the detection threshold in young and elderly subjects



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ABSTRACT

Objective: Vibration detection threshold of the foot sole was compared to the psychophysical estimate of vibration in a wide range of amplitudes in young (20–34 years old) and elderly subjects (53–67 years old).

Methods: The vibration detection threshold was determined on the hallux, 5th metatarsal head, and heel at frequencies of 25, 50 and 150 Hz. For vibrations of higher amplitude (reaching 360 μ m), the Stevens power function ($\Psi = k * \Phi^n$) allowed to obtain regression equations between the vibration estimate (Ψ) and its physical magnitude (Φ), the n coefficient giving the subjective intensity in vibration perception. We searched for age-related changes in the vibration perception by the foot sole.

Results: In all participants, higher n values were measured at vibration frequencies of 150 Hz and, compared to the young adults the elderly had lower n values measured at this frequency. Only in the young participants, the vibration detection threshold was lowered at 150 Hz.

Conclusion: The psychophysical estimate brings further information than the vibration detection threshold which is less affected by age.

Significance: The clinical interest of psychophysical vibration estimate was assessed in a patient with a unilateral alteration of foot sensitivity.

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1. Introduction

An electrophysiological study in humans (Kennedy and Inglis, 2002) reported the presence of both slow (Merkel and Ruffini corpuscles) and fast (Meissner and Pacinian corpuscles) adapting receptors in the foot sole, with far greater numbers of the latter (71% of tested units). These cutaneous mechanoreceptors detect the changes in the application of mechanical loads on the plantar surface during gait and standing. Skin mechanoreceptors can be classified into four groups based on their afferent firing properties [fast adapting (FA) vs. slow adapting (SA)] and receptive field size [type I (small defined boundaries), vs. type II (large undefined boundaries)]. Johansson et al. (1982) found that SAI and SAII skin afferents were activated by low vibration frequencies between 2 and 32 Hz whereas FAI were activated between 8 and 64 Hz and FAII between 64 and 400 Hz. Electrophysiological studies have

shown that the cutaneous afferents from the plantar surface project on the somatosensory cortex leading to a perceptual representation (Kandel et al., 2012). There are several studies indicating that plantar cutaneous load receptors contribute to controlling the standing balance and postural reflexes in healthy subjects (Wu and Chiang, 1997; Meyer et al., 2004). Indeed, balance problems are often related to cases where reduced plantar sensitivity occurs.

Examination of the vibration sense is widely used as a clinical examination in neurology and it is usually done at the medial or lateral malleolus. Many studies also measured the vibration detection threshold of the sole in healthy subjects in an attempt to compare normal values to those measured in aged individuals and diabetic patients (Kenshalo, 1986; Kekoni et al., 1989; Kowalzik et al., 1996; Wells et al., 2003; Lin et al., 2005; Perry, 2006; Hennig and Sterzing, 2009; Gu and Griffin, 2011; Schlee et al., 2009; Strzalkowski et al., 2015). On the other hand, very few data are found on the magnitude of the vibration estimate of the foot sole in response to the increased amplitude of the vibratory stimulus. To determine the estimate of vibrations delivered to the skin of the hand, Verillo et al. (2002) already used a

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psychophysical approach based on the method of Absolute Magnitude Estimation (AME). They showed that the subjective magnitude of vibration was substantially lower at all intensities in the older group. But these authors did not compare their data to the vibration detection threshold. Kenshalo (1986) proposed a method of single ramp-and-hold skin vibrations to explore the vibration perception at the level of the thenar eminence and the plantar foot. The methods cited above give an approach of the global gain of the sensory detection but no information on the threshold of perception.

The main objective of the present study was to propose a psychophysical approach of the relationship between the estimate (Ψ) of vibratory stimuli applied on the foot sole and the physical magnitude of the stimuli (Φ) using the Stevens power function, $\Psi = k * \Phi^n$. The n coefficient measured the gain in perception. Independently, the vibration detection threshold was determined in each participant. The second objective was to compare values of n and detection threshold in two groups of young (20–34 years old) and elderly subjects (53–67 years old) to identify significant age-related changes in the perception of a mechanical stimulation by the foot sole. This approach could be useful to the diabetologists and the podiatrists who have to diagnose patients at risk of diabetic neuropathy.

2. Methods

2.1. Subjects

Twenty healthy female and male subjects were explored. All were free of foot pain and had no antecedent of trauma or surgery of the feet and legs. None were involved in an exercise program. They were separated into two groups of 10 individuals according to their age range (20–34 years old/53–67 years old). Their characteristics are shown in Table 1.

This research adheres to the principles of the latest revision of the *Declaration of Helsinki*. The protocol was submitted to and approved by our institutional committee (CPP Sud Mediterranée 1). The procedures were carried out with the adequate understanding and written consent of the subjects.

Table 1 Characteristics of subjects.

Sex	Age	Weight	BMI
	Year	kg	kg/m ²
Group I: 20–34 years old			
CF M	20	65	21
TG M	21	104	30
EF F	21	62	22
RF M	21	74	23
JG F	22	48	20
VD M	22	71	20
LM F	22	57	20
VR F	33	61	21
CC F	34	57	21
DL M	22	68	21
Group II: 53–67 years			
BV M	53	70	23
JMG M	53	70	24
PG F	53	78	30
GL M	57	90	28
MF F	57	48	18
RG M	59	105	33
JPW M	62	75	25
JGS M	64	98	31
SR F	64	49	20
YJ M	67	100	30

BMI: body mass index.

2.2. Vibration sensitivity

The participants sat comfortably with their eyes closed and wore head phones to eliminate auditory cues associated with the onset of the vibration.

Skin sensitivity was evaluated using vibration testing at three frequencies (25, 50, and 150 Hz) at each one of three foot plantar locations (hallux, fifth metatarsal head, and heel). The vibration frequencies were chosen to target the activation of three different skin receptors in the glabrous skin of the foot (25 Hz for SAI, 50 Hz for FAI, and 150 Hz for FAII) based on the frequencies known to best recruit individual mechanoreceptors in the foot sole (Johansson et al., 1982; Lowrey et al., 2014). Sinusoidal vibrations were applied to the foot sole via a plastic probe (width: 2 mm; length: 5 mm) attached to a minishaker (model 201, Ling Dynamic Systems, Royston, UK). As recommended by Lowrey et al. (2014). prior to the onset of each trial the probe of the minishaker was placed in contact with the foot sole and a preload force of 2N was applied, manipulated by a vertical adjustment of the shaker and confirmed with a force transducer (model K13 - 0.02 kN, Scaime, Annemasse, France). Fig. 1 gives a schematic representation of the device.

Our vibrator device allowed to deliver different amplitudes of vertical motions of the probe and seven levels were retained (1, 2, 5, 10, 15, 20 and 25 arbitrary units). The vibration motion expressed in μm was measured using an accelerometer attached to the probe (model EOAS S114 D2500, MAES France, Les Clayessous-Bois, France) when applying a force of 2N on the probe. Fig. 2 shows the values of the vibration amplitudes measured at the three vibration frequencies. The vibration magnitude depended on its frequency and varied in a range of 10–360 μm at 25 Hz, 10–330 μm at 50 Hz, and 10–180 μm at 150 Hz. The three frequencies were tested at one site before moving on to the next site to minimize the total testing time. The testing frequencies were randomized at each foot sole location. The testing order of the foot sole location was also randomized across the participants. Both feet were tested in each participant.

First, the vibration detection threshold in each plantar location was determined by considering the lowest detectable load at each vibration frequency.

Second, a step increase in the vibration amplitude was performed at each of the vibration frequencies, the lowest amplitude corresponding to the detection threshold. Two trials were performed at each frequency. Judgements of increased stimuli intensity were recorded on a 1–10 cm visual analog scale. The participant's specific standards for 1 and 10 on this scale were established in pilot tests in which the lowest and the highest detected vibration stimuli were presented twice in order to acquaint the subjects with the full range of loads. After this

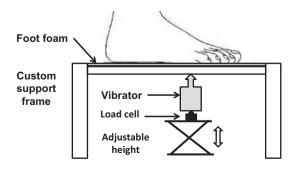


Fig. 1. Schematic representation of the vibration device including the foot support frame, the vibration probe and the load cell measuring the force applied on the foot sole

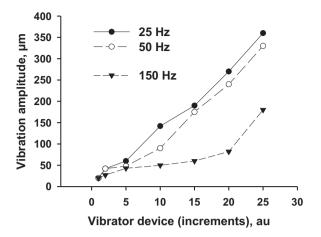


Fig. 2. Calibration of the vibration amplitude at three vibration frequencies.

acclimatization, the experimenter remained silent during further tests and the participants indicated their estimate immediately after each step increase in vibration amplitude. The right and left feet were used for all skin sensory testing. The whole duration of a trial consisting in progressive increase then decrease in vibration amplitude was 5 min.

2.3. Data analyses

The Stevens power function (Stevens, 1957), $\Psi = k^* \Phi^n$ was used to quantify the perceptual performance, where Ψ is the

estimate and Φ the vibratory stimulus. As previously performed (Balzamo et al., 1995; Scharf et al., 1986; Vie et al., 2015), the exponent n in this function was determined by a linear regression analysis between Napierian logarithmic (Ln) transformations of stimuli and estimation data using Excel program allowing to obtain the Ln Ψ = Ln k + (n * Ln Φ) relationship. The n coefficient is the slope of the Stevens power function and measures the changes in perception between the extreme values of loads and the Lnk coefficient could hypothetically correspond to the detection threshold.

As shown in Fig. 3 for the Ψ vs. Φ relationships obtained in the same subject, the logarithmic transformation closely approached a linear relationship. To determine statistical inter-individual differences in vibration sensation, ANOVA for repeated measures was used to compare $\operatorname{Ln} k$ and n coefficients with their standard errors. Significance was accepted if p < 0.05.

3. Results

3.1. Determination of vibration detection thresholds

At each plantar location and each vibration frequency, the subject indicated the magnitude of the lowest perceptible load. In all participants, no differences in the detection threshold were found between the right and left feet. In the young participants the vibration detection threshold was significantly lowered at 150 Hz in the three plantar locations (Fig. 4). In the elderly, the detection threshold did not decrease at 150 Hz and, compared to that measured in the young participants, it was significantly elevated in the 5th metatarsal head and the heel.

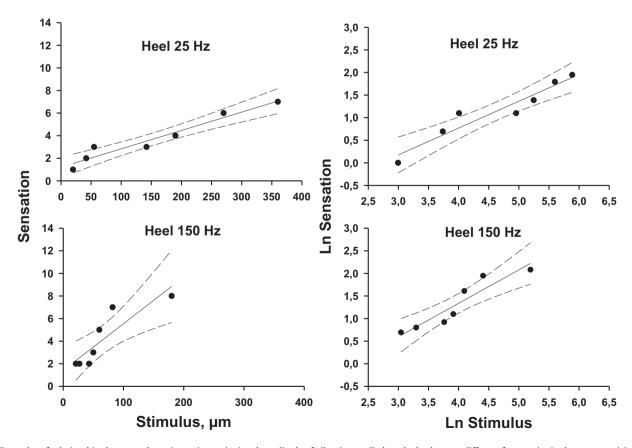


Fig. 3. Examples of relationships between the estimate (sensation) and amplitude of vibration applied on the heel at two different frequencies in the same participant. The Napierian logarithmic transformation of stimuli and estimation data (right panels) ($\text{Ln } \Psi = \text{Ln } k + (n^* \text{Ln } \Phi)$ relationship) closely approaches linear regression lines compared to the regression line drawn on pair raw values of vibration estimate and magnitude (expressed in μ m) (left panels).

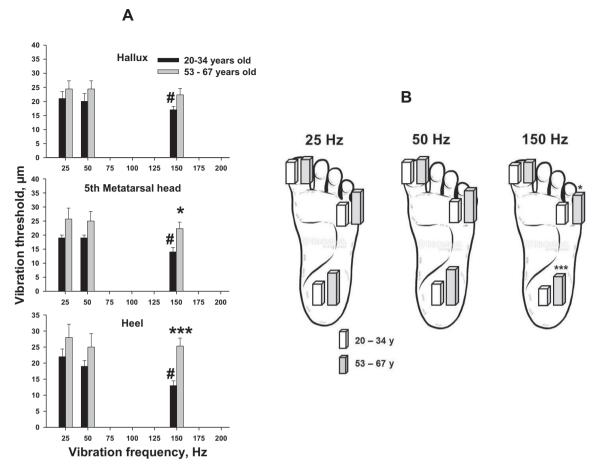


Fig. 4. Changes in the vibration detection threshold with aging (Mean value \pm SEM). A: Only in the younger subjects the vibration detection threshold was significantly lowered when the 150 Hz frequency was used to activate the skin afferents in the hallux, 5th metatarsal head, and the heel (symbol #: p < 0.05). In the elderly, the vibration detection threshold did not vary with the vibration frequency and was significantly higher than in young subjects in the 5th metatarsal head and the heel (p < 0.05; p < 0.001). B: Schematic representation of the intergroup differences between the vibration thresholds in the three plantar locations (p < 0.05; p < 0.001).

3.2. Determination of the Lnk and n coefficients

A total of 360 regression equations were calculated in the 20 participants (both feet, three plantar locations, three vibration frequencies). The n and Lnk values were only considered when the analysis of variance confirmed the significance against zero (p < 0.05) of the R coefficient of linear regression. This was verified for 342 regression equations. Fig. 5 gives the mean \pm SEM of individual values of n and Lnk coefficients obtained in each group of participants. All Lnk values were negative and thus any decrease in absolute value of Lnk should indicate elevated sensitivity to the lowest loads, i.e., a lowered detection threshold. In all participants, the Lnk value did not significantly vary with the vibration frequency, whereas the n values were significantly higher at the 150 Hz vibration frequency in the three plantar locations. No differences in Lnk and n values were found between the right and left feet in all participants.

In the elderly, the n coefficient was significantly less when the vibration sensitivity was tested at 50 Hz in the 5th metatarsal head and the heel and at 150 Hz in the three plantar locations. No intergroup differences in $\operatorname{Ln} k$ values were noted.

In the three plantar locations, we found significant negative correlations between the *n* coefficient and the age of subjects but only at the vibration frequency of 150 Hz (Fig. 6).

4. Discussion

4.1. Main results

The originality of the present study was to explore in young adults and the elderly the psychometrical estimate (Ψ) of a plantar vibration in a wide range of magnitudes (Φ) and to compare data to the vibration detection threshold measured in the same subjects. The slope n of the linear regression between pair values of Ψ and Φ had the dimension of a gain of vibration perception. The psychometrical approach showed that: (1) in both groups of participants, the n value was significantly higher at the 150 Hz vibration frequency in the three plantar locations and no differences were found between the feet; (2) the elderly subjects had lower *n* values determined at 150 Hz in the three plantar locations and at 50 Hz in both the 5th metatarsal head and the heel; (3) negative correlations between the *n* values and age were obtained at 150 Hz in the three plantar locations; (4) in the youngest participants the vibration detection threshold was significantly lowered at 150 Hz in the three plantar locations while, in the elderly, it did not vary at 150 Hz. On the other hand, the Lnk coefficient cannot serve to evaluate the detection threshold because it did not significantly vary with the vibration frequency and no intergroup differences were found.

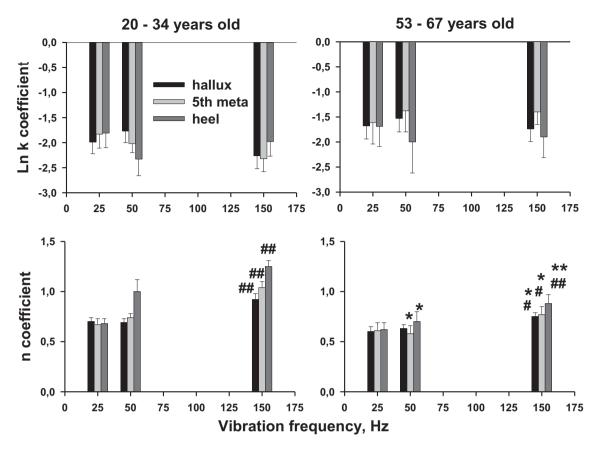


Fig. 5. Mean value (\pm SEM) of Lnk and n values of the linear regressions obtained in each participant at each plantar location between the estimate (sensation) and the stimulus. Symbol # indicates that n values measured at the 150 Hz vibration frequency were significantly higher than those measured at 25 and 50 Hz (*p < 0.01; $^{**}p$ < 0.01). Asterisks were used to depict significant intergroup differences between n values at the same vibration frequency (*p < 0.05; $^{**}p$ < 0.01). No difference was measured at the 25 Hz frequency.

We conclude that the psychophysical estimate of the vibration sensation (n coefficient) and the measurement of vibration detection threshold bring complementary information on the mechanosensitivity of the foot sole.

4.2. Comparison with literature data on the vibration detection threshold

The values of the vibration detection threshold reported by our participants were in the range of those given by Strzalkowski et al. (2015) at 40 Hz (12–17 $\mu m)$ and 250 Hz (2–6 $\mu m)$, and by Lowry et al. at 250 Hz (6–15 $\mu m)$. As in the present study, both previous ones had shown that the vibration detection threshold was lowered when the vibration frequency increased.

Our study confirms the elevation of the plantar vibration detection threshold in the elderly (Kenshalo, 1986; Wells et al., 2003; Lin et al., 2005; Perry, 2006) and this was also shown for the hand (Gescheider et al., 1994, 1996; Verillo et al., 2002). In their very well documented study in 484 subjects aged from 20 to 86 years, Lin et al. (2005) said that the age was significantly correlated with the vibratory detection threshold of the foot. Perhaps due to the limited number of participants in our study, we did not obtain a correlation between the age and the detection threshold. Wells et al. (2003) reported that the detection thresholds for fast-adapting type I receptor-mediated frequencies were age invariant whereas those for fast-adapting type II (FA-II) receptor-mediated frequencies increased with age. Compared to the data obtained in our young participants, the plantar vibration detection threshold of the elderly was selectively elevated at the 150 Hz frequency

which only activates the FA-II receptors (Johansson et al., 1982), corroborating the observations by Wells et al. (2003) and also Lin et al. (2005). These age-related changes in vibration perception were measured in the 5th metatarsal head and the heel, and not in the hallux.

4.3. Data on the psychophysical vibration estimate

We can only compare our data to those reported by Verillo et al. (2002) who determine the estimate of vibrations delivered to the skin of the hand. They did not report the consequence of increased vibration frequency on the vibration estimate but they showed that the subjective magnitude of vibration was substantially lower at all intensities in their older group.

In all our participants, we measured in the three plantar locations higher n values at the 150 Hz vibration frequency which selectively activate the fast adapting type II receptors, suggesting that the sensory pathways carried by these receptors prevail. Our observations corroborate electrophysiological data. Indeed, Kennedy and Inglis (2002) have shown a great number of FA-II receptors in the human foot sole compared to the slow-adapting (SA) and type I fast-adapting (FA-I) ones, which are respectively activated between vibration frequencies of 2 and 32 Hz, and 8 and 64 Hz (Johansson et al., 1982).

There was an age-dependent decrease in n values measured at the sole 150 Hz vibration frequency in the three plantar locations, confirming the age-dependent elevation of the vibration detection threshold of FA-II receptors. The reduced plantar sensitivity here found in elderly subjects agrees with their balance problems

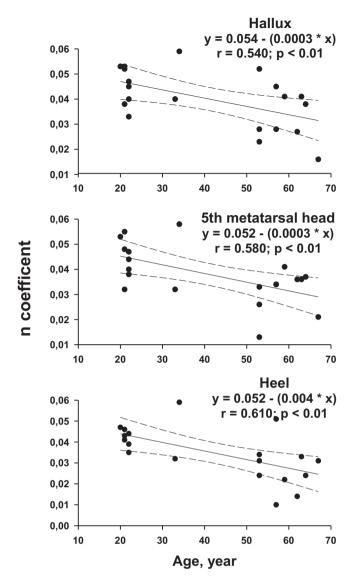


Fig. 6. Linear regressions with 95% confidence intervals obtained between the n coefficient of the Ln Ψ = Lnk + (n * Ln Φ) relationship and the age of participants in response to the 150 Hz vibration frequency applied on the hallux, 5th metatarsal head or the heel.

(Wu and Chiang, 1997; Meyer et al., 2004). Compared to the detection threshold, our psychophysical approach brings new information because in the elderly the n coefficient was also reduced in the hallux. Thus, the n coefficient of the relationship between estimate and vibration amplitude was more affected by age than the detection threshold. Gescheider et al. (1996) have already reported that the discriminative capacities of the hand of elderly were mostly affected for stimuli above the detection threshold. In our study, the n coefficient mostly depends on the highest amplitude of the vibration stimuli.

The Lnk coefficient being not dependent on the vibration frequency and the age of subjects, we conclude that it does not represent a valuable estimate of the vibration detection threshold.

4.4. Clinical relevance

We examined a 66 y old male patient who related posterior pinch disk of the 3rd to the 5th lumbar metamere assessed by X ray images, leading to altered sensitivity on the course of the left external popliteal nerve. Fig. 7 represents the *n* values measured

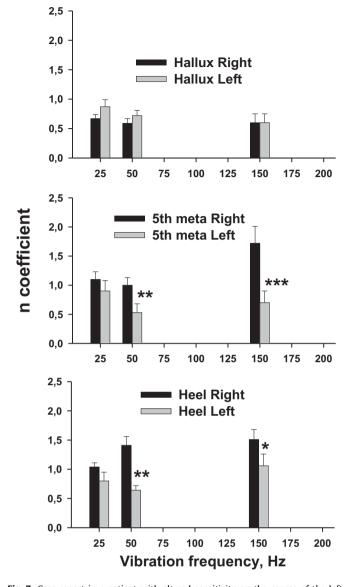


Fig. 7. Case report in a patient with altered sensitivity on the course of the left external popliteal nerve due to posterior pinch disk of the 3rd to the 5th lumbar metamere. The n coefficient measured in the three plantar locations was significantly lower in the left 5th metatarsal head and left heel, i.e., at the locations of the altered clinical sensitivity (p < 0.05; p < 0.01; p < 0.001).

in the three plantar locations of both feet, and shows significantly lower n values at the 50 and 150 Hz vibration frequencies in the left 5th metatarsal head and the left heel, i.e., the locations of his altered clinical sensitivity which seem to prevail on the FA-I and FA-II sensory pathways.

5. Conclusions

We have completed the goals of the present study. Indeed, the psychophysical approach of the relationship between the n estimate of a vibratory stimuli applied on the foot sole and its physical magnitude brings valuable and reproducible information on the gain of perception of plantar loads. The vibration detection threshold was less informative because it did not vary with age and also did not depend on the vibration frequency in our elderly participants. It merits to be underlined that the whole vibration trial, including the determination of the detection threshold followed by the progressive increase in vibration magnitude, needed less than 5 min and the determination of the n coefficient of the Sevens'

function using basic Excel software was easy. Further studies using this new method are needed to assess pathological alterations of the sole somaesthesia in diabetic patients who often consult diabetologists and podiatrists.

Conflict of interest

The authors declare they have no conflict of interest.

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References

- Balzamo, E., Burnet, H., Zattara-Hartmann, M.C., Jammes, Y., 1995. Increasing background inspiratory resistance changes somatosensory sensations in healthy man. Neurosci. Lett. 197, 125–128.
- Gescheider, G.A., Bolanowski, S.J., Hall, K.L., Hoffman, K.E., Verillo, R.T., 1994. The effects of aging on information-processing channels in the sense of touch: I. Absolute sensitivity. Somatosens. Mot. Res. 11, 345–357.
- Gescheider, G.A., Edwards, R.R., Lackner, E.A., Bolanowski, S.J., Verillo, R.T., 1996. The effects of aging on information-processing channels in the sense of touch: III. Differential sensitivity to changes in stimulus intensity. Somatosens. Mot. Res. 13, 73–80.
- Gu, C., Griffin, M.J., 2011. Vibrotactile thresholds at the sole of the foot: effect of vibration frequency and contact location. Somatosens. Mot. Res. 28, 86–93.
- Hennig, E.M., Sterzing, T., 2009. Sensitivity mapping of the human foot: thresholds at 30 skin locations. Foot Ankle Int. 30, 986–991.
- Johansson, R.S., Landstrom, U., Lundstrom, R., 1982. Responses of mechanoreceptive afferent units in the glabrous skin of the human hand to sinusoidal skin displacements. Brain Res. 244, 17–25.
- Kandel, E., Schwartz, J., Jessell, T., 2012. Principles of Neural Science, 4th ed. McGraw-Hill Medical, New York.

- Kekoni, J., Hämäläinen, H., Rautio, J., Tukeva, T., 1989. Mechanical sensibility of the sole of the foot determined with vibratory stimuli of varying frequency. Exp. Brain Res. 78, 419–424.
- Kennedy, P.M., Inglis, J.T., 2002. Distribution and behaviour of glabrous cutaneous receptors in the human foot sole. J. Physiol. 538, 995–1002.
- Kenshalo Sr., D.R., 1986. Somesthetic sensitivity in young and elderly humans. J. Gerontol. 41, 732–742.
- Kowalzik, R., Hermann, B., Biedermann, H., Peiper, U., 1996. Two-point discrimination of vibratory perception on the sole of the human foot. Foot Ankle Int. 17, 629–634.
- Lin, Y.H., Hsieh, S.C., Chao, C.C., Chang, Y.C., Hsieh, S.T., 2005. Influence of aging on thermal and vibratory thresholds of quantitative sensory testing. J. Periph. Nerv. Sys. 10, 269–281.
- Lowrey, C.R., Perry, S.D., Strzalkowski, N.D., Williams, D.R., Wood, S.J., Bent, L.R., 2014. Selective skin sensitivity changes and sensory reweighting following short-duration space flight. J. Appl. Physiol. 116, 683–692.
- Meyer, P.F., Oddsson, L.I., De Luca, C.J., 2004. The role of plantar cutaneous sensation in unperturbed stance. Exp. Brain Res. 156, 505–512.
- Perry, S.D., 2006. Evaluation of age-related plantar-surface insensitivity and onset of age of advanced insensitivity in older adults using vibratory and touch sensation test. Neurosci. Lett. 392, 62–67.
- Scharf, B., Buus, S., 1986. Audition I: stimulus, physiology, threshold. In: Boff, K.T., Kaufman, I., Thomas, J.P. (Eds.), Handbook of Perception and Human Performance, Vol. 1. Wiley, New York, pp. 253–268.
- Schlee, G., Sterzing, T., Milani, T.L., 2009. Foot sole skin temperature affects plantar foot sensitivity. Clin. Neurophysiol. 120, 1548–1551.
- Stevens, S.S., 1957. On the psychological law. Psychol. Rev. 64, 153-181.
- Strzalkowski, N.D., Triano, J.J., Lam, C.K., Templeton, C.A., Bent, L.R., 2015. Thresholds of skin sensitivity are partially influenced by mechanical properties of the skin on the foot sole. Physiol. Rep. 3. http://dx.doi.org/10.14814/phy2.12425.
- Verillo, R.T., Bolanowski, S.J., Gescheider, G.A., 2002. Effect of aging on the subjective magnitude of vibration. Somatosens. Mot. Res. 19, 238–244.
- Vie, B., Nester, C.J., Porte, L.M., Behr, M., Weber, J.P., Jammes, Y., 2015. Pilot study demonstrating that sole mechanosensitivity can be affected by insole use. Gait Posture 41, 263–268.
- Wells, C., Ward, L.M., Chua, R., Inglis, J.T., 2003. Regional variation and changes with ageing in vibrotactile sensitivity in the human footsole. J. Gerontol. A Biol. Sci. Med. Sci. 58, 680–686.
- Wu, G., Chiang, J.H., 1997. The significance of somatosensory stimulations to the human foot in the control of postural reflexes. Exp. Brain Res. 114, 163–169.