SIMILARITIES IN AGE DIFFERENCES IN HEAT PAIN PERCEPTION AND THERMAL SENSITIVITY

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Age differences in the thresholds for heat pain, warmth and cold were studied in 64 healthy persons from 17 to 63 years of age (32 women, 32 men). The stimuli were applied to the thenar and the dorsum pedis with a contact thermode. The thresholds increased significantly with age in all modalities on the foot, but not on the hand. Furthermore, the quotients of the individual foot and hand thresholds revealed a significant relative increase in all thresholds on the foot. The length of the afferent pathways seems to influence the degree of age-related changes both in heat pain perception and in thermal sensitivity, resulting in a distal-proximal pattern of age-dependent decline.

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According to the most comprehensive reviews, the evidence so far for age changes in pain perception is conflicting (1-4). However, this may be due mainly to differences in the stimulation techniques, sites of stimulation, and psychophysical methods used. A majority of the studies on age changes in the pain threshold have found a decrease in pain sensitivity with increasing age. This is especially true where thermocutaneous stimulation has been applied. Up to now there have been only a few studies of age changes in pain tolerance threshold and discrimination ability, and the results have been mixed.

There is a good deal of evidence that sensitivity to temperature, touch and vibration declines with age (3-6). The decline in sensitivity is usually most pronounced in the lower extremities (7-14), which suggests that the length of the afferent pathways is of great importance in somatosensory aging. Therefore, a distal-proximal pattern of somatosensory decline has been assumed to be a usual accompaniment of aging (15). To explain this pattern and other similarities between normal aging and neuropathological changes in the peripheral nervous system, some authors have postulated a distal axonopathy as the aging mechanism underlying somatosensation (6,15).

The aim of the present study was to find out whether the age-dependent changes in pain sensitivity have a topographic distribution similar to those of the other somatosensory modalities, i.e. with a distal-proximal shift. If so, a distal-proximal pattern should be demonstrable. To test this hypothesis, we assessed pain thresholds at two sites, on the hand and on the foot. As a control for having a representative sample with respect to somatosensory aging, we also measured thermal sensitivity because its age-dependent decline is well known and shows a distal-proximal pattern (8,9,11,12).

METHOD

Subjects

A total of 64 subjects were recruited for three age groups: 17 to 29 (n=20), 30 to 44 (n=22) and 45 to 63 (n=22) years of age. The corresponding means were 23.8 (SD=3.6), 36.8 (SD=5.3) and 51.2 (SD=5.4) years. Each group consisted of half men and half women. To enable us to study changes in pain and thermal sensitivity in relation to nonpathological aging, prior to the experiment we assessed the subjects' current neurological status including lower tendon reflexes, the motor and sensory status of the legs, and lumbosacral motion. Furthermore, we took a history to exclude individuals with any disorders that lead to somatosensory impairment. Pathological skin changes at the sites of measurement were excluded by visual inspection.

Apparatus and Procedure

The stimulator used was a temperature-controlled contact thermode with a stimulation surface of 1.6 x 3.6 cm^2, mounted on an articulated arm. Contact pressure could be adjusted and was held at 0.4 N/cm^2. The apparatus also included a thermode controller with a microcomputer for managing thermal stimulation and an IBM personal computer for controlling the procedures and giving a basic evaluation. Integrated into the response panel were visual signalling devices. Acoustic cues were delivered by the sound generator of the personal computer. The apparatus (PATH Tester MPI 100) had been developed earlier in the Department of Neurology of the Max Planck Institute for Psychiatry in cooperation with Phywe Systeme GmbH (Göttingen) (for details see 16).

The subjects sat upright at a table. For measurement on the hand, they placed the thenar of the hand on the thermode. For measurement on the foot, the thermode was attached to the lateral dorsum pedis with the long edge at a distance of about 1 cm from the toes.

Determination of the pain threshold

Beginning at 40 °C, 8 heat stimuli were applied with a rate of temperature change of 0.7 °C/s. The subjects were instructed to press a button as soon as they felt pain. Each time they pressed the button, the temperature returned to the base value at a cooling rate of 2.0 °C/s. The stimulus intervals lasted at least 10 s. The pain threshold was calculated as the mean of the peak temperatures of the last 5 stimuli. The start of each trial was announced visually and acoustically, but the stimulus was presented with a pseudo-randomized delay of between 1 and 3 s.

Determination of the warmth and cold thresholds

Starting at a temperature of 32 °C, 7 warm stimuli and then 7 cold stimuli were administered. The rate of the temperature change was again 0.7 °C/s. The subjects had to press a button as soon as they noticed a change in temperature. Thereupon, the temperature returned to the base value (2.0 °C/s). The mean differences between the base temperature and the peak temperature in the 2 sets of 7 trials were the measures of the warmth and cold thresholds. The stimuli were delayed between 1 and 3 s (pseudo-randomized intervals) after the visual and acoustic signals for the start of a trial.

The thresholds for warmth, cold and pain were determined in that order, twice a session at each site, always beginning with the hand.

Evaluation

For each modality (pain, warmth, cold) and each point of stimulation (hand, foot) a separate regression analysis was computed with the independent variable "age" and the dependent variable "threshold". The p values for the linear and quadratic trend were assessed via the F test of the change in explained variance (F change). Furthermore, the relationship between the age-dependent changes in threshold found on the hand and on the foot was evaluated. Because of the marked differences in the distributions for the different thresholds, the threshold values for each distribution were first transformed into a standard scale with a mean of 100 and a standard deviation of 10. Then individual foot/hand quotients were computed and a regression analysis was performed in the manner described.

RESULTS

Table I gives the thresholds for the three

Table I - Pain thresholds and thresholds for sensitivity to warmth and cold (mean ± SD; ° C) for the three age groups: 17 to 29 (A, n = 20), 30 to 44 (B, n = 22), and 45 to 63 (C, n = 22) years of age; all subjects assessed twice.

	A	B	C
Pain			
Hand	45.6 ± 2.5	45.2 ± 2.5	45.7 ± 1.8
Foot	44.9 ± 1.5	44.8 ± 1.7	45.7 ± 1.2
Warmth			
Hand	1.3 ± 0.7	1.9 ± 1.0	1.6 ± 0.9
Foot	4.5 ± 1.9	6.1 ± 2.8	6.2 ± 3.2
Cold			
Hand	0.8 ± 0.3	1.0 ± 0.4	0.9 ± 0.4
Foot	1.4 ± 1.0	1.7 ± 1.0	2.2 ± 1.6

age groups.

For the heat pain threshold on the hand neither the linear nor the quadratic trend showed a significant change with increasing age (Table II and Fig. 1). For this threshold on the foot, however, the linear trend was highly significant, indicating a threshold elevation. The positive quadratic trend was not significant. The quadratic regression curves for stimulation on the hand and on the foot showed distinct age courses, with estimated threshold elevations from 15 to 65 years of 0.6 °C on the hand and 2.2 °C on the foot (Fig. 1).

The thresholds for warmth and cold on the foot increased in a highly significant

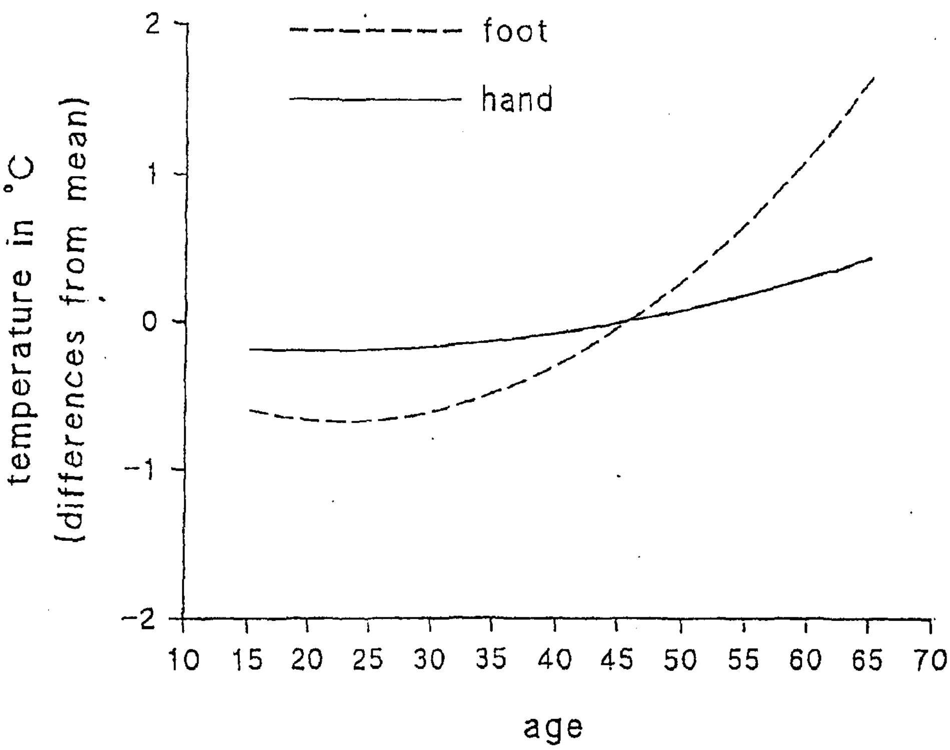

FIG. 1 - Quadratic regression curves with "age" as the independent variable and "threshold" as the dependent variable for the pain threshold (n = 128) measured on the hand and on the foot.

Table II - Results of the regression analysis "threshold on age" for the linear and the quadratic trend with the explained variance by trend (R^2 change), the degrees of freedom (DF), the value of F change and the p value.

		R^2	DF	F	p
Pain					
Hand	linear	0.0040	126,1	0.5014	0.480
	quadratic	0.0004	125,2	0.0512	0.821
Foot	linear	0.1085	126,1	15.3399	<0.001
	quadratic	0.0149	125,2	2.1195	0.148
Warmth					
Hand	linear	0.0247	126,1	3.1960	0.076
	quadratic	0.0723	125,2	10.0094	0.002
Foot	linear	0.0789	126,1	10.7312	0.001
	quadratic	0.0011	125,2	0.1433	0.706
Cold					
Hand	linear	0.0100	126,1	1.2709	0.262
	quadratic	0.0273	125,2	3.5463	0.062
Foot	linear	0.1058	126,1	14.9105	<0.001
	quadratic	<0.0001	125,2	0.0001	0.993

linear fashion with age (Table II and Fig. 2). The quadratic regression curves showed estimated threshold elevations from 15 to 65 years of 3.3 °C for warmth and 1.7 °C for cold. On the hand, in contrast, no threshold increases were observed. Instead, for the warmth threshold there was a significant negative quadratic trend, with a threshold

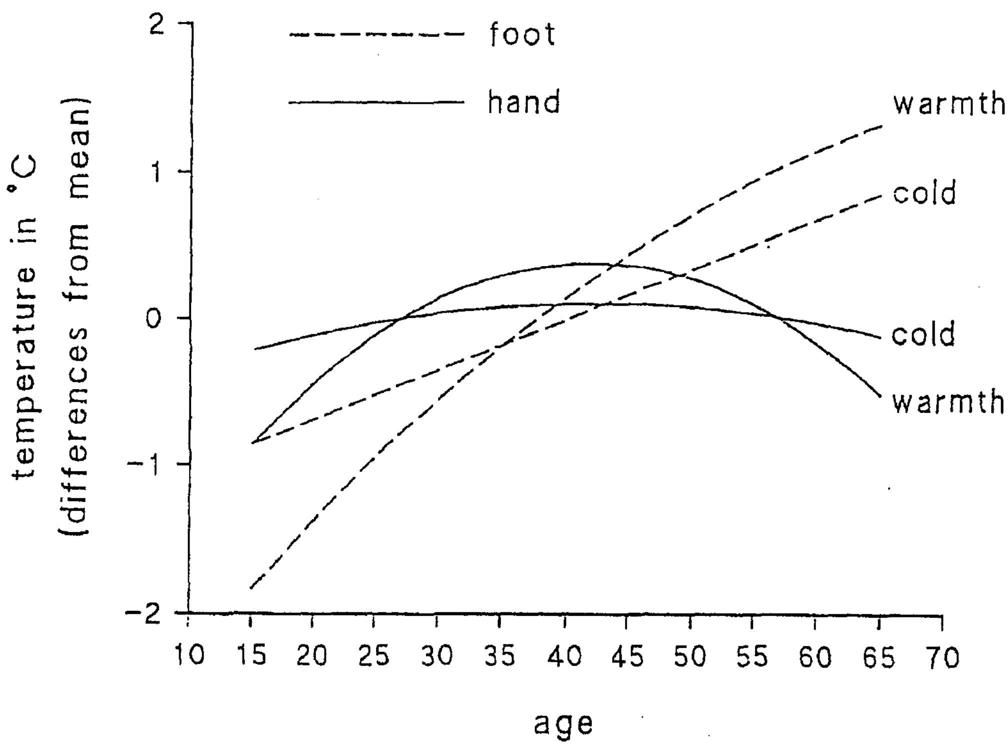

FIG. 2 - Quadratic regression curves with "age" as the independent variable and "threshold" as the dependent variable for the thermal sensitivity thresholds (warmth, cold) measured on the hand and on the foot (n = 128 in each case).

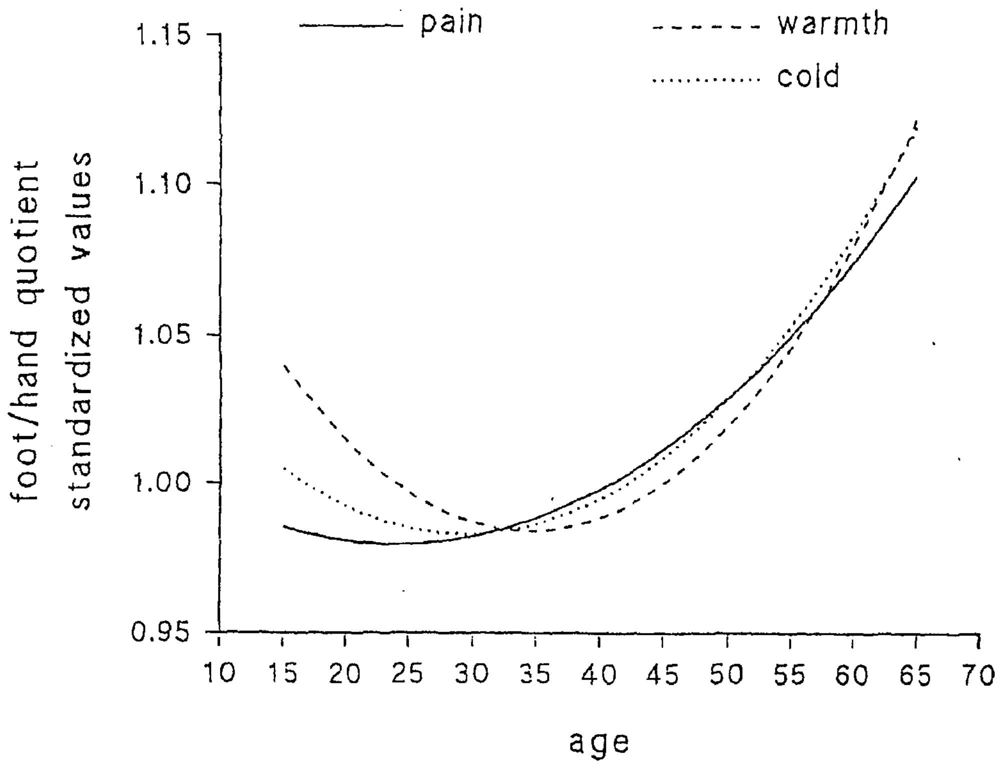

FIG. 3 - Quadratic regression curves with "age" as the independent variable and "foot/hand quotient" as the dependent variable (standardized threshold values) for the pain thresholds and the thermal sensitivity thresholds (warmth, cold) ($n = 128$ in each case).

maximum at 42 years.

The individual foot/hand quotient for the pain threshold increased in a highly significant linear fashion with age (Table III and Fig. 3). The quadratic regression curve suggests that the increase began only within the fourth decade because of a strong, but nevertheless nonsignificant quadratic trend. The individual foot/hand quotients for the warmth and cold thresholds had a quite similar age course, with a weaker linear and a more pronounced quadratic trend for the

Table III - Results of the regression analysis "foot/hand quotient on age" for the linear and the quadratic trend with the explained variance by trend (R^2 change), the degrees of freedom (DF), the value of F change and the p value.

	R^2	DF	F	p
Pain				
linear	0.0883	126,1	12.2023	<0.001
quadratic	0.0143	125,2	1.9966	0.160
Warmth				
linear	0.0149	126,1	1.9061	0.170
quadratic	0.0313	125,2	4.0981	0.052
Cold				
linear	0.0481	126,1	6.3632	0.013
quadratic	0.0199	125,2	2.6732	0.105

warmth threshold (Table III and Fig. 3). The relative increase in the thresholds on the foot as compared with those on the hand seemed to occur only from the end of the third (cold) and the fourth (warmth) decade on, respectively.

DISCUSSION

This study provides evidence that within the age limits of 17 and 63 years the threshold for heat pain increases with age on the foot, but not on the hand. The difference between the age-related changes at the two sites began in the fourth decade, as indicated by a marked increase in the foot/hand quotient starting at this age. The kind of age change in the pain threshold was similar to that found for temperature sensitivity in the present study and also to that found in other somatosensory systems (7-14).

Inasmuch as we were able to replicate the findings of other studies with respect to thermal sensitivity (8,9,11,12), our subjects can be considered to be representative samples of their respective age groups. This strengthens our conclusion that pain sensitivity appears to decrease in a distal-proximal pattern with increasing age, as is known to happen in other somatosensory modalities.

The causes of this phenomenon remain to be clarified. They seem not to be related to the diameter of the primary afferents because modalities with large (vibration, touch) and small (warmth, cold, pain) fibers appear to be affected similarly. It can be assumed that longer nerve fibers are more vulnerable to the consequences of the age-dependent slowing of axonal transport than shorter (17). This can lead to an earlier loss of regenerative capacities and to the phenomenon of a distal axonopathy especially in longer fibers (6,14). Whether the age-dependent reduction in nerve conduction velocity reflects the same processes is unclear because it is at least partially due to the cumulative myelination deficits (18), which are irrelevant for the C-fiber modalities (warmth, pain).

However, it is unlikely that our findings of a reduced heat pain and thermal sensitivity on the foot are produced only by age changes of the skin: the free nerve endings of the nociceptive and thermoceptive afferents are mainly located near the epidermal-dermal junction (19). The flattening of the junction and the thinning of the epidermis and dermis with increasing age (20) may indeed result in more frequent damage to the free nerve endings, but also in a decrease in the thermal resistance, which would tend to appear as heightened sensitivity.

Only a few studies have addressed the question of site-dependent age differences in pain perception up to now. Two studies appear to contradict our findings. Schludermann and Zubeck (21) found a more pronounced age-related elevation in the pain threshold for short than for long nociceptive pathways. They had a different experimental design, using a constant radiation technique and a time criterion for the pain threshold. Kenshalo (12) found no increase in heat pain threshold at all, either on the hand or on the foot. His design was similar to ours, including use of a contact thermode. Because he did not find an age-related decline in cold sensitivity on the foot, which was a result of our study and also of several others (8,9,11), we speculate that his group of elderly subjects had fewer deficits than the subjects in the other aging studies. In contrast, Mitchell and Schady (12) obtained results similar to ours. They observed a more marked age-related decrease in thermal and vibratile sensitivity on the foot than on the hand, and they found no age changes in heat pain perception on the hand, but highly significant increases on the foot.

Additional studies are necessary to resolve these inconsistencies. Inasmuch as the hypothesis of a similarity between age changes in pain perception and age changes in other somatosensory modalities is supported by our findings and by those of Mitchell and Schady (12), we feel it would be an appropriate basis for further studies in this area.

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