European Journal of Applied Physiology (2019) 119:771–780
https://doi.org/10.1007/s00421-018-04068-4

ORIGINAL ARTICLE

Body regional heat pain thresholds using the method of limit and level: a comparative study

Sungjin Park[1] · Sang-Hyun Roh[1] · Joo-Young Lee[1,2]

Received: 20 February 2018 / Accepted: 31 December 2018 / Published online: 14 January 2019

Abstract

Purpose The purpose of this study was to compare cutaneous heat pain thresholds using the method of limit and level.
Methods Sixteen young males (23.2 ± 3.2 year, 174.9 ± 4.9 cm, and 70.1 ± 8.6 kg) participated in this study. The thermode temperature increased at a constant rate of 0.1 °C s^{-1} from 33 °C for the method of limit, whereas the method of level consisted of 3 s heat pulses increasing from 44 °C to 50 °C in 100 s separated by 5 s intervals. All measurements were conducted on 14 body regions (the forehead, neck, chest, abdomen, upper back, upper arm, forearm, waist, hand, palm, thigh, calf, foot, and sole) in 28 °C, 35% relative humidity.
Results The results are as follows. Heat pain thresholds were on average 3.2 ± 2.1 °C higher for the method of level than for the method of limit ($P < 0.05$). Second, the correlation coefficient between values by two methods was 0.819 ($P < 0.01$). Third, lower body regions (thigh, calf, and sole) had higher heat pain thresholds than upper body regions (chest) by the method of level only ($P < 0.05$). Fourth, body regional subcutaneous fat thickness showed no relationship with heat pain thresholds except the upper arm.
Conclusion These results indicated that cutaneous heat pain thresholds vary based on the type of heat stimuli and body regions. The method of limit could be applied for predicting accumulated thermal pain starting from moderate heat, whereas the method of level may be applicable for predicting acute heat pain to flames or high heat.

Keywords Heat pain thresholds · Method of limit · Method of level · Subcutaneous fat thickness · Body regional difference · Burn

Abbreviations

ASTM	American Society for Testing and Materials
ISO	International Organization for Standardization
SG	Substantia gelatinosa
T_{re}	Rectal temperature
T_{sk}	Skin temperature
TC	Thermal comfort
TRP	Transient receptor potential (TRP)
TS	Thermal sensation

Communicated by George Havenith.

✉ Joo-Young Lee
leex3140@snu.ac.kr
http://comfortlab.snu.ac.kr

Sungjin Park
puzzlingus@snu.ac.kr

Sang-Hyun Roh
shtkdgus011@snu.ac.kr

1 COMFORT Laboratory, College of Human Ecology, Seoul National University, Bld #222-#room 306, 1 Gwanak-ro, Gwanak-gu, Seoul 08826, South Korea

2 Research Institute for Human Ecology, Seoul, South Korea

Introduction

Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage" and classified as nociceptive, inflammatory, or neuropathic pain (IASP 1994). The three stimulations for pain are thermal, mechanical, and chemical. Among the three types of pain, heat pain sensitivity has been explored by multiple testing algorithms, which could be divided into the method of limit and level. The method of limit measures thermal thresholds providing continuous heat stimulation, whereas the method of level measures thermal thresholds providing intermittent heat stimulation. The method of limit is a time-dependent protocol and subjects are asked to push a button as soon as a change in linearly increasing or decreasing temperature is perceived. The method of level is a time-independent protocol that presents a trapezoid waveform, which is called 'forced choice', because subjects are forced to choose with specific thermode temperatures presented (Bakkers et al. 2013).

Accumulated studies suggest that transient receptor potential (TRP) channels are the main attributor for the distinct thermal sensitivities. TRPV1 is a noxious heat-activated channel with a thermal activation threshold of about 43 °C and marks a population of unmyelinated C fibers (Caterina et al. 1997; Julius 2013). TRPV2 is activated by high temperatures with a threshold of ~52 °C (Tominaga 2007) and expressed in the myelinated sensory Aδ fibers, which transmit nociceptive information much faster than C fibers (Tominaga 2007). Heat pain sensations are mediated by medium-diameter myelinated Aδ and small-diameter unmyelinated C fibers (Meyer et al. 1994). Along with those studies at molecular levels, holistic studies with human subjects have been conducted on cutaneous thermal thresholds, but deviations are wide according to the experimental conditions. Heat sensations have been reported to occur at 43 °C (Burnett and Dallenbach 1927), 40–46 °C (Lowenstein and Dallenbach 1930), or 45 °C skin temperature (Hensel 1981; Nafe and Wagoner 1936), whereas heat pain sensation has been reported to occur from 43 to 51 °C (Lowenstein and Dallenbach 1930). Thermal sensation is evoked due to the change of skin temperature in the range of 13–45 °C and heat pain sensation occurs at temperatures above 45 °C (Jones and Berris 2002). For human subjects, the difficulty remains that heat sensation is not able to be clearly separated from heat pain (Hensel 1981). A low-temperature burn can occur at approximately 44 °C when the skin sustains exposure for approximately 6 h (ASTM C1055 2003). From 44 °C to about 51 °C, the time required for skin damage decreases by approximately 50% for each 1 °C (ASTM C1055 2003).

As described above, great variability of heat pain thresholds was found and the differences are attributed to differences in the experimental conditions of body regions, adapting temperature, intensity and amount of the previous stimulation, duration and rates of stimulation, and hour and date of measurement (Chery-Croze 1983; Jones and Berris 2002). For example, values obtained from most human subject studies were from a couple of body sites such as the forearm, face, hand, or foot, but cutaneous thermal thresholds had body regional differences. Moreover, cutaneous pain serves to warn for extreme thermal exposure. Lee et al. (2010) tested cutaneous warm thresholds using the method of limit and found that the calf is the most thermally insensitive and the face is the most sensitive body site among 12 body sites tested. Although several studies have already compared regional distribution of heat pain sensitivity, little is known on regional variations across the whole body. Defrin et al. (2006) found that heat pain thresholds from five body sites (chest, forearm, thigh, hand, and foot) were the lowest on the chest (mean 42 °C) and peaked on the foot (44.5 °C) with the method of limit, but there were no regional differences in the pain thresholds when adopting the method of level.

Although both the methods of limit and level are commonly used in heat pain thresholds measurement, the difference in values between two methods has rarely been examined. Bakkers et al. (2013) conclude that the method of limit is less time consuming, but several studies favor the method of level, because its reproducibility is better. As mentioned before, Defrin et al. (2006) found significant differences in heat pain thresholds among five regions with the method of limit, but no regional differences were found with the method of level. The differences between two methods may be explained by a phenomenon of the first and second heat pain. According to Julius and Basbaum (2001), the first onset of pain is related to A fibers, which are fast and thick, while the second pain is related to C fibers. Aδ fibers, which are thicker than C fibers, have conduction velocities in the range of 12–30 m s^{-1}, whereas C fibers have velocities in the ranges of 0.5–2 m s^{-1}. Because the method of level is quick to respond to fast and high intensity heat, and the method of limit is good for catching accumulated heat starting from low-intensity heat, it can be assumed that methodological characteristics may distinguish the first from second pain.

Although studies on thermal pain have been done extensively for a long time, the understanding of methodological and regional differences in cutaneous heat pain is still far from clear. Defrin et al. (2006) investigated the five regions (the chest, forearm, thigh, and the dorsal surface of the hand and foot), but no pain thresholds on the head, back, calf, or other body regions were compared with the two methods. Therefore, the purpose of the present study was to investigate body regional heat pain thresholds over numerous body parts covering each segment using the method of limit and level. We hypothesized that cutaneous heat pain threshold by the method of level would be higher than those by the method of limit, and the differences would vary according to body regions.

Methods

Subjects and experimental conditions

Sixteen healthy Korean young males (23.2 ± 3.2 years in age, 174.9 ± 4.9 cm in height, 70.1 ± 8.6 kg in body weight, and 1.85 ± 0.12 m^2 in body surface area) participated in this study. Subcutaneous fat thickness was measured three times on the posterior neck (11.6 ± 1.5 mm), chest (8.8 ± 2.6 mm), abdomen (16.9 ± 6.9 mm), upper back (scapular) (11.3 ± 1.6 mm), upper arm (triceps)(9.4 ± 2.3 mm), anterior forearm (6.3 ± 1.4 mm), lower back (10.9 ± 1.3 mm), medial thigh (8.0 ± 1.7 mm), and lateral calf (9.6 ± 3.6 mm) ($P < 0.05$ between regions) using a ultrasound measurement device (BFI SM 506, SEIKOSHA, Japan), and the mean and standard deviation of the nine body areas was 9.8 ± 3.2 mm. Body surface area was calculated using Lee et al. (2015). All subjects were free of skin disorders, neurological illnesses, and other medical conditions. Subjects visited the laboratory twice. On the first visit, heat pain threshold detection was practiced, and then, the both methods of limit and level were performed. On the second visit, cutaneous fat thickness and other anthropometric items were measured. All tests were performed in a climate room and subjects (wearing shorts and undershorts only) were seated in a comfortable recliner posture at an air temperature of 28 °C and 35%RH. The room was kept quiet, so that subjects could concentrate on their perceptions. All tests were performed between 9:00 AM and 1:00 PM to avoid any possible effects of circadian rhythm. Measurement sites, if necessary, were shaved. Standardized instructions, purpose, and potential risks of this study were given, and a training session for every test was performed. Subjects were prohibited from consuming alcohol and heavy exercise 24 h prior to their participation. All subjects were volunteers and signed the informed consent form prior to the participation. This study was approved by the Institutional Review Board of Seoul National University (IRB No. 1704/003-009).

Measurements

All measurements were conducted using a thermal stimulator (Intercross-210, Intercross Co., Japan, stimulating probe surface area: 1×1 cm^2) and repeated three times at each of the 14 body sites. The values of three repetitions were averaged. The order of measurements of the 14 sites was randomized to avoid the order effect. We had at least 1-min interval between stimulating different body regions. For safety, the cut-off temperature of the stimulating probe was set at 50 °C at which point the test automatically terminated at that point. When the subject did not report any pain sensation and the limit of 50 °C was reached, the heat pain threshold on the body region was regarded as over 50 °C. For the measurements on the neck, upper back, and waist regions, subjects sat on the recliner and we measured the heat pain in the rear side of the subjects. The probe was put on the skin to the direction of gravity without any artificial pressure by hand, but for the neck, back, and waist regions, the probe was contacted to the skin in the vertical direction. To keep the contact pressure of the probe in a similar range, the same researcher held and put the probe on the skin throughout the experiment, while the other researchers managed the main body of the device for starting, stopping, and recording in the climate room. All researchers wore their lab gowns during the measurements to minimize any possible influence of touch or body scents. The male and female researchers were present during the tests in the climate room.

All pain thresholds were measured by both methods of limit and the method of level. Subjects practiced several times with the thermal stimulator until they were able to discern what the heat pain sensation for both methods of limit and level. For the method of limit, the stimuli of the probe started from baseline skin temperature (33 °C) and increased at a constant rate of 0.1 °C s^{-1} until the subject reported feeling pain sensation by pressing a button (Fig. 1, left). The rate of 0.1 °C s^{-1} was based on the previous studies (Kim et al. 2017; Lee et al. 2010). To avoid any confusion between cutaneous warmth, hotness, and pain sensations, we provided a standardized instruction to subjects. In the instruction, warm sensation was defined as initially sensed warmth, hot sensation was a hotness on the skin after perceiving the warm sensation, and heat pain sensation was defined as a mixed sensation of hotness and pain (like stinging) (Fig. 1, left). Subjects pushed the button of the thermal stimulator as soon as they felt heat pain (initial heat pain). The method of limit has previously been utilized by Verdugo and Ochoa (1992), Yarnistky et al. (1992), Reulen et al. (2003), Lee et al. (2010), and Kim et al. (2017).

For the method of level, the stimuli of predetermined levels of intensity and duration were utilized. The starting baseline temperature was set at 33 °C which is reflective

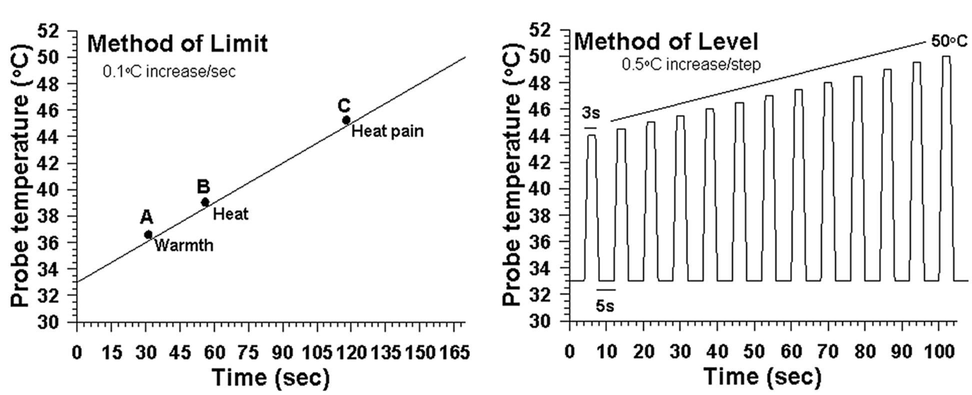

Fig. 1 Method of limit (left) and method of level (right). In the left figure, points when warmth, heat, and heat pain sensations are perceived over time are represented as points A, B, and C. In the present study, subjects expressed all the three points for the trials of the method of limit to avoid any confusion between the heat and heat pain sensation. The point C was regarded as the heat pain threshold for the method of limit

of mean skin temperature in comfort. The thermode temperature increased from the baseline temperature of 33 °C to the first stimuli of 44 °C at the rate of 10 °C s^{-1}. The method of level consisted of 3 s heat pulses increasing from 44 to 50 °C in 100 s separated by 5 s intervals. Subsequent stimuli were of progressively 0.5 °C higher intensity (Fig. 1, right). There might be a variety for the method of level in terms of baseline temperature, the first and last stimuli temperatures, the speed of temperature change, inter-stimulus intervals, the duration of stimulus, or gradual increase in stimulus temperature. Reulen et al. (2003) recommended a trapezoid temperature–time graph (a graph that temperature is maintained for several seconds on the upper temperature) over a triangle graph (a graph that lowering temperature as soon as reaching the upper temperature) for the method of level. In particular, the 3-s duration of stimulus and the 5-s interval were chosen as being appropriate through pilot tests (e.g., when the thermode was put on the skin for 1 or 2 s, subjects did not recognize the heat stimuli, whereas heat could be accumulated in the skin during over 4-s stimulating. To get rid of previously perceived heat, at least 5 s were required). The subject was instructed to press the button as soon as pain was perceived. At the first stimuli, the subject was asked about thermal sensation as none, slightly warm, warm, or hot. If the subject pressed the button as soon as the thermode with the first stimuli of 44 °C was contacted to the skin, the heat pain threshold on the body region was regarded below 44 °C.

Along with pain threshold, skin temperature was continuously measured on the 14 sites using a data logger (LT-8A, Gram Corporation, Japan, 0.01 °C of resolution; 5 s interval) during the pain threshold measurement. The initial skin temperature was recorded at the beginning of the measurement of heat pain thresholds with the method of level. All measurements for skin temperature were performed on the left side of the body except for the forehead, neck, upper back, and waist which were measured on the center of the body. When measuring heat pain thresholds with the method of level, the subjects were asked for their initial thermal sensation. The purpose of asking for their initial thermal sensation was to ascertain how the initial stimuli of 44 °C for 3 s were felt on different body sites. The initial thermal sensation was scaled as none (1), slightly warm (2), warm (3), and hot (4).

Data analysis

Statistical analysis was performed using SPSS v. 24.0. Normality was confirmed by Kolmogorov–Smirnov and Shapiro test ($P > 0.05$). Differences in pain thresholds by methods (two methods) and body regions (14 regions) were tested using a repeated-measures two-way ANOVA with Tukey's post hoc test. Pearson's correlation coefficients between measured items were performed. Values were presented as mean and standard deviation (SD). A P value of 0.05 or less was considered statistically significant. Heat accumulated on the skin surface through conductive heat transfer between the thermode and the skin layer was calculated by Fourier's law of thermal conduction (Eq. 1). The heat flow was compared through the methods of limit and level. For the calculation, we used the thickness of 75 μm and thermal conductivity of 0.6155 $W{\cdot}m^{-1}{\cdot}K^{-1}$ of the skin epidermis, according to ISO 13506 (2014). We assumed that there was no heat loss to the air while contacting the thermode to the skin, the specific heat of the skin was identical on the 14 body regions, and the specific heat and density of the skin were identical during heating. The surface area of the thermode contacting the skin was 1 cm^2:

$$J = -k\frac{dT}{dx} \quad \text{[Eq. 1]}$$

[Method of limit]

$$Q = \int J \times (\mathrm{SA})\,dt$$
$$J = -k \times (-0.1t) \times (75\ \mu m)^{-1}$$
$$Q = \int [-k \times (-.01t) \times (1\ cm \times 1\ cm) \times (75\ \mu m)^{-1}$$
$$= 1/15 \times k \times t^2$$
$$t : \Delta T/0.1$$

[Method of level]

$$Q = J \times (\mathrm{SA}) \times (3s)$$
$$J = -k \times \Delta(T_f - T_i) \times (75\ \mu m)^{-1},$$
$$Q = J \times (SA) \times (3s)$$
$$= -k \times \Delta(T_f - T_i) \times (1\ cm \times 1\ cm) \times (75\ \mu m)^{-1},$$

where, J: heat flux in Joule, k: thermal conductivity in W/m K, T: temperature in K, x: displacement, $dT = -0.1$ sK ($\longrightarrow$ 0.1 °C/s), and SA: surface area.

Results

There was no significant interaction effect between methods and body regions ($F = 0.430$, $P = 0.959$). Cutaneous heat pain thresholds with the method of level were 3.2 ± 0.5 °C higher when compared to values by the method of limit (Fig. 2; Table 1; on average 46.7 ± 0.8 °C for the method of level and 43.6 ± 0.5 °C for the method of limit). We re-calculated heat pain thresholds by the method of level of which the values expressing as 44 °C and 50 °C were removed. For the initial stimuli of 44 °C for 3 s by the method of level, there were 24 cases of 224 cases (10.7%) that responded

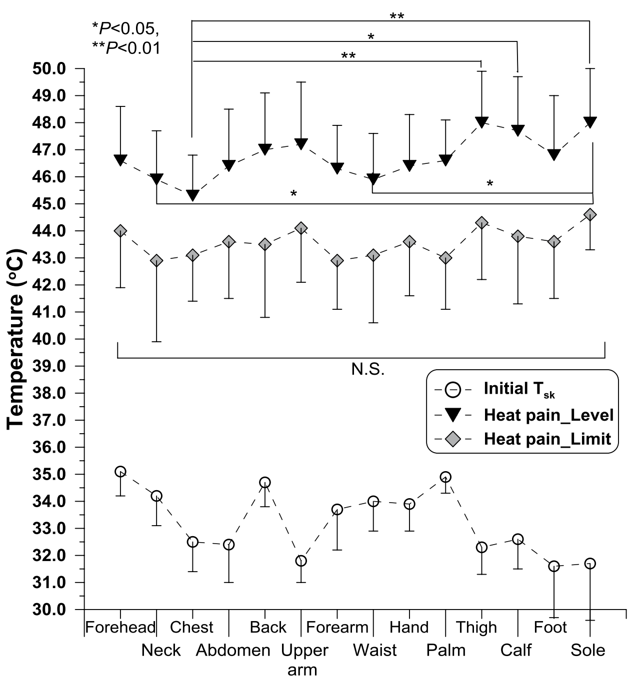

Fig. 2 Heat pain thresholds with the method of level and limit and initial skin temperatures on the 14 body sites. Values were expressed as mean and SD of 16 subjects. *Significant difference between the chest and the other 13 body sites. Differences in pain thresholds between the method of level and limit were all significant on the 14 body sites (*$P<0.05$, **$P<0.01$, and ***$P<0.001$)

as heat pain, whereas 12 cases of 224 cases (5.4%) showed no responses at the maximum temperature of 50 °C. That showed on average 46.9 ± 0.6 °C with no difference with the originally calculated values (Table 1). Higher pain thresholds for the method of level corresponded to all 14 body regions (all $P<0.05$). The greatest and smallest differences between the two methods were on the calf (3.9 °C difference) and the chest (2.2 °C difference), respectively. Heat pain thresholds with the method of level showed significant differences by body regions ($P<0.05$, Fig. 2). Values on the chest (45.3 ± 1.5 °C) were significantly lower than those on the thigh (48.0 ± 1.9 °C, $P=0.006$), calf (47.7 ± 2.0 °C, $P=0.031$), and sole (48.0 ± 2.0 °C, $P=0.008$). For the method of limit, no significant difference in the pain thresholds was found among the 14 body sites, although the lower leg showed relatively higher thresholds than the other body regions (Fig. 2; Tables 1, 2).

High agreements were found between the two methods, showing that the correlation coefficients (r) between pain thresholds from the two methods were 0.82 (14 body regions, $P<0.001$, Fig. 3a) and 0.58 (16 subjects, $P=0.017$, Fig. 3b). There were significant differences in the initial thermal sensation for the 14 body sites ($P<0.05$). Subjects felt warmer on the chest and less warm on the back, calf, foot and sole. We calculated total heat flow accumulated in the skin until the pain thresholds by the method of limit and level. On all 14 body regions, total heat flow required to cause cutaneous pain sensation was higher for the method of

Table 1 Heat pain thresholds with the method of level and limit on the 14 body sites

Body region	Heat pain threshold method of limit (°C)	Method of level				
		Heat pain threshold (°C)	Heat pain threshold without the cases of [a] and [b] (°C)	Cases of expressing the heat pain at 44 °C stimulus (n)[a]	Cases of non-expressing the heat pain at 50 °C stimulus (n)[b]	Homogeneous subsets[†]
Forehead	44.0 ± 2.1	46.6 ± 2.0	47.2 ± 1.7	2	0	abc
Neck	42.9 ± 3.0	45.9 ± 1.8	46.4 ± 1.7	2	0	a
Chest	43.1 ± 1.7	45.3 ± 1.5	45.8 ± 1.4	4	0	a
Abdomen	43.6 ± 2.1	46.4 ± 2.1	47.0 ± 1.9	2	0	abc
Back	43.5 ± 2.7	47.0 ± 2.1	47.1 ± 1.7	2	2	abc
Upper arm	44.1 ± 2.0	47.2 ± 2.3	47.1 ± 1.4	3	4	abc
Forearm	42.9 ± 1.8	46.3 ± 1.6	46.6 ± 1.4	2	0	abc
Waist	43.1 ± 2.5	45.9 ± 1.7	46.2 ± 1.6	2	0	a
Hand	43.6 ± 2.0	46.4 ± 1.9	46.7 ± 1.8	2	0	abc
Palm	43.0 ± 1.9	46.6 ± 1.5	46.8 ± 1.3	1	0	abc
Thigh	44.3 ± 2.1	48.0 ± 1.9	48.0 ± 1.6	1	2	bc
Calf	43.8 ± 2.5	47.7 ± 2.0	47.6 ± 1.9	0	1	abc
Foot	43.6 ± 2.1	46.8 ± 2.2	47.2 ± 2.0	1	0	abc
Sole	44.6 ± 1.3	48.0 ± 2.0	47.5 ± 1.9	0	3	c
Mean ± SD	43.6 ± 0.5	46.7 ± 0.8	46.9 ± 0.6	Total 24 cases	Total 12 cases	

Values were expressed as mean and SD of 16 subjects. For the method of level, the case numbers of expressing as 44 °C and 50 °C are presented

[†]Homogeneous subsets in the results by the method of level were classified by the Tukey's post hoc test, where [a, b], and [c] represent statistically different groups among the 14 body regions

Table 2 Heat flow accumulated in the skin by the method of limit and level, and relationships between subcutaneous fat thickness and heat pain thresholds

Body region	Subcutaneous fat thickness (mm)	Heat flow			Correlation coefficients between subcutaneous fat and pain thresholds[c]	
		Method of limit (J)[a]	Method of level (J/3 s)[b]	*P* value	r^2	*P* value
Forehead		174.1 ± 65.2	4.27 ± 0.71	< 0.001		
Neck	11.6 ± 1.5	160.1 ± 90.1	4.18 ± 0.71	< 0.001	0.075	0.783
Chest	8.8 ± 2.6	173.0 ± 59.8	4.13 ± 0.59	< 0.001	− 0.248	0.355
Abdomen	16.9 ± 6.9	187.4 ± 68.3	4.45 ± 0.71	< 0.001	0.174	0.519
Back	11.3 ± 1.6	169.5 ± 70.9	4.47 ± 0.76	< 0.001	0.353	0.181
Upper back	9.4 ± 2.3	221.4 ± 76.6	4.89 ± 0.78	< 0.001	0.596	0.015
Forearm	6.3 ± 1.4	151.8 ± 54.4	4.34 ± 0.59	< 0.001	0.050	0.855
Waist	10.9 ± 1.3	158.9 ± 70.3	4.14 ± 0.61	< 0.001	− 0.331	0.211
Hand		179.5 ± 63.5	4.38 ± 0.67	< 0.001		
Palm		151.2 ± 59.3	4.35 ± 0.47	< 0.001		
Thigh	8.0 ± 1.7	222.9 ± 72.0	5.11 ± 0.66	< 0.001	− 0.032	0.906
Calf	9.6 ± 3.6	201.2 ± 72.1	4.95 ± 0.66	< 0.001	− 0.156	0.565
Foot		199.0 ± 66.1	4.68 ± 0.77	< 0.001		
Sole		236.6 ± 48.6	5.14 ± 0.74	< 0.001		
Mean ± SD		184.7 ± 66.9 J	4.53 ± 0.67 J	< 0.001		
				N.S		

[a]Converted to 1.74 J/s (an average of 106 s passed starting from 33 °C until perceiving heat pain)

[b]Converted to 1.51 J/s (3 s were contacted to the skin)

[c]Based on the values from method of level

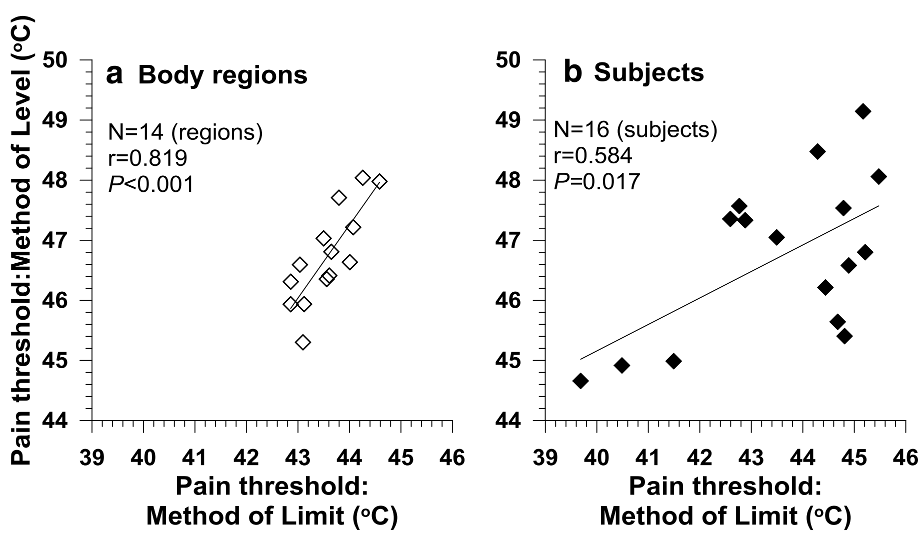

Fig. 3 Relationships between heat pain thresholds by the methods of limit and level for the 14 body regions (**a**) and subjects (**b**)

level than the method of limit ($P < 0.001$, Table 1). However, the values per unit time showed no significance difference between the methods (1.74 J s^{-1} for the method of limit vs. 1.51 J s^{-1} for the method of level). Subcutaneous fat thickness did not show any correlation with heat pain thresholds obtained by the method of level or limit, except for the upper arm ($r = 0.60$, $P = 0.015$, $N = 16$).

Discussion

Method of level vs. method of limit

We found that cutaneous heat pain thresholds over the numerous body parts covering each segment were 43.6 ± 0.5 °C for the method of limit and 46.7 ± 0.8 °C for the method of level. Our findings from the method of limit are slightly lower compared to the previous research. For example, van den Bosch et al. (2017) showed that heat pain threshold on the hand using a method of limit was 45.9 ± 4.2 °C (N = 69 children and adolescents, 3 × 3 cm^2, 1 °C·s^{-1}). Method of limit for heat pain thresholds has been studied by Verdugo and Ochoa (1992), Yarnisky et al. (1994), and others, while the reports based on the method of level (Dyck et al. 1993) are relatively rare. Levy et al. (1989) and Reulen et al. (2003) have compared both methods for warm and cool thermal thresholds with similar interests as the present study. Their conclusions are, however, not sufficient to make a decision on whether one method is better than another method, because there are differences in reaction time, the effect of rate of temperature change of the thermode, thermode size, or the number of examiners. Levy et al. (1989) tested diabetic patients and concluded both methods are suitable for clinical thermal testing, though the method of limits is quicker and, thus, may be more appealing in its application. Reulen et al. (2003) concluded that using the method of level with the trapezoid temperature–time graph as used in the present study is preferred in practice, but application of the method of limit with different speed of stimuli combined gives comparable results. However, in the present study, heat pain threshold with the method of level was, on average, 3.2 °C higher than those with the method of limit. The present study suggests that using the method of limit would be more appropriate when dealing with thermal pain related to therapeutic or thermal use of heat such as hot packs where heat gradually accumulates, whereas the method of level would be better for cases involving sudden large changes in temperature such as flash fire or flames, which is related that the sensory fibers involvement differs between the method of limit and the method of level.

Values by the method of level are less dependent to surface area stimulated compared to the values by the method of limit. We set the rate of increasing speed at 0.1 °C·s^{-1} for the method of limit, which could be regarded as a low rise rate. At low rise rates of the stimulus temperature (< 2.0 °C·s^{-1}), pain threshold responses may be based on the activation of C fibers (Yarnitsky and Ochoa 1990; Yeomans and Proudfit 1996), whereas, at high rise rates, they may be based on the activation of thin Aδ fibers (Defrin et al. 2006a, b; Pertovaara et al. 1988). Temporal and spatial summation is more pronounced for the C fiber mediated second pain than for the Aδ fiber mediated first pain (Arendt-Nielsen 1998). Aδ fibers elicit a rapid, first phase of pain, which is sharp in nature, whereas C fibers evoke a second wave of dull pain (Belemonte and Cervero 1996).

More discussion concerning the influence of temperature change rate on the cutaneous pain thresholds is needed. Lower thresholds were found for 0.2 °C·s^{-1} than for 2.0 °C·s^{-1} in rabbits (Lynn 1979). The surface temperature thresholds were found to be 41.9 °C for stimulus ramp rates of 5.8 °C·s^{-1}, 40.1 °C for rate of 0.85 °C·s^{-1}, and 39.6 °C for rate of 0.095 °C·s^{-1} (Tillman et al. 1995). Defrin et al. (2006a, b) found that the pain threshold difference was as large as 4 °C measured in the range of 0.5–40 °C·s^{-1}. Although Nielsen and Arendt-Nielsen (1998) did not find any change in human C nociceptor firing thresholds between the three rates of temperature rise used (0.3 °C·s^{-1}, 2.0 °C·s^{-1}, and 6.0 °C·s^{-1}), the relatively low rate of 0.1 °C s^{-1} in the present study should be considered if comparing to the other studies.

In addition, we calculated total heat flow accumulated in the skin until perceiving cutaneous pain sensation using Fourier's law of thermal conduction. The total heat was approximately 41 times greater for the method of limit than for the method of level, which is related to time passed by the pain thresholds. For the method of limit, subjects felt the sense of pain after 106 s, on average, but only 3 s for the method of level. These results indicate that heat pain sensation is close to a function of temperature, itself, rather than a function of heat flow accumulated. Of course, the 3.1 °C difference between the two methods cannot be explained by the function of temperature, but the role of accumulated heat flow should be required on the basic role of temperature stimulated. It seems that the heat flow accumulated in the skin would be a more critical factor for burn prediction than pain prediction.

Body regional differences of heat pain thresholds

As discussed above, the regional differences were more obvious for the method of level than the method of limit. We found that heat pain thresholds were higher for the lower body and foot when compared to the face and upper body for both methods of limit and level. The neck, chest, and waist had significantly lower heat pain thresholds than the thigh or sole in the present study. As mentioned, very few studies compared the heat pain thresholds over the whole body, but several studies agreed to that the lower legs, especially feet, had higher thresholds than the head or trunk (Dyck 1993; Hardy et al. 1952). Hardy et al. (1952) found that the highest pain thresholds were on the heel of the foot and the lowest thresholds on the lower back, buttocks, and thighs when using a thermal radiant method. Similarly, the highest values were found in the legs and feet (Dyck et al. 1993; Lynn and Perl 1977; Meh and Denislic 1994) or the hand and foot (Taylor et al. 1993), but the lowest thresholds were in the face and arms (Dyck et al. 1993; Meh and Denislic 1994), the neck and abdomen (Lynn and Perl 1977), or the forearm and calf (Taylor et al. 1993). Cold pain showed lower thresholds in the foot than hand (Greenspan et al. 1993), but contradictory results with no differences between the hands and feet were found in Yarnitsky et al. (1994).

Body regional differences of heat pain thresholds are considered to be affected by the biomechanical characteristics of the skin. The previous studies (Zahorska-Markiewicz et al. 1988) have suggested altered pain sensitivity with obesity. Price et al. (2013) found decreased heat pain sensitivity only on excess subcutaneous fat (the abdomen area) in the obese groups compared to non-obese groups. In this regard, we examined the relationships between subcutaneous fat thickness and pain thresholds, but significant relationships were not found except the upper arm. Because the cutaneous heat pain receptors are located in the dermis over the subcutaneous fat, no relationship could be predictable. However, when taking together previous and the present studies, it needs that the real relationship should be explored in sufficient sample size with the wide range of subcutaneous fat thickness.

Another factor for the regional differences might be explained to some extent by the characteristics of non-glabrous (i.e. hairy skin) and glabrous skin. The heat pain threshold for non-glabrous skin in human is lower than those for glabrous skin (Greenspan et al. 1993; Harrison and Davis 1999). Glabrous skin is fivefold thicker and has more epidermal layers compared to non-glabrous skin (Cormack 1987), which may affect the rate of heat transfer to the nociceptors in the previous studies. Tillman et al. (1995) found that the heat threshold for C fiber heat nociceptors was determined by receptor depth. However, we did not found any tendency of having lower heat pain sensitivity on the non-glabrous skin than the glabrous skin.

Along with the subcutaneous fat thickness and non-glabrous skin, the third explanation for the regional difference could lie in the differences between the peripheral innervation densities of the nerves subserving the two skin types. There is a ‘silent’ nociceptor which is defined as a receptor that cannot be activated (Xu and Lu 2011) and differences in the density of the silent nociceptors may be one of reasons for the regional differences. Furthermore, latency might be another reason for the regional difference. There is a clear latency in that the time to detect temperature stimuli had a range of 0.7–1.1 s for the fingertip and 0.4–1.1 s for the arm (Campbell and Lamotte 1983). However, relatively little regional differences in pain thresholds were found unlike cutaneous warm or cold thresholds. Non-glabrous skin seems more sensitive to pain than glabrous skin (Taylor et al. 1993; Pertovaara et al. 1996), but less sensitive for warm and cold detection (Greenspan et al. 1993). However, there should be more discussion in further studies, because we did not measure peripheral nerve innervation or latency to detect cutaneous heat pain.

Limitations

The strength of the present study is that all values were from the numerous body parts covering each segment using both representative methods of limit and level. One of the limitations is, however, that the minimum temperature of 44 °C and maximum temperature of 50 °C were set for the method of level: Out of the total, 10.7% (24 of 224 cases) reported heat pain sensation early at 44 °C and 5.4% (12 of 224 cases) were automatically terminated at 50 °C. Even though the percentages of 5.4% and 10.7% in the present study are not that severe when compared to the 41% which showed no response at 50 °C from van den Bosch et al. (2017), such set temperatures should be discussed in advance in further studies.

Most of all, values of cutaneous pain sensitivity obtained from the present study differ from the previous studies because of differences in stimulus intensity, duration, area, and modality. There are various stimulus modalities available to induce cutaneous pain, such as electrically transduced heat pain, radiant heat pain, contact heat pain using a thermode, or chemically induced heat pain (capsaicin or mustard oil). The surface area of thermodes differs between studies showing 5, 7, 9, 12, and 26 cm^2 (Bakkers et al. 2013). As it is reported that a larger thermode results in lower thresholds, the present results use a relatively smaller sized thermode (1 cm^2). This may be why higher thresholds were found in this study. The mean heat pain threshold decreased significantly from 45.6 to 43.5 °C as the stimulus dermatome area increased from 3.14 to 15.70 cm^2 (Nielsen and Arendt-Nielsen 1997). Such spatial summation refers to an increase in pain perception when larger areas of stimulation are used (Bakkers et al. 2013; Raja et al. 1999).

We used the 3-s stimulus at every step in the method of level, and found that a longer stimulus duration leads to a lower heat pain threshold (Nielsen and Arendt-Nielsen 1998; Pertovaara et al. 1996). For the method of limit, the rate of temperature change during testing affects thresholds. A higher rate results in higher thresholds (Pertovaara and Kojo 1985; Pertovaara et al. 1996; Yarnitsky and Ochoa 1990, 1991) and greater intra-subject variability (Hilz et al. 1995; Nielsen and Arendt-Nielsen 1998). As most previous studies using the method of limits set the rate of increase at 1–4 $°C·s^{-1}$ (Bakkers et al. 2013), the rate of increase at 0.1 $°C·s^{-1}$ in the present study may cause relatively lower thresholds. The smaller size of the thermode with both methods and lower rate of increase with the method of limit in the present study compared to the other studies should be considered. Baseline temperature of the thermode and environmental temperature may affect pain thresholds, but it was reported that skin temperature within the range of 25–35 °C seem to be have a little influence on cutaneous pain sensitivity (Pertovaara et al. 1996). Due to the lack of standardized methods to test cutaneous pain thresholds, the present results should be interpreted within the present experimental settings with healthy young males.

Acknowledgements This research was supported by Nano·Material Technology Development Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT and Future Planning (No. 2016M3A7B4910) and by the Fire Fighting Safety and 119 Rescue Technology Research and Development Program funded by the Ministry of Public Safety and Security ('MPSS-Fire Fighting Safety-2015-76'). We thank the subjects for their participation and Jung-Mi Ha, Wojin Joe, and Andrew Gorski for their technical supports.

Author contributions Its publication has been approved by all co-authors. All authors have contributed to the planning, preparation, data collection, analysis, and the writing of this manuscript, such that their contributions satisfy all the requirements of authorship.

Complaince with ethical standards

Conflict of interest There are no conflicts of interest.

References

Arendt-Nielsen L (1998) Experimental pain research-experimental and clinical aspects (reviews). J Jpn Soc Pain Clinic (JJSPC) 5(4):455–462

ASTM C1055-03 (2003) Standard guide for heated system surface conditions that produce contact burn injuries. American Society of Test and Materials, West Conshohocken

Bakkers M, Faber CG, Peters MJ, Reulen JP, Franssen H, Fischer TZ, Merkies IS (2013) Temperature threshold testing: a systemic review. J Peripheral Nerv Syst 18:7–18. https://doi.org/10.1111/jns5.12001

Belemonte C, Cervero F (1996) Neurobiology of nociceptors. Oxford University Press, Oxford

Burnett NC, Dallenbach KM (1927) The experience of heat. Am J Psychol 38(3):418–431

Campbell JN, LaMotte RH (1983) Latency to detection of first pain. Brain Res 266:203–208

Caterina MJ, Schumacher MA, Tominaga M, Rosen TA, Levine JD, Julius D (1997) The capsaicin receptor: a heat-activated ion channel in the pain pathway. Nature 389:816–824

Chery-Croze S (1983) Painful sensation induced by a thermal cutaneous stimulus. Pain 17(2):109–137

Cormack DH (1987) Ham's histology. WB Saunders, Philadelphia, pp 450–474

Defrin R, Givon R, Raz N, Urca G (2006a) Spatial summation and spatial discrimination of pain sensation. Pain 126(1–3):123–131. https://doi.org/10.1016/j.pain.2006.06.026

Defrin R, Shachal-Shiffer M, Hadgadg M, Peretz C (2006b) Quantitative somatosensory testing of warm and heat-pain thresholds: the effect of body region and testing method. Clin J Pain 22(2):130–136

Dyck PJ, Zimmerman I, Gillen DA, Johnson D, Karnes JL, O'brien PC (1993) Cool, warm, and heat-pain detection thresholds testing methods and inferences about anatomic distribution of receptors. Neurology 43(8):1500–1508

Greenspan JD, Taylor DJ, McGillis SLB (1993) Body site variation of cool perception thresholds, with observations on paradoxical heat. Somatosens Mot Res 10(4):467–474

Hardy JD, Wolff HG, Goodell H (1952) Pricking pain thresholds in different body areas. Exp Biol Med 80(3):425–427

Harrison JLK, Davis KD (1999) Cold-evoked pain varies with skin type and cooling rate: a psychophysical study in humans. Pain 83:123–135

Hensel H (1981) Thermoreception and temperature regulation. Academic Press, London

Hilz MJ, Glorius S, Beric A (1995) Thermal perception thresholds: influence of determination paradigm and reference temperature. J Neurol Sci 129:135–140

IASP (1994) Part III: pain terms, a current list with definitions and notes on usage. In: Merskey H, Bogduk N Classification of chronic pain, 2nd edn. IASP Press, Seattle, pp 209–214 IASP Task Force on Taxonomy

ISO 13506 (2014) Protective clothing against heat and flame—test method for complete garments—prediction of burn injury using an instrumented manikin. International organization Standardization

Jones LA, Berris M (2002) The psychophysics of temperature perception and thermal-interface design. In: 10th Symposium on haptic interfaces for virtual environment and teleoperator systems, 2002. HAPTICS 2002. Proceedings, pp 137–142. IEEE

Julius D (2013) TRP channels and pain. Annu Rev cell DeV Biol 29:355–384. https://doi.org/10.1146/annurev-cellbio-101011-155833

Julius D, Basbaum AI (2001) Molecular mechanisms of nociception. Nature 413(6852):203–210. doi

Kim YB, Jung D, Park J, Lee JY (2017) Sensitivity to cutaneous warm stimuli varies greatly in the human head

Lee JY, Saat M, Chou C, Hashiguchi N, Wijayanto T, Wakabayashi H, Tochihara Y (2010) Cutaneous warm and cool sensation thresholds and the inter-threshold zone in Malaysian and Japanese males. J Therm Biol 35(2):70–76

Lee JY, Park J, Park H, Coca A, Kim JH, Taylor NAS, Son SY (2015) What do firefighters desire from the next generation of personal protective equipment? Outcomes from an international survey. Ind Health 53(5):434–444. https://doi.org/10.2486/indhealth.2015-0033

Levy D, Abraham R, Reid G (1989) A comparison of two methods for measuring thermal thresholds in diabetic neuropathy. J Neurol Neurosurg Psychiatry 52:1072–1077

Lowenstein L, Dallenbach KM (1930) The critical temperatures for heat and for burning heat. Am J Psychol 42:423–429. https://doi.org/10.2307/1415441

Lynn B (1979) The heat sensitization of polymodal nociceptors in the rabbit and its independence of the local blood flow. J Physiol (Lond) 287:493–507

Lynn B, Perl ER (1977) A comparison of four tests for assessing the pain sensitivity of different subjects and test areas. Pain 3(4):353–365

Meh D, Denislic M (1994) Quantitative assessment of thermal and pain sensitivity. J Neurol Sci 127:164–169

Meyer RA, Ringkamp M, Campbell JN, Raja SN (1994) Peripheral mechanisms of cutaneous nociception. In: McMahon SB, Koltzenburg M (eds) Wall and Melzack's textbook of pain. Elsevier, London, pp 3–34

Nafe JP, Wagoner KS (1936) The Experiences of warmth, cold, and heat. The J Psychol 2(2):421–431. https://doi.org/10.1080/00223980.1936.9917471

Nielsen J, Arendt-Nielsen L (1997) Spatial summation of heat induced pain within and between dermatomes. Somatosens Mot Res 14(2):119–125

Nielsen J, Arendt-Nielsen L (1998) The influence of rate of temperature change and peak stimulus duration on pain intensity and quality. Somatosens Motor Res 15:220–229. https://doi.org/10.1080/08990229870781

Pertovaara A, Kojo I (1985) Influence of the rate of temperature change on thermal thresholds in man. Exp Neurol 87:439–445

Pertovaara A, Thomas MJ, Kenneth CL (1988) Cutaneous pain and detection thresholds to short CO2 laser pulses in humans: evidence on afferent mechanisms and the influence of varying stimulus conditions. Pain 34(3):261–269

Pertovaara A, Kauppila T, Hämäläinen MM (1996) Influence of skin temperature on heat pain threshold in humans. Exp Brain Res 107(3):497–503

Price RC, Asenjo JF, Christou NV, Backman SB, Schweinhardt P (2013) The role of excess subcutaneous fat in pain and sensory sensitivity in obesity. Eur J Pain 17(9):1316–1326. https://doi.org/10.1002/j.1532-2149.2013.00315.x

Raja SN, Meyer RA, Ringkamp M et al (1999) Peripheral neural mechanisms of nociception. In: Wall PD, Melzack R (eds) Textbook of pain. Churchill, London, pp 11–57

Reulen JPH, Lansbergen MDI, Verstraete E, Spaans F (2003) Comparison of thermal thresholds tests to assess small nerve fiber function: limits vs. levels. Clin Neurophysiol 114(3):556–563

Taylor DJ, McGillis SL, Greenspan JD (1993) Body site variation of heat pain sensitivity. Somatosens Mot Res 10(4):455–465

Therm J, Biol 69:132–138. https://doi.org/10.1016/j.jtherbio.2017.07.005

Tillman DB, Treede RD, Meyer RA, Campbell JN (1995) Response of C fiber nociceptors in the anaesthetized monkey to heat stimuli: estimates of receptor depth and threshold. J Physiol 485(3):753–765

Tominaga M (2007) The role of TRP channels inthermosensation. In: Liedtke WB, Heller S (eds) TRP ion channel function in sensory transduction and cellular signaling cascades. CRC Press/Taylor & Francis, Boca Raton, pp 271–286

Van den Bosch GE, van Dijk M, Tibboel D, Valkenburg AJ (2017) Thermal quantitative sensory testing in healthy Dutch children and adolescents standardized test paradigm and Dutch reference values. BMC Pediatrics 17:77. https://doi.org/10.1186/s12887-017-0827-7

Verdugo R, Ochoa JL (1992) Quantitative somatosensory thermotest: a key method for functional evaluation of small calibre afferent channels. Brain 115(3):893–913

Xu F, Lu T (2011) Introduction to skin biothermomechnics and thermal pain. Science Press Beijing, Springer, New York

Yarnitsky D, Ochoa JL (1990) Studies of heat pain sensation in man: perception thresholds, rate of stimulus rise and reaction time. Pain 40(1):85–91

Yarnitsky D, Ochoa JL (1991) Differential effect of compressionischaemia block on warm sensation and heat-induced pain. Brain 114:907–913

Yarnitsky D, Simone DA, Dotson RM et al (1992) Single C nociceptor responses and psychophysical parameters of evoked pain: effect of rate of rise of heat stimuli in humans. J Physiol 450(1):581–592

Yarnitsky D, Sprecher E, Tamir A (1994) Variance of sensory threshold measurements: discrimination of feigners from trustworthy performers. J Neurol Sci 125:186

Yeomans DC, Proudfit HK (1996) Nociceptive responses to high and low rates of noxious cutaneous heating are mediated by different nociceptors in the rat: electrophysiological evidence. Pain 68(1):141–150. https://doi.org/10.1016/S0304-3959(96)03177-6

Zahorska-Markiewicz B, Zych P, Kucio C (1988) Pain sensitivity in obesity. Acta Physiol Pol 39(3):183–187