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Spatial variation in sensitivity as a factor in measurements of spatial summation of warmth and cold

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Abstract

Perception of cutaneous heating and cooling depends strongly on stimulus size. Although this dependence has been attributed solely to spatial summation, topographical variations in temperature sensitivity may also play a role. These variations, which differentially affect perception of small stimuli, may have led to overestimation of spatial summation. This possibility was investigated by measuring detection thresholds and perceived intensity for heating and cooling on the volar surface of the forearm using a multiple-thermode stimulus array. By keeping the array in place throughout each testing session we were able to measure threshold sensitivity and suprathreshold responsiveness at eight individual sites and for combinations of these sites having total stimulus areas of 0.64–5.12 cm^2. When spatial summation was calculated in the traditional way by averaging the data for all stimuli of each size, the results agreed closely with previous estimates of summation for warmth and cold. When calculations were based instead on the most sensitive test site for each stimulus size, estimates of summation were reduced by about two-thirds. This outcome indicates that the spatial heterogeneity of thermal sensitivity likely contributed to estimates of spatial summation reported in earlier psychophysical studies. A schematic model of cutaneous thermoreception is presented that shows how neural summation and the density of innervation may combine to produce the psychophysical effects of increasing stimulus size (*spatial enhancement*).

Key words: *spatial summation, temperature, warm receptors, cold receptors, psychophysics*

Introduction

Spatial summation is a defining characteristic of cutaneous temperature sensitivity. In no other sensory system does perception depend so strongly on stimulus size. The magnitude of this dependency was first demonstrated by Hardy and Oppel (1937), who found that doubling the area of stimulation on the forehead reduced the intensity of infrared radiation needed to perceive warmth by 42%. Although Jenkins (1940) subsequently reported a smaller effect of stimulus area using punctate conductive stimuli, Kenshalo *et al.* (1967) eventually confirmed Hardy and Oppel's (1937) results for conductive as well as radiant heating, and for body sites other than the forehead. Hardy and co-workers (Herget *et al.*, 1941) were also first to quantify the effect of stimulus size on perception of suprathreshold heating. Using a flicker-fusion task and a simple type of intensity scaling, Hardy and co-workers found near reciprocity between stimulus area and radiant flux. Three decades later Marks and Stevens (1971) applied modern psychophysical scaling to warmth perception and found complete reciprocity between size and radiation intensity at low levels of heating, but a lesser effect of size as intensity rose. When plotted on log–log coordinates the psychophysical functions for different stimulus areas converged near the threshold for heat pain. Marks and Stevens surmised that spatial summation of warmth was served by different neural mechanisms at low and high levels of heating, or possibly that lateral inhibition began to counteract summation as stimulation intensified.

A year after their benchmark work on warmth, Hardy and Oppel (1938) conducted a clever but crude experiment on spatial summation of cold in which they produced "cold radiation" by exposing blocks of dry ice to the skin through cardboard shutters of different size. Their results indicated that summation of cold was similar in magnitude to summation of warmth. Four decades later Rózsa and Kenshalo (1977) used more precise Peltier technology and found a large effect of stimulus size on the ability to discriminate different levels of cooling. Stevens and Marks (1979) went on to study perception of suprathreshold cold and reported strong but incomplete spatial summation over a wide range of temperatures.

Hardy and Oppel's (1937) original use of the term "spatial summation" to explain their psychophysical results was based on the belief that afferent activity in temperature-sensitive neurons converged and summated both in the periphery and in the CNS. An observation that heating the hand and forehead together produced lower warmth thresholds than heating either alone (Hardy and Oppel, 1937) was attributed to summation within the CNS, and evidence that spatial effects were greater

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for relatively small areas (<3–$5\,cm^2$) (Herget *et al.*, 1941) was consistent with the idea that summation occurred within the receptive fields of branching axons in the periphery. The latter assumption, which grew out of the failure to link temperature spots to morphologically distinct receptors (see Dallenbach, 1927), was central to thinking about spatial effects in thermoreception (Hardy and Oppel, 1937; Jenkins, 1940, 1941; Melzack *et al.*, 1962; Kenshalo *et al.*, 1967). Summation was thought to be required for perception of warmth and cold no matter how small the stimulus. Later reports of complete reciprocity between area and intensity at low levels of heating (Stevens and Marks, 1971; Marks and Stevens, 1973; Stevens *et al.*, 1974; Marks *et al.*, 1976) and between pairs of stimuli presented across the midline of the body (Marks and Stevens, 1973; Rózsa and Kenshalo, 1977) confirmed the fundamental importance of summation for temperature perception.

However, current understanding of the anatomy and physiology of thermoreception contradicts the assumption of peripheral summation and complicates the interpretation of previous psychophysical results. The receptive fields of low-threshold warm and cold fibers are now known to be single spots only a few millimeters in diameter (Hensel and Iggo, 1971; Darian-Smith *et al.*, 1973, 1979a, b; Dubner *et al.*, 1975; Hallin *et al.*, 1981), and surveys of temperature sensitive neurons have shown that low-threshold fibers are extremely rare in cutaneous nerves (Beck *et al.*, 1974; Hallin *et al.*, 1981; Leem *et al.*, 1993). Whereas small receptive fields and a paucity of fibers are both consistent with the low density of "warm spots" that were reported in most spot-mapping studies (see Norrsell *et al.*, 1999), the same two facts undermine the old belief that temperature is sensed via a web of free nerve endings. Whereas summation within this web was considered a requirement for perception, punctate receptive fields implied that it was possible to sense warmth when only a *single* warm fiber was stimulated.

In addition, the discovery of temperature-sensitive nociceptors (Bessou and Perl, 1969; Beck *et al.*, 1974; Torebjörk, 1974; Georgopoulos, 1976; Price and Dubner, 1977) made it clear that intense thermal stimuli were not mediated solely by the senses of warmth and cold. Indeed, the existence of heat-sensitive nociceptors explained early observations that detection of small stimuli sometimes required such intense radiation that subjects reported "pain" or "heat" rather than warmth (Hardy and Oppel, 1937). Recently, the involvement of nociceptors in "warmth" perception was clearly demonstrated in a study which showed that warmth sensitivity in humans is even more sparsely distributed than previously thought (Green and Cruz, 1998). Patches of skin several cm^2 in area were found on the forearm in which the detection threshold for heating equaled or exceeded the physiological thresholds of C-heat-sensitive nociceptors ($\sim 41°C$; Bessou and Perl, 1969; Croze *et al.*, 1976; Van Hees and Gybels, 1981; Yarnitsky *et al.*, 1992). Thresholds within these "warmth-insensitive fields" (WIFs; Green and Cruz, 1998) averaged 43.0°C, compared to 35.4°C on immediately adjacent skin.

WIFs, the abrupt changes in sensitivity at the edges of these areas, and the potential for perception without summation, all raise questions about attributing the effects of stimulus size solely to spatial summation, particularly for small stimulus areas (e.g., $<5\,cm^2$). First, when the location of stimulation varies from trial to trial, as has been the case in virtually all psychophysical studies of summation, smaller stimuli will sometimes fall within WIFs, whereas larger ones will more often stimulate one or more warm fibers. Thus thresholds for small stimuli will be "biased" because some percentage of thresholds will be mediated by nociceptors rather than by warm fibers. Second, because warm fibers are not all equally sensitive, larger stimuli have a higher probability of stimulating the most sensitive "spots" within a region, and so should have lower thresholds by chance alone. We therefore hypothesized that previous psychophysical measurements of the effect of stimulus size on warmth included a topographic factor that may have led to overestimation of spatial summation, particularly for smaller stimuli. We further speculated that the same factor influenced estimates of spatial summation of cold. Although studies of punctate sensitivity typically found higher spatial densities for cold spots than for warm spots, this was not always the case (Dallenbach, 1927), and Melzack *et al.* (1962) reported pronounced spatial variations in cold sensitivity despite using a temperature that was sufficiently low (10°C) to engage high-threshold cold fibers and nociceptors as well as low-threshold cold fibers (Georgopoulos, 1976; LaMotte and Thalhammer, 1982; Campero *et al.*, 1996; Simone and Kajander, 1996).

These hypotheses were tested by estimating the contribution of local variations in thermal sensitivity to changes in detection and perceived intensity as a function of stimulus size. We used a multiple-thermode array to measure the sensitivity and responsiveness of all segments of a fixed field of stimulation, then calculated summation as the difference between the results for the most sensitive of these segments vs those for the entire field of stimulation. The data supported the hypothesis that spatial variations in sensitivity can influence psychophysical estimates of spatial summation for warmth and cold.

Method

Three separate experiments were conducted to study the effect of stimulus area on (1) detection of heating, (2) detection of cooling, and (3) perceived intensity of heating and cooling.

Subjects

Two groups of subjects served in the three experiments: 18 (4 males and 14 females, average age = 27.0 years) served in experiment 1, and 7 of these individuals plus 11 others (a total of 9 males and 9 females, average age = 27.7 years) served in experiments 2 and 3. All subjects were recruited in and around the Yale University campus and were paid for their participation.

Equipment

The temperature stimuli for all three experiments were produced using a 4 × 4 array of 0.64 cm^2 Peltier thermoelectric modules (hereafter referred to as the *array*) that was constructed in the Pierce Laboratory machine and electronics shop. The 8 mm × 8 mm Peltier modules were chosen for use because they are of sufficient size to produce reliable and measurable changes in skin temperature, and because they approximate the receptive field size of warm fibers after thermal spread is taken into account (Darian-Smith *et al.*, 1979a). The 16 modules are independently controlled and thermally isolated from one another. Thermal isolation was achieved by spacing the modules 2 mm apart atop 16 separate chambers of a water-circulated heat sink. The stimulating surface of each module is a machined copper plate (8 mm (8 mm (0.96 mm) with a 40-gauge copper constantin thermocouple epoxied into a 0.5 mm deep groove in its center. The thermocouples provide continuous temperature feedback through a 16-channel computer interface (InstruNet) and stimulus temperature is controlled via LabView Software. The software enables the experimenter to specify the base (adapting) temperature, duration of stimulation, rate of temperature change, and target temperature for each thermal module within ± 0.1°C.

The array is mounted on a three-way microscope stage which is in turn attached via a lockable ball joint to a floor-mounted positioning arm. The lockable ball joint enables adjustment of the angle of the array to accommodate the contour of the body part to be tested. The array and its positioning system stand beside a modified dental chair in which the subject can be seated or reclined. In this study all testing was conducted on the subject's right forearm as it rested volar side up on a foam-padded armrest.

The array was placed on the widest part of the forearm. After adjusting its angle to parallel the surface of the forearm, the array was lowered until all 16 modules made full contact with the skin. The positioning arm was then locked pneumatically and any additional slight adjustments in vertical or horizontal position were made using the vernier controls on the microscope stage. Because precise and steady placement of the array was crucial in all three experiments, two removable steel pins (1-mm diameter) held in brackets attached to the outside of the array served as positioning guides. With the array in place against the arm the experimenter touched the tips of the pins to an inkpad, slid them through guide holes in the bracket until they touched the skin, then removed them. The pins left a pair of 1-mm marks that were used to check the position of the array periodically throughout the testing session. Slight movements of the subject's arm over time were detected by reinserting and noting any misalignment with the ink marks. Misalignments were then corrected by adjusting the position of the array until the pins aligned with the dots. The pins and marks were used in the same manner to reposition the array after rest periods.

All testing was conducted in a laminar-flow environmental chamber with air temperature and relative humidity controlled at 25°C and 30%, respectively.

Experimental design and procedure

Experiments 1 and 2: spatial effects on detection of heating and cooling In the first two experiments we measured the effect of varying total stimulus area on the detection thresholds for heating and cooling. Area was varied by manipulating the number of Peltier modules activated, and thresholds were measured using the ascending method of limits. For heating thresholds (exp. 1) temperature was increased from a base temperature of 33°C at the rate of 0.5°C/s, and for cooling thresholds (exp. 2) temperature was decreased from the same base at the same rate. Subjects signaled the moment a sensation appeared by pressing a hand-held switch that recorded the temperature with a resolution of ± 0.1°C. When the button was pressed the temperature of the thermodes returned to 33°C. Note that use of a more sensitive forced-choice

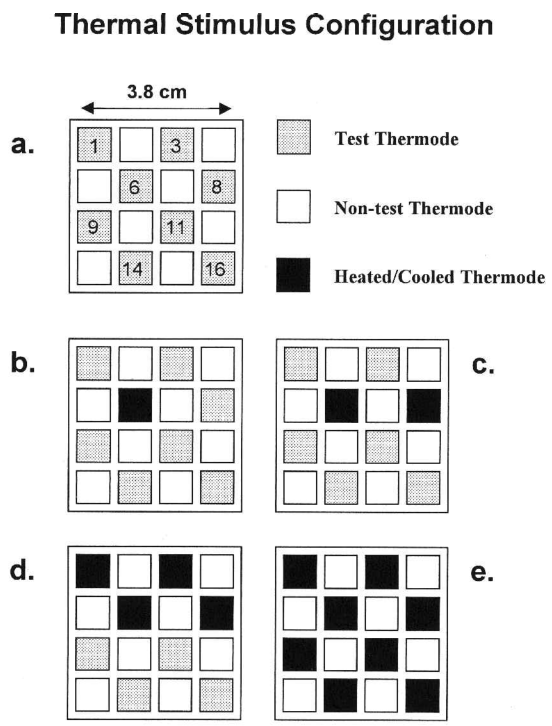

FIGURE 1. Spatial configuration of the Peltier thermode array with examples of stimuli having different total surface areas. (a) Shaded and numbered squares indicate the eight thermodes that were used throughout the study. (b)–(e) Examples of stimuli having surface areas of 0.64 cm^2 (thermode #6), 1.28 cm^2 (thermodes #6 and 8), 2.56 cm^2 (thermodes #1, 3, 6, 8) and 5.12 cm^2 (thermodes #1, 3, 6, 8, 9, 11, 14, 16), respectively.

procedure was impractical given the large number of thresholds that were needed to survey sensitivity for each of 15 different stimuli (at fixed sites) multiple times in each testing session. The 0.5°C/s rate was chosen as a compromise between slower rates that would significantly lengthen the testing session, and faster ones that would introduce a very large reaction time bias into the data.

Before data collection began all subjects served in a practice session to familiarize them with the psychophysical procedure and give them experience making threshold (detection) judgments for heating and cooling. In the practice sessions and in regular sessions the array was positioned against the volar surface of the right forearm for at least 5 min prior to testing to allow the test site to become adapted to the 33°C base temperature. The subjects were told that on each trial the experimenter would signal the beginning of a trial by saying "ready, go", and that they should then attend to the skin beneath the array and be ready to press a hand-held button the moment a sensation of heating or cooling appeared. Because it was likely that some test sites would lack low-threshold sensitivity to warmth or cold, the subjects were told that they should be alert for sensations such as pricking, burning, or stinging, and to press the button if one or more of these qualities appeared. Thus the task was referred to as detection of "heating" or "cooling" rather than only detection of warmth or cold. Subjects were encouraged to ask questions throughout the practice session to help them become comfortable with the task and with the qualities of sensations they experienced.

In the practice session and during data collection the surface area of stimulation was varied by energizing 1, 2, 4 or 8 modules (corresponding to areas of 0.64, 1.28, 2.56 and 5.12 cm^2) on each trial. Use of 8 of the 16 modules throughout practice and testing enabled the stimuli to be arranged in a checkerboard pattern that minimized thermal interactions between adjacent modules (Fig. 1). The spatial sequence of thermode activation was pseudo-randomized across trials as follows: [14 + 16], [9], [11], [1 + 3 + 6 + 8], [14], [16], [9 + 11], [6 + 8], [3], [1], [9 + 11 + 14 + 16], [6], [8], [1 + 3], [1 + 3 + 6 + 8 + 9 + 11 + 14 + 16]. This order maximized the time between thermal stimulation at each site while varying in unpredictable ways the number of modules heated or cooled across trials. Pilot tests indicated that although subjects could sometimes tell if the stimulus was large or small, their ability to judge the size and location of stimulation within the array was poor. A minimum of 15 s elapsed between the end of one trial and the beginning of the next, which together with the time required for the measurement of each threshold resulted in an approximate 3-min interval between stimulation at a given site. However, because the eight-module stimulus included sites that had been heated or cooled on immediately preceding trials, adaptation was minimized by inserting a 2-min break prior to this stimulus. The full stimulus sequence was presented only once in practice sessions but three times in test sessions. Repeating the sequence in test sessions required that we also insert a 2-min pause after the eight-module stimulus to reduce the potential for adaptation at the beginning of the second and third replicates.

Experiment 3: spatial effects on perceived intensity of heating and cooling The array was used in the same manner and configuration as in the preceding two experiments. However, in this experiment the subjects' task was to rate the intensity of sensations produced by heating and cooling. Two warm temperatures (36 and 40°C) and two cold temperatures (28 and 20°C) were tested over the same stimulus areas (0.64–5.12 cm^2) as in the detection task. Heating stimuli were chosen that would provide clearly differentiable levels of sensation without also stimulating heat-sensitive nociceptors (Bessou and Perl, 1969; Croze *et al.*, 1976; Van Hees and Gybels, 1981; Yarnitsky *et al.*, 1992). Cold stimuli were selected which produced a range of sensations comparable in intensity to those produced by the heating stimuli.

Intensity ratings were obtained using the Labeled Magnitude Scale (LMS), a category-ratio scale (Borg, 1982) developed by Green *et al.* (1993, 1996) for the purpose of quantifying the subjective magnitude of multi-modal stimulation. Subjects again started the experiment with a practice session, which this time included directions in and familiarization with the intensity scaling task. Intensity ratings were made by moving a cursor (via a mouse) to the position on the LMS that corresponded to the strength of whatever sensation was felt. After receiving general instructions the subject was read a list of 16 examples of common thermal sensations that ranged from weak (e.g., the warmth of a cat sitting on your lap) to very intense (e.g., dipping your hand in scalding hot water) for both cooling and heating. After the experimenter discerned from this exercise that the subject understood the rating scale, blocks of seven cooling (25°C) and seven warming (39°C) stimuli were given using a subset of the stimulus areas administered in the experiment proper.

Subjects served in four separate sessions, one for each of the test temperatures, with the order of temperatures varied across subjects. The sequence of spatial stimuli was the same as before, as were the intervals between trials and between the end of one sequence and the beginning of another. Three replicate ratings were obtained for each combination of temperature and stimulus area.

Data analysis

Detection thresholds Within-subject estimates of the threshold for each combination of temperature and surface area were calculated by taking the median value of the three replicates. Medians were used to minimize the effect of occasional false-positive responses during the slow (±0.5°C/s) temperature ramps. Premature termination of the temperature ramp could be particularly problematic when stimulation fell within WIFs, where thresholds for heating could be 10°C or more above the baseline temperature (Green and Cruz, 1998). In such cases subjects needed to remain vigilant and patient for 20 s or longer as they waited for a sensation to appear.

Estimates of the detection threshold for each surface area were calculated in two ways: (1) by averaging all of the thresholds for each stimulus size ("simple averaging" method), and (2) by averaging the thresholds for only the most sensitive sites for each stimulus size ("sensitive-site" method). The simple averaging method rests on the assumption that sensitivity to temperature is uniform in the skin, hence the location of stimulation can be ignored. To calculate the threshold for the 0.64 cm^2 stimulus, thresholds for all eight single-module stimuli were averaged; for the 1.28 cm^2 stimulus the four, two-module stimuli were averaged; for the 2.56 cm^2 stimulus the two, four-thermode stimuli were averaged; and for the 5.12 cm^2 stimulus the single threshold for the eight-module stimulus was averaged across subjects.

The sensitive-site method takes into account the heterogeneity of temperature sensitivity by calculating the effects of stimulus size relative to the most sensitive region of skin within a test field. Accordingly, thresholds were based on arithmetic means across subjects of the threshold for the most sensitive site for each surface area. For example, for each subject the single-module (1, 3, 6, 8, 9, 11, 14 or 16) that yielded the lowest median threshold over three replicates was taken as the estimate for the 0.64 cm^2 area, and these values were then averaged arithmetically across subjects. The same procedure was used for the 1.28 and 2.56 cm^2 areas.

Intensity ratings Replicate intensity ratings for each site were averaged arithmetically within subject. However, because ratings obtained using the LMS tend to be log-normally distributed across subjects (Green *et al.*, 1993), the subject means were converted to $\log_{10}$ prior to averaging across subjects.

To evaluate spatial factors in perception of suprathreshold warmth and cold, across-subject estimates of perceived intensity were calculated in the same two ways that thresholds were, i.e., as simple averages and in terms of the most sensitive (responsive) site within each surface area.

Statistical analyses (ANOVAs and *post hoc* Tukey tests) were performed on the log-mean values, and the level of significance was set at $p < 0.05$.

Results

Experiments 1 and 2: detection thresholds

Thresholds for detection as a function of stimulus area for both heating and cooling are displayed in Figure 2. Filled triangles show the results calculated as simple averages across all stimuli for each surface area, and filled circles show the results calculated in terms of the most sensitive site for each area. The two approaches gave very different results. The detection threshold for heating derived using the traditional averaging method was 2.5°C lower for the 5.12 cm^2 stimulus than for the 0.64 cm^2 stimulus. In contrast, the sensitive-site analysis yielded only a 0.6°C decline in threshold over the eight-fold change in area. A repeated measures ANOVA revealed a significant two-way interaction between stimulus area and the method of analysis ($F(3,51) = 40.8$, $p < 0.0001$), and Tukey HSD tests confirmed that thresholds for the two smallest areas were significantly higher for the averaged data than for the sensitive-site data ($p < 0.05$).

The results were similar for cooling: simple averaging indicated a +2.3°C gain in sensitivity over the eight-fold difference in area, whereas the sensitive-site analysis showed only a +0.9°C gain. The same interaction between area and method of analysis ($F(3,51) = 40.1$, $p < 0.0001$) was found for cold, as well as significant differences between methods for the smaller two areas ($p < 0.05$).

The lesser effects of area obtained with the sensitive-site analysis suggest that spatial summation of warmth and cold may be overestimated by simple averaging. If summation is taken as the gain in sensitivity over and above the threshold for the most sensitive site within an area of stimulation, summation could account for only 24% ($100 \times (0.6/2.5)$) of the total effect of stimulus size on the heating threshold, and only 39% ($100 \times (0.9/2.3)$) of the effect of stimulus size on the cooling threshold.

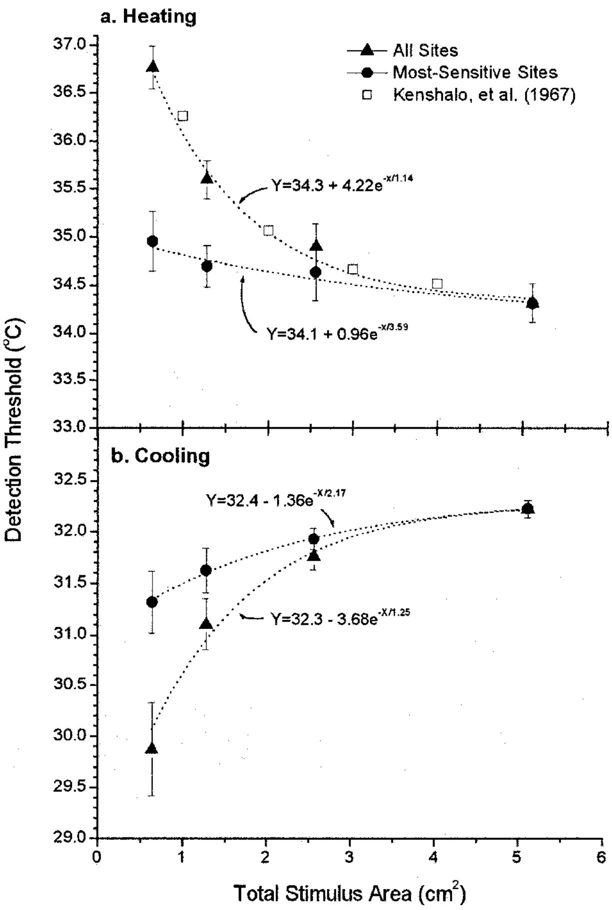

FIGURE 2. The results of the detection task are shown for heating (a) and cooling (b) calculated by simple averaging of all sites of each stimulus area (triangles) or by averaging only the most sensitive sites for each stimulus area (circles). Dotted lines denote exponential functions fitted to both sets of data for both methods of analysis (all $r > 0.93$). Open squares show good agreement between the rate of change in threshold across area calculated by simple averaging and warmth detection thresholds on the forearm reported by Kenshalo *et al.* (1967, Fig. 1) for conductive and radiant heat stimuli. To account for differences in the absolute value of thresholds between studies, a constant of 1.0°C was added to the Kenshalo *et al.* data. Error bars denote SEMs.

For both methods of analysis the data are well described by first-order exponential decay functions (all values of $r > 0.95$). The best-fitting functions, shown in Figure 2 as dotted lines, illustrate that the effect of area on detection declines toward an asymptote as stimulus size increases. Despite the very different rates of change over area for the "averaged" and "sensitive site" data, the two methods predict threshold values for very large stimuli that are within ± 0.2°C of one another for both heating and cooling. For heating the asymptotic value is approximately 34.2°C, corresponding to a minimum ΔT of $+1.2$°C, and for cooling it is approximately 32.4°C, or a minimum ΔT of (0.6°C. Concurrence between these estimates is, of course, abetted by use of the same threshold estimate for the 5.12 cm^2 area in both analyses.

The open squares in Figure 2a show data adapted from Kenshalo *et al.* (1967, Fig. 1), which were obtained on the forearms of two subjects who had received "intensive training in making judgments of threshold warm sensations" (p. 510). A constant of 1°C was added to the Kenshalo *et al.* data to bring them into register with the simple-averaging data. The nearly identical rate of change in sensitivity as a function of stimulus area is notable because Kenshalo *et al.* compared conductive and radiant heating and concluded that both forms of stimulation produced "complete" summation of stimulus energy. That is, on log–log coordinates the relationship between stimulus area and either radiation intensity or temperature change (ΔT) was linear with a slope near −1.0. However, plotting the simple-averaging data in the same way resulted in a slope of only −0.5. The lower slope is a byproduct of the higher thresholds in the present study, which render the effects of stimulus area proportionally smaller. The higher thresholds can be attributed to differences in methodology between the two studies. Whereas Kenshalo *et al.* tested just two, highly trained subjects using 3-s temperature pulses in a yes–no task, we tested a group of inexperienced subjects using a slow temperature ramp in a task that depended on reaction time. Reaction time would be expected to add a few tenths of a degree to each threshold measurement, and temporal summation, which for warmth has a critical duration of about 1 s (Stevens *et al.*, 1973), would work against detection of the temperature ramp at latencies significantly less than 1 s. When we adjusted our results by subtracting 1.0°C from the threshold for each stimulus area, plotting the simple-averaging data on log–log coordinates produced a linear function with a slope of −0.82 ($r = -0.99$). The same operation resulted in a slope of only −0.42 ($r = -0.94$) for the sensitive-site data.

Experiment 3: suprathreshold heating and cooling

The results for suprathreshold heating and cooling are shown in Figures 3 and 4, where $\log_{10}$ of perceived intensity is plotted as a function of stimulus area along a logarithmic axis. Plotted in this way the data are well described as linear functions (dotted lines; all $r \geq 0.96$), which means that at all four temperatures perceived intensity can be expressed as a power function of stimulus area. The equations for the power function are given in the figures.

Two aspects of the results deserve special attention. First, in accord with the threshold data, simple averaging led to a much larger effect of stimulus size on perceived intensity than did averaging across the most sensitive sites. For example, simple averaging gave a power function with an exponent (slope) of 1.0 for 36°C (Fig. 2a), which means that perceived intensity increased in direct proportion to stimulus area. This result agrees with the data of Stevens and Marks (1971) for low intensity warmth, which was taken as evidence of

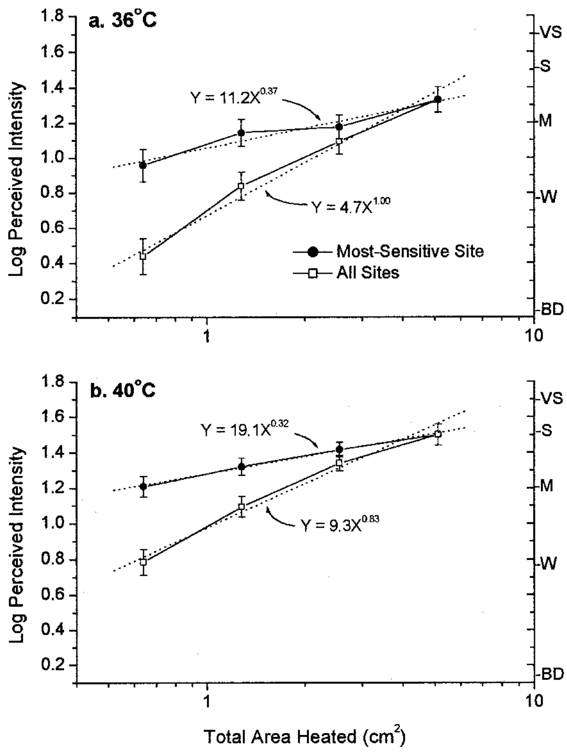

FIGURE 3. $\log_{10}$ intensity ratings as a function of stimulus size for 36°C (a) and 40°C (b) calculated as averages of all sites of each stimulus area (triangles) or as averages of the most sensitive sites for each stimulus area (circles) are plotted as a function of stimulus size on a logarithmic axis. The best-fitting linear equations are depicted by dotted lines. The adapting temperature was 33°C. Alphabetic characters on the right *y*-axis correspond to the semantic descriptors of sensation intensity of the rating scale (LMS) that was used in the experiment: BD = barely detectable; W = weak; M = moderate; S = strong; VS = very strong. The error bars denote SEMs.

complete spatial summation. In contrast the sensitive-site analysis yielded an exponent of only 0.37, which predicts that doubling stimulus size will increase perceived intensity by only 29%. Second, the exponents of the sensitive-site functions show remarkable consistency across temperature, varying between 0.32 and 0.37, whereas exponents for the averaged data vary more widely (0.67–1.0) and tend to be lower at the more extreme temperatures. However, the inverse relationship between power function exponent and thermal intensity reached statistical significance only for cooling. A repeated measures ANOVA of the cold data revealed a three-way interaction among method of analysis, temperature, and area ($F(3,51) = 3.16$, $p < 0.05$), while a separate analysis on the heating data showed that the same interaction fell short of significance ($F(3,51) = 2.02$, $p = 0.12$). This outcome was unexpected in light of the data of Stevens and Marks (1979) which showed that for suprathreshold cooling the effect of stimulus area stayed nearly constant across temperature. On the other hand, the average exponent for perceived cold as a function of stimulus area in the Stevens and Marks study was 0.79, which compares well with the exponents of 0.80 and 0.67 that we obtained for 28 and 20°C, respectively (Fig. 3).

Discussion

The present results support the hypothesis that topographic variations in sensitivity can significantly influence measurements of spatial summation in the temperature senses. Variations in sensitivity may account for two-thirds or more of the gain in sensitivity from enlarging stimulus area up to 5.12 cm², which places in question the common practice of attributing this gain solely to spatial summation. We therefore suggest (and hereafter use) the term *spatial enhancement* to describe the psychophysical effect of stimulus size on temperature perception.

The approach we took of selecting and averaging the most sensitive sites within a field of stimulation might be criticized on the basis that doing so will necessarily reduce the effect of increasing stimulus size. However, this would not be true if the sensitivity of the skin were homogeneous. Moreover, because sensitivity is markedly heterogeneous, it makes sense to base psychophysical inferences about spatial summation on the advantage accrued by stimulating an entire area compared to stimulating the most sensitive region within the area.

The idea that the heterogeneity of thermal sensitivity complicates psychophysical measurements of summation is not new. Hardy and Oppel (1937) noted that studying summation on the back and arm

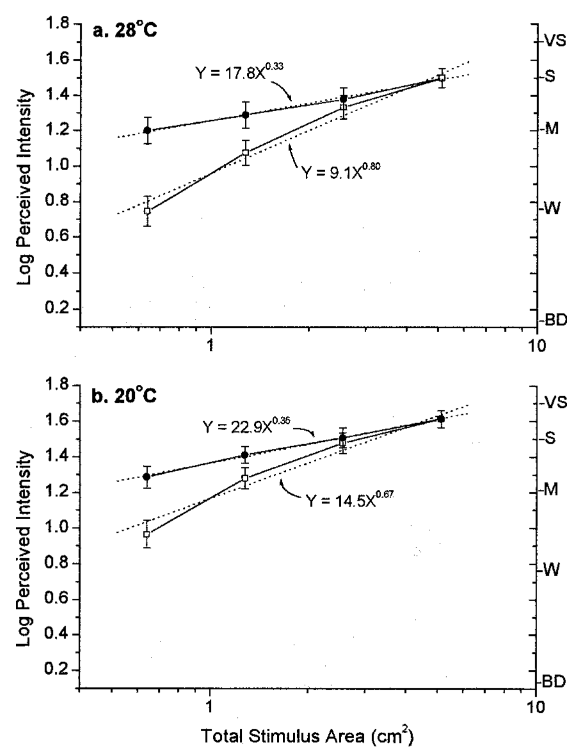

FIGURE 4. Same as Figure 3, but for cooling to 28°C (a) and 20°C (b).

was problematic because those sites were "highly variable in sensitivity from place to place, [therefore] nothing could be made of the data without further knowledge of end organ distribution" (p. 535). They chose to work on the forehead because they believed it had uniform warmth sensitivity. However, informal tests in our laboratory revealed gaps in warmth sensitivity on the forehead that were comparable to those we had found on the forearm (Green and Cruz, 1998). The radiant heat stimuli of Hardy and Oppel may not have been sufficiently focused to detect these discontinuities (Kenshalo *et al.*, 1967), or alternatively, their impression of uniform sensitivity may have arisen because ". . . no care was taken. . . to insure the testing of the same spot each time" (p. 533). Trial-to-trial variations in sensitivity cannot be linked to spatial variations in sensitivity unless stimulus location is controlled.

Whatever the explanation, the near reciprocity between area and intensity that Hardy and Oppel reported almost certainly resulted in part from the heterogeneity of warmth sensitivity on the forehead, and subsequent findings of complete or nearly complete reciprocity for warmth and cold (e.g., Hardy and Oppel, 1938; Herget *et al.*, 1941; Kenshalo *et al.*, 1967; Stevens and Marks, 1979) were likely influenced to varying degrees by the same spatial factor. Support for this view comes from the necessity of using larger stimuli to study summation on body regions that have lower thermal sensitivity (Stevens and Marks, 1971; Stevens *et al.*, 1974). In their study of suprathreshold warmth on the forehead and back, Stevens and Marks (1971) employed stimuli on the back that were about 20 times larger than those used on the forehead. Given the widely accepted view that the warmth sense was served by a plexus of axons, it appeared that larger stimuli were needed because ". . . in terms of *unit area*, the forehead is much more sensitive to warmth than is the back" (p. 393). We can now infer that larger stimuli may be required on the back because a lower density of warm fibers there causes small stimuli to go undetected at low levels of stimulation, and to evoke only burning or pricking at high levels of stimulation.

Evidence of spatial summation

While the present results reveal that spatial enhancement is not attributable entirely to spatial summation, they also provide further evidence that neural summation does indeed occur. The close agreement in results for warmth and cold in the sensitive-site analysis also raises the intriguing possibility that summation may be nearly equivalent for warmth and cold. Threshold differences between the most sensitive site and all eight sites were 0.9°C for cold vs 0.6°C for warmth, and for suprathreshold stimulation the slopes of the best fitting power functions for the two warm and two cold temperatures differed by no more than 0.05 (0.32–0.37). We can hypothesize that summation causes a 0.2–0.3°C drop in threshold per doubling of area, and an increase in perceived intensity that approximates a cube root function of stimulus size.

But it is also possible that point-to-point differences in sensitivity obscure the full magnitude of spatial summation within the low-threshold thermal systems, particularly when stimulus size is small. At locations on the skin where a single sensitive receptor can mediate detection, summation may not have a chance to take place among less sensitive receptors (see section Schematic model below). By this logic the potential for summation should be greater for larger stimuli that have a higher probability of stimulating multiple receptors with similar (high) sensitivities. Topography of sensitivity may therefore figure more importantly in spatial enhancement over a range of small stimulus areas like those tested here, whereas neural summation may play a more dominant role for larger areas. Theoretically, the lowest possible thresholds for warmth and cold would be reached when very large stimuli activate the most sensitive receptors in the skin, and summation occurs among them (Hardy and Oppel, 1937).

It should be possible to assess neural summation directly by identifying skin sites that have equivalent sensitivity and/or suprathreshold responsiveness, then measuring detection and perceived intensity when the sites are stimulated together and alone. We plan to take advantage of the 16-thermode array to conduct such experiments, which will also enable us to test the hypothesis that summation occurs in similar amounts for warmth and cold.

Schematic model of spatial factors in cutaneous temperature sensitivity

Based on current understanding of the sensory physiology of thermoreception, we have constructed a schematic model of how topographic and integrative factors may contribute to spatial enhancement (Fig. 5). The model is based on five assumptions: (1) thermal innervation is punctate and heterogeneous; (2) warm fibers and cold fibers exhibit a range of sensitivities; (3) adequate stimulation of a single temperature receptor is sufficient to trigger warmth or cold, i.e., spatial summation is not required for temperature perception; (4) central convergence of afferent pathways takes place, i.e., spatial summation occurs; and (5) where cold fibers and warm fibers are absent, thermal sensitivity is mediated by temperature-sensitive nociceptors. The model as it pertains to heat sensitivity is shown in Figure 5.

The first two assumptions receive ample support from electrophysiological data, whereas the remaining three are inferred from indirect yet persuasive psychophysical evidence. That warmth and cold can be evoked by adequate stimulation of single fibers is supported by the small size of receptive fields and the

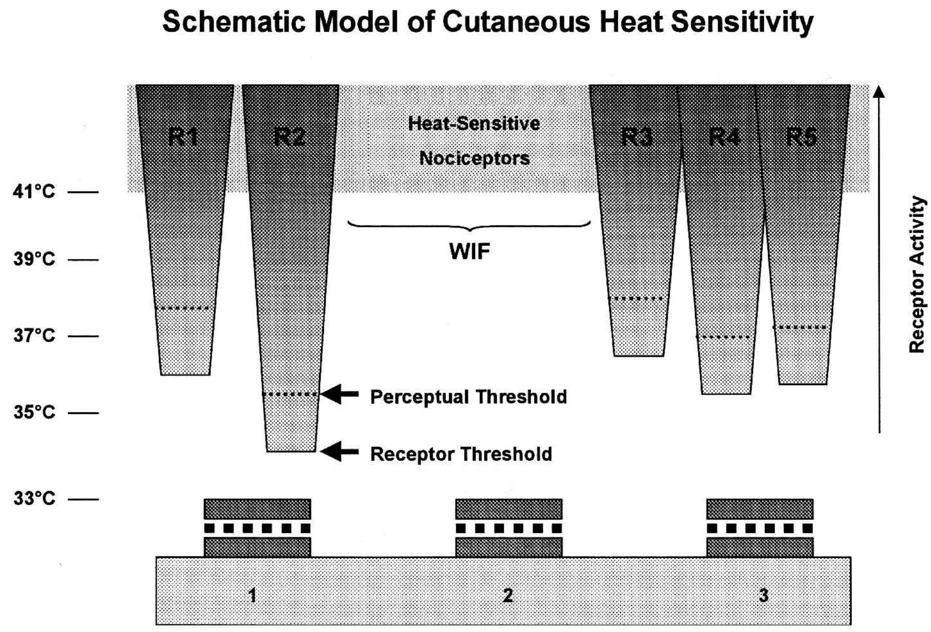

FIGURE 5. Schematic model of cutaneous heat sensitivity in a hypothetical patch of skin. The receptive fields and relative sensitivities of five different low-threshold warm fibers (R1–R5) are represented by the shaded vertical cones. The base of each cone represents the skin temperature at which each receptors' dynamic discharge increases significantly above its adapted level at 33°C ("receptor threshold"); the dotted horizontal line within each cone represents the level of activation in a given receptor neuron which alone would be adequate to trigger a sensation of warmth ("perceptual threshold"). A denser field of heat-sensitive nociceptors is represented by the stippled area above 41°C. WIF = warmth-insensitive field. Three Peltier thermodes (1–3) are pictured at separate locations at the bottom of the figure. See text for descriptions of how heating at each of these skin sites may be mediated by the warm receptor(s) and/or nociceptors that lie beneath the thermodes in the skin.

existence of "temperature spots". Although some spots may be served by more than one receptor, it is unlikely that all are. The clearest evidence of spatial summation comes from studies of additivity between separate skin sites, including across the midline (Marks and Stevens, 1973; Rózsa and Kenshalo, 1977). Lastly, the logical assumption that nociceptors mediate detection and perception when no low-threshold thermoreceptors lie within the stimulated area is supported qualitatively by reports of burning and stinging from small heat stimuli (e.g., Hardy and Oppel, 1937), and quantitatively by evidence that thresholds inside WIFs (Green and Cruz, 1998) agree closely with the thresholds of C-heat sensitive nociceptors (Van Hees and Gybels, 1981; Yarnitsky *et al.*, 1992).

The model depicts a patch of skin several centimeters in area that contains five irregularly spaced, low-threshold warm receptors (R1–R5) that have different sensitivities. If thermode #1 were heated the threshold for detection at that location would be mediated solely by R2. Excitation of R2 would increase with temperature until at about 35°C its dynamic response would be adequate to produce the perception of warmth. If thermode #2 were heated, the absence of a low-threshold warm fiber at that site would cause detection to be mediated by nociceptors at or above 41°C. In this case the subject's first indication of heating would be burning, stinging or pricking. If thermode #3 were heated, it would begin to evoke dynamic responses in receptors R4 and R5 at temperatures just above 36°C. Because the activity of these neurons would be summated centrally, the perceptual threshold would be reached at a lower temperature than if either were stimulated alone. Note however that in this hypothetical patch of skin, if temperature were slowly increased at all three thermodes detection would still occur via R2, since stimulation of that "most sensitive site" would trigger warmth before excitation of R4 and R5 was adequate to do so. If instead the five receptors had similar thresholds, the opportunity for spatial summation would be maximized and activating all three thermodes would produce a significantly lower threshold than would any one thermode alone. The same effect could be achieved by dramatically enlarging stimulus size, which would increase the probability of stimulating multiple receptors that have low thresholds. The combined effects of topography and summation for smaller stimuli, and summation alone for larger stimuli, may account for Hardy and co-workers' (Herget *et al.*, 1941) observation that the effect of increasing stimulus size was more pronounced for smaller stimuli.

Figure 5 also illustrates how suprathreshold sensations may vary in intensity and quality depending upon the location and surface area of the stimulus, and why at higher levels of stimulation the topographic component of spatial enhancement should also tend to decrease. As temperature rises the lateral spread of heat (depicted here by widening receptive fields at higher temperatures) will increase the probability that every thermode will stimulate at least one warm receptor, and as the threshold of heat pain is approached heat-sensitive nociceptors, which innervate the skin much more densely than do warm fibers (Hallin *et al.*, 1981), begin to respond. These two factors may help explain Stevens and Marks' (1971) finding of a diminishing effect of stimulus size as radiation intensity rose toward the heat pain threshold. The same trend, although not statistically significant, was found in the present data between 36 and 40°C (Fig. 2). However, a preponderance of psychophysical evidence indicates that significant spatial enhancement occurs above the heat pain threshold (Machet-Pietropaoli and Chery-Croze, 1979; Kojo and Pertovaara, 1987; Price *et al.*, 1989, 1992; Douglass *et al.*, 1992), and there is physiological evidence of neural integration within receptive fields of single nociceptors in the periphery as well as evidence of convergence within the CNS (e.g., Torebjörk *et al.*, 1984; Douglass *et al.*, 1992). Spatial enhancement of heat pain therefore conforms to the early ideas about warmth innervation, perhaps because many of the undifferentiated nerve endings seen in tissue samples from temperature spots (Dallenbach, 1927) that were thought to be warm fibers and cold fibers were actually nociceptors.

The schematic model should also apply to perception of cooling, although the relationship between nociception and low-threshold cold fibers is less well understood and may be more complex (Georgopoulos, 1976; LaMotte and Thalhammer, 1982; Campero *et al.*, 1996; Simone and Kajander, 1996). The latter fact, plus the relatively higher density of cold fibers compared to warm fibers, may explain why in previous studies suprathreshold spatial enhancement was reported to be less for cold than for warmth, but remained more constant across temperature (Stevens and Marks, 1979).

Summary and conclusions

Prior studies of spatial summation were based on the assumption that sensitivity was effectively homogeneous within the area of measurement. Here we have shown that topographical variations in temperature sensitivity can contribute to psychophysical measurements of the effect of stimulus size (*spatial enhancement*) on both detection and perception of heating and cooling. These variations, which differentially affect perception of small stimuli, may have led to overestimations of spatial summation. Our results therefore reaffirm Hardy and Oppel's (1937) forgotten observation that psychophysical measurements of spatial summation cannot be meaningfully interpreted unless local variations in sensitivity are taken into account.

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