Age and Gender Differences in Skin Sensory Threshold Assessed by Current Perception in Community-Dwelling Japanese

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The purpose of this study was to investigate age and gender differences in current perception thresholds (CPT) in Japanese citizens. CPT values at frequencies of 2000, 250 and 5 Hz reflect different types of peripheral sensory nerve functions. Since there have been only a limited number of reports which investigated CPT values in community-dwelling people, little is known about variations with age and gender. The present study therefore concentrated on a large population of 1632 individuals (men; 818 mean age $\pm$ standard deviation 59.4 $\pm$ 10.9, women; 814, 59.4 $\pm$ 11.1) in a Japanese community. Significant gender differences in CPT values at 250 and 5 Hz were observed. Multiple comparisons among 4 age groups (40s, 50s, 60s and 70s) showed age-related differences in CPT values at 2000 and 250 Hz in both genders. However, age and gender interactions with reference to CPT values appeared to be different between these latter two frequencies. At 5 Hz, only men showed age-related variations. These results indicated gender differences in fiber-specific aging changes. *J Epidemiol*, 2000 ; 10 : S33-S38.

gender influence, current perception thresholds, neurometer, CPT, age-related change

INTRODUCTION

The Neurometer (Neurotron Inc, Baltimore, USA) is a computerized automated neurodiagnostic device that can measure peripheral sensory function quantitatively ¹. Compared with other conventional quantitative sensory parameters, such as thermal or vibration sensation thresholds ^{2,3}, current perception threshold (CPT) testing with the Neurometer has several merits. First, the device can stimulate three different types of sensory peripheral nerve fibers (A β , A δ and C fibers) selectively ⁴. Second, its capacity for measuring peripheral sensory function is barely affected by skin conditions, such as skin thickness or skin temperature and it can maintain an electrical current despite alterations in skin resistance ⁵. Therefore, a high reproducibility of CPT values is possible ⁵. Third, application of this machine is relatively easy compared with other quantitative sensory testing methods ⁵. For reasons of selectivity, reproducibility, and ease of handling, this method is particularly appropriate for quantitative estimation of peripheral sensory nerve function ⁶.

There have been many clinical investigations into diabetic neuropathy ⁷⁻¹⁰, carpal tunnel syndrome ^{11,12} and other peripheral neuropathy ¹³ with the Neurometer. The results indicated its potential advantages for epidemiological studies of peripheral neuropathy.

However, little is known about age and gender effects on CPT values because there have only been a limited number of epidemiological studies on community-living people. The effects of aging ¹⁴ or gender ¹⁵ on CPT values were investigated in only small populations with less than 200 subjects. In the present case, we examined age and gender differences in CPT values obtained from a relatively large community-dwelling population.

MATERIALS AND METHODS

A longitudinal study of aging (National Institute for Longevity Sciences-Longitudinal Study of Aging: NILS-LSA) has been conducted since November, 1997. In this study, participants are stratified random samples of community-dwelling

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people, aged 40 to 79 years old in Obu-shi and Higashiura-cho, located in Aichi prefecture, Japan. Mail orders for participation to this study were delivered to people selected randomly from resident registration records. The responders were invited to our facility. After explanation of this study, those giving written informed consent were invited to our facility on a subsequent day for evaluation of aging. Detailed examinations included medical evaluation, sensory aging evaluation, body composition analysis and anthropometry, physical function evaluation, nutritional analysis, and psychological tests. The plan was to evaluate 2400 men and women longitudinally every two years. CPT testing was performed on all participants as part of the medical examination. The total number of subjects who received CPT testing was 1632 who attended from November, 1997 to September, 1999.

CPT testing with the Neurometer was performed in a relatively quiet room with the subject seated. The stimulus site was located on the left index finger. The device emits sinusoidal alternating currents at 2000, 250 and 5 Hz at intensities from 0 to 10 mA. This constant current output automatically compensates for alterations in skin resistance and provides a standardized stimulus independent of different skin thickness, degree of skin dryness or perspiration, or drying of the electrode paste¹¹⁾. Electrical stimulus was initially increased until a specific sensation was reported by the subject. Short stimuli were then applied at progressively lower amplitudes until a minimal, but consistent threshold was detected. One CPT value corresponded to 10 μ A. All measurements of CPT values for a single participant were carried out at one time within an average period of about 5 minutes. The intra- and interrater reliability in this method is shown in Table 1. As previously described, the coefficient of variation of CPT measures was frequency dependent, with the smallest coefficient of variation at 2000 Hz and the largest at 5 Hz⁵⁾.

Data analysis was performed with the SAS release 6.12 statistical package (SAS Institute, Cary, NC). First, we analyzed CPT values across genders with the UNIVARIATE procedure. Second, comparisons between both genders for the same age categories were made using the TTEST procedure. Multiple

comparisons among four age groups (40-49, 50-59, 60-69, and 70-79 years) in each gender were carried out using the GLM procedure (Tukey). Finally, correlation coefficients between age and CPT values at each frequency in each gender were calculated with the CORR procedure. Statistical significance was taken as $p < 0.05$.

RESULTS

The age and gender distributions of all participants are shown in Table 2. The mean age for men was 59.4 ± 10.9 years (mean $\pm$ standard deviation), and for women 59.4 ± 11.1 years. Figures 1, 2 and 3 show histograms of CPT values at each frequency for both genders and Tables 3, 4 and 5 summarize the statistical characteristics. The results of overall comparisons between genders at each frequency were as follows: 2000 Hz, no significant difference; 250 Hz, women showed lower CPT values than men ($p < 0.001$); 5 Hz, women showed lower CPT values than men ($p < 0.001$). At 2000Hz, there were no gender differences across the same age groups. At 250Hz, significant gender differences were seen for those in their 40s and 60s. At 5Hz, significant gender differences were seen in the 40s and 50s age groups. The results of multiple comparisons among the four age groups for each gender were as follows: in men, there were significant differences between the 40s and 70s groups at 2000 ($p < 0.05$) and 250 Hz ($p < 0.05$). At 5 Hz, there was a significant difference between the 40s and 60s groups ($p < 0.05$). In women, at 2000Hz, there were significant differences between those in their 40s and 60s ($p < 0.05$), and 70s groups ($p < 0.001$). At 250Hz, there was a significant difference between the 40s and 70s groups, and at 5 Hz there were no significant differences among the four age groups. Correlation coefficients between age and CPT values were as follows: 2000Hz: men, $r = 0.115$, $p < 0.01$; women, $r = 0.177$, $p < 0.001$; 250 Hz: men, $r = 0.108$, $p < 0.01$; women, $r = 0.142$, $p < 0.001$; 5Hz: men, $r = -0.088$, $p < 0.05$; women; $r = 0.056$, not significant.

Table 1. Intra- and interrater reliability.

	correlation coefficient	prevalence of difference (%)		C.V. (%)
		≤ 10 CPT values	≤ 20 CPT values	
Intrarater (n=13)				
2000Hz	0.97 (p<0.001)	85	92	4.7
250Hz	0.95 (p<0.001)	69	92	12.0
5Hz	0.97 (p<0.001)	77	100	15.3
Interrater (n=13)				
2000Hz	0.97 (p<0.001)	54	92	5.6
250Hz	0.98 (p<0.001)	77	100	10.7
5Hz	0.86 (p<0.001)	85	85	26.7

c.v. : coefficient of variation

DISCUSSION

To our knowledge, this is the first report of age and gender differences in CPT values obtained from community-dwelling people in Japan. There are no reference CPT values in Japan, but in the United States, reference values have been used to examine peripheral sensory function with the Neurometer^{11,12}. These values were as follows: 2000Hz: 243 ± 68 (mean $\pm$ standard deviation), 250Hz: 91 ± 35 , 5Hz: 50 ± 21 . Compared with

our study, the number of participants assessed to obtain these reference values was limited. Furthermore, there was no consideration of age and gender differences in the United States data on a limited number of subjects.

Our results showed gender differences in CPT values at 250 and 5 Hz, but were in disagreement with one previous report of women having lower thresholds than men at all three frequencies¹⁵. This discrepancy may be due to differences in the sample size and participant selection method. Selection in our study was performed randomly. Furthermore, the number of our participants, stratified by age and gender, was relatively large. The selection method in the previous study was not described and there were only 60 subjects. Therefore, our results are expected to provide reliable CPT values for community-dwelling people.

Our results demonstrated age-related changes in CPT values differed with different frequencies. At 2000 Hz, at which A β fibers are stimulated⁴, both men and women showed age-related changes in multiple comparisons. At 250Hz, corresponding

Table 2. Age and gender distribution of subjects.

Age Groups	Men	Women
40-49	199	204
50-59	207	201
60-69	205	200
70-79	207	209
Total	818	814

Figure 1. Histogram of CPT values at 2000Hz.

Figure 2. Histogram of CPT values at 250Hz.

to A δ fibers ⁴, age-related changes were also seen in both genders. In both cases, participants in their 40s showed lower CPT values than those in their 70s. On the other hand, at 5 Hz, which represents the function of C fibers ⁴, only men showed a difference in multiple comparisons, having a negative correlation between age and CPT values ($r = -0.088$, $p < 0.05$). The fact that the correlation coefficient was negative in contrast to those at 2000 and 250 Hz, indicated that the age and gender effects on CPT values at 5 Hz involve different mechanisms compared with higher frequencies.

Animal studies have shown that myelinated fibers are affected by aging, whereas unmyelinated fibers hardly change ¹⁶. These results suggest that age-related changes in peripheral nerves mainly relate to changes in the myelin sheath. A β and A δ fibers are both myelinated ¹⁷, while C fibers are unmyelinated ¹⁷. These differences in peripheral nerve fiber structure could affect age-related changes in CPT values at each fre-

quency. The results of our study are thus consistent with the animal data.

Despite the structural similarity between A β and A δ fibers, age and gender interactions with regard to CPT values were different between 2000 and 250 Hz. At 2000 Hz, there was no gender difference in aging effects on CPT values, with no significant gender differences among any age groups. On the other hand, at 250 Hz, women in their 40s showed significantly lower CPT values compared with their male counterparts, but not in the 70s group. These results indicated the aging effect on CPT values at 250 Hz is more significant in women compared with men. One previous study suggested a gender difference in myelinated fiber density, which could lead to better myelinated nerve function in women ¹⁸. This result indicated a structural difference in myelinated fibers between both genders, which may be related to our result. Further investigation is required with reference to age and gender influences on

Figure 3. Histogram of CPT values at 5 Hz.

Table 3. Age-related distribution of CPT values at 2000 Hz.

Age	Men	Women	Gender difference (p value)
40-49	229 ± 60	219 ± 58	n.s.
50-59	233 ± 62	232 ± 61	n.s.
60-69	240 ± 58	235 ± 56	n.s.
70-79	248 ± 68	248 ± 66	n.s.
Total	238 ± 63	234 ± 62	n.s.

mean ± standard deviation,

* : $p < 0.05$, *** : $p < 0.001$, n.s. : not significant

Table 4. Age-related distribution of CPT values at 250 Hz.

Age	Men	Women	Gender difference (p value)
40-49	92 ± 40	79 ± 40	< 0.01
50-59	96 ± 44	89 ± 47	n.s.
60-69	100 ± 44	89 ± 39	< 0.01
70-79	104 ± 50	98 ± 43	n.s.
Total	98 ± 45	89 ± 43	< 0.001

mean ± standard deviation,

* : $p < 0.05$, *** : $p < 0.001$, n.s. : not significant

Table 5. Age-related distribution of CPT values at 5 Hz.

Age	Men	Women	Gender difference (p value)
40-49	72 ± 40	50 ± 30	< 0.001
50-59	68 ± 38	55 ± 33	< 0.001
60-69	61 ± 35	56 ± 36	n.s.
70-79	63 ± 44	57 ± 36	n.s.
Total	66 ± 40	55 ± 34	< 0.001

mean ± standard deviation, * : $p < 0.05$, n.s. : not significant

CPT at these higher frequencies.

As shown in Table 5, a significant gender difference in CPT values at 5 Hz in middle- aged people was found. No previous studies detected such age and gender interaction at this frequency. Presumably, the results reflect the large number of participants in our study and the associated high statistical power. At this frequency, the Neurometer stimulates C fibers selectively, conveying noxious stimuli ¹⁷. The electrically stimulated pain threshold is known to be similar to that of clinical pain due to activation of C fibers ¹⁹. Thus, CPT values at 5 Hz may have relevance to the pain threshold due to electrical stimulation. In fact, CPT stimulus at 5 Hz is sensed as 'burning' or 'stinging' and is unpleasant at increased stimulus levels. On the other hand, stimulus at 2000 Hz is sensed as 'buzzing' or 'tingling' without unpleasant pain at increased stimulus ⁵. Gender differences in the pain threshold, especially the electrical stimulation pain threshold are well known ²⁰. With electrical pain stimulation, women show a significantly lower electrical pain threshold than men ²⁰. This biological mechanism is considered to depend on central processing for noxious stimuli ²⁰. Significant variations at 5 Hz between men and women in the 40s and 50s groups in our study may be related to this.

Our results also showed age-related changes in CPT values at 5 Hz were only seen in men. Taking into account the fact that unmyelinated fibers are thought to be hardly affected by aging ¹⁶, the age-related change at 5 Hz in men may be a consequence of aging changes in the central processing system for noxious stimuli, rather than in peripheral sensory nerve fibers themselves. The lack of gender differences in CPT values at 5 Hz in the 60s and 70s groups is consistent with this hypothesis.

Our study had some limitations. For example, a detailed neurological examination was not performed. Patients with peripheral neuropathies are reported to show significantly higher CPT values compared with normal subjects ^{15,17}. It is probable that age and gender interaction on CPT values obtained from our subjects, who were confirmed to be normal by detailed neurological examination, may be different from our results. A second limitation is the limited period of training for CPT testing. In the NILS-LSA, evaluations for participants are scheduled in a relatively busy time schedule. Thus, participants must take CPT testing without sufficient knowledge of the sensation of this current.

The present results indicated the important effects of age and gender on CPT values at different frequencies in clinical or epidemiological studies. CPT testing appears to have strong potential to provide useful information in epidemiological or clinical studies because of its comparability and reproducibility. Recently, new CPT application techniques for the determination of neuroselective electrical pain perception thresholds have been used ²². Studies have been conducted on the effects of narcotics ²³ and local analgesics ⁴ with this new application. Our results indicated significant age and gender interaction in CPT values at 5 Hz, which is associated with pain thresholds.

In epidemiological or clinical studies with the Neurometer, especially with such new applications, age and gender differences should be considered when interpreting results.

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