The distribution of cutaneous sudomotor and alliesthesial thermosensitivity in mildly heat-stressed humans: an open-loop approach

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The distribution of cutaneous thermosensitivity has not been determined in humans for the control of autonomic or behavioural thermoregulation under open-loop conditions. We therefore examined local cutaneous warm and cool sensitivities for sweating and whole-body thermal discomfort (as a measure of alliesthesia). Thirteen males rested supine during warming (+4°C), and mild (−4°C) and moderate (−11°C) cooling of ten skin sites (274 cm^2), whilst the core and remaining skin temperatures were clamped above the sweat threshold using a water-perfusion suit and climate chamber. Local thermosensitivities were calculated from changes in sweat rates (pooled from sweat capsules on all limbs) and thermal discomfort, relative to the changes in local skin temperature. Thermosensitivities were examined across local sites and body segments (e.g. torso, limbs). The face displayed stronger cold (−11°C) sensitivity than the forearm, thigh, leg and foot ($P = 0.01$), and was 2–5 times more thermosensitive than any other segment for both sudomotor and discomfort responses ($P = 0.01$). The face also showed greater warmth sensitivity than the limbs for sudomotor control and discomfort ($P = 0.01$). The limb extremities ranked as the least thermosensitive segment for both responses during warming, and for discomfort responses during moderate cooling (−11°C). Approximately 70% of the local variance in sudomotor sensitivity was common to the alliesthesial sensitivity. We believe these open-loop methods have provided the first clear evidence for a greater facial thermosensitivity for sweating and whole-body thermal discomfort.

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Thermal stimulation of cutaneous, and some deep body, tissues drives powerful and highly developed behavioural and autonomic thermoregulatory responses in humans. The magnitude of these responses to such stimulation quantifies the thermosensitivity of that tissue. It is well established that cutaneous thermosensitivity is lower than that of the body core in driving autonomic responses (Stolwijk & Hardy, 1966; Nadel *et al.* 1971; Wyss *et al.* 1975), and possibly the alliesthesia-related sensory responses that underlie thermoregulatory behaviour (Cabanac *et al.* 1972). However, the skin experiences much larger temperature fluctuations, which can drive the autonomic and sensory responses (Cabanac *et al.* 1972; Bothorel *et al.* 1991), yet it remains unknown, despite several studies, whether or not these thermosensitivities are uniform among skin sites in humans. This is primarily due to methodological shortcomings within the few studies in which thermoeffector responses have been directly measured, but under closed-loop experimental conditions (Nadel *et al.* 1973; Crawshaw *et al.* 1975; Libert *et al.* 1984). Therefore, in this study, we tested the hypothesis that, under open-loop conditions, achieved by clamping the untreated tissue temperatures, regional differences would exist for cutaneous thermosensitivities for sweating, and for thermal discomfort, as a measure of thermal alliesthesia.

Two lines of evidence support the notion that localized differences may exist in cutaneous thermosensitivities for sweating and thermal discomfort. First, neurophysiological evidence has shown a higher density of thermal afferents arising from the face, with little or no apparent convergence at the thalamus (Poulos & Molt, 1976; Hellon & Dawson, 1979). A high density and unique pattern of thermoafferent flow from scrotal skin has also been observed at the midbrain in rats (Hellon & Mitchell, 1975; Schingnitz & Werner, 1980), consistent with a greater local thermosensitivity (Waites, 1961; Ingram & Legge, 1972; Schingnitz & Werner, 1980). Second,

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several human studies, investigating the local nature of transient cutaneous thermosensitivity, have observed a higher relative sensitivity for the face in relation to local temperature sensation (Hardy & Oppel, 1938; Kenshalo *et al.* 1967; Stevens *et al.* 1974).

At present, however, our understanding of differential cutaneous thermosensitivity underlying thermoregulation in humans is based wholly upon observations derived from closed-loop experiments, which we believe represent an inappropriate experimental model to address this topic, since the temperatures of untreated thermosensitive tissues are not clamped. Under closed-loop conditions, local perturbations of skin temperature elicit whole-body changes in effector activity, which in turn modify the temperature of other thermosensitive tissues, such that the nett thermal perturbation is minimized. Closed-loop thermosensitivities have been estimated from: (a) the temperature change of untreated tissues following the thermoeffector response (Hales & Hutchinson, 1971; Ingram & Legge, 1972); (b) non-thermoregulatory responses, such as inspiratory effort (Burke & Mekjaviæ, 1991); and (c) the magnitude of thermoeffector responses (Nadel *et al.* 1973; Crawshaw *et al.* 1975). The last approach provides the most direct determination of thermosensitivity. However, by definition, it also requires that changes in thermoeffector activity are primarily driven by changes in thermoafferent flow arising from the stimulated skin site, and this requirement cannot be satisfied under closed-loop conditions. Clamping the temperatures of unstimulated thermosensitive structures to open the control loops is especially important when investigating localized cutaneous thermosensitivity (Jessen, 1981), since the sensitivity of such sites is very low relative to the combined sensitivity of unstimulated tissues, and some non-thermal influences. Indeed, the failure of previous groups (Nadel *et al.* 1973; Crawshaw *et al.* 1975) to apply such thermal clamps represents the principal methodological limitation of human research in this area.

We have developed a method whereby thermoregulatory control loops in humans can be held open for extended periods while discrete skin sites are thermally stimulated, without modifying the temperature of adjacent skin or core tissues (Cotter *et al.* 1995). In a preliminary study using this method (Patterson *et al.* 1998), we found no differences in the warm or cool sensitivities for sweating responses for the face, arm, forearm or hand. However, given the low relative thermosensitivity of the skin, we considered the possibility that our local thermal stimuli may have been inadequate, due either to the size of the stimulus or the design of the apparatus for its application. We also wished to extend this investigation to include upper- and lower-body skin sites, as well as preselected segmental combinations of sites. Accordingly, we refined this method and undertook the present study to provide an open-loop, whole-body assessment of localized cutaneous thermosensitivities in humans.

Methods

Warm and cool thermosensitivities for sudomotor drive and whole-body thermal discomfort were assessed during open-loop heating and cooling of 10 discrete skin sites: face (forehead and cheeks), chest, abdomen, lower back, lateral (upper) arm, dorsal forearm, hand (distal palm, fingers and dorsal surface), anterior thigh, lateral leg and foot (toes and dorsal surface). These local sites were chosen so that both local and segmental (grouped) thermosensitivities could be investigated separately. Segmental data were obtained by averaging the local thermosensitivities across several sites: face, torso (chest, abdomen and back), upper limb (arm, forearm and hand), lower limb (thigh, leg and foot), limb extremities (hand and foot) and proximal limb surfaces (forearm, arm, leg and thigh).

Water-perfused patches were used to change local skin temperature (T_{skl}) at the 10 sites individually, as explained under Procedures below, with the order of stimulation balanced as fully as possible across sites. Patch sizes were limited to the maximal treatable facial area (274 cm^2; ~1.4% skin surface). The remaining skin and core tissues were thermally clamped using a water-perfusion suit that covered 93% of the skin surface, and a climate chamber. Three trials, conducted at the same time of day (within subjects) and 14 days apart, were required for each subject. All procedures were approved by the Human Research Ethics Committee, University of Wollongong, in accordance with the Declaration of Helsinki.

Subjects

Thirteen physically active males participated, after providing written, informed consent (mean ± s.d. age 27.1 ± 6.7 years, height 1.79 ± 0.06 m, mass 75.9 ± 7.5 kg and surface area 1.94 ± 0.06 m^2). Subjects were instructed to avoid physical training, alcohol (for at least 20 h) and caffeinated drinks (for at least 4 h) prior to attendance, and to consume 20 ml H_2O (kg body mass)$^{-1}$ on the morning of each trial, in addition to their normal fluid intake.

Procedure

Upon arrival at the laboratory, subjects dressed in a bathing costume, and were weighed and fitted with three core temperature thermistors, before resting supine on a wire-mesh bed in a climate chamber during preparation (~1 h; 28°C; relative humidity ~60%). Climatic conditions were then set to achieve a hot-humid state (35.8°C, s.d. 0.2°C, and relative humidity 55.2%, s.d. 0.2%). The suit and all patches were initially perfused with warm water (36.7°C). This combination of water and air

temperatures ensured the clamping of core temperature and a highly uniform, whole-body skin temperature. This isothermal clamp primed the sudomotor response, optimizing the extent to which sweat secretion could increase and decrease without saturation and cessation in response to local cutaneous warming and cooling, respectively (Cotter *et al.* 1995). Body mass losses during testing were less than 1 kg, so rehydration was not undertaken until after each trial.

When the sweat traces indicated that stable and generalized sweating was present, 10 min of baseline data were recorded before the first T_{skl} stimulus. Stimuli consisted of warming (W_{+4}) or cooling (C_{-4}) T_{skl} by 4°C for 10 min, commencing from an adapting skin temperature of 36.3°C (S.D. 0.1°C). An additional, stronger cooling stimulus (C_{-11}) was applied for 5 min, immediately following local warming, to achieve a T_{skl} change (ΔT_{skl}) of −11°C from 40.3°C (S.D. 0.2°C), at a peak rate of approximately $-8°C\,min^{-1}$. This stimulus, which was not totally independent of the effects of W_{+4}, was used because we had previously demonstrated a low cutaneous sensitivity for mild (−3°C) cooling (Patterson *et al.* 1998). The W_{+4} and C_{-11} treatments were always applied 60–80 min before the C_{-4} treatment at a given site. A 10 min recovery separated each C_{-11} and W_{+4} treatment between sites, during which recovery to the pretreatment T_{skl} was expedited by perfusing the patch with water of the opposing temperature for 35–50 s.

Apparatus and measurements

Water-perfusion system. The perfusion suit contained 140 tubes, each 1 m long, arranged such that the long-sleeved jacket and full-length trousers received water in parallel (Paul Webb Associates, Yellow Springs, OH, USA). Water was supplied at $2.5\,l\,min^{-1}$ to the suit and patches, but at $1.0\,l\,min^{-1}$ to a patch during T_{skl} treatment, from heated water baths (type VFP, Grant Instruments Ltd., Shepreth, Cambridgeshire, UK) connected to coolers (type CK2, Grant Refrigeration Systems). Approximately 93% of the skin surface area was incorporated within the suit, yet its lattice design, and the mesh bed, maximized skin exposure to the environment. Perfusion patches were constructed from identical tubing, arranged in parallel, with 2–3 mm separations. The effectiveness of the patches was improved relative to our previous study (Patterson *et al.* 1998) by making them more pliable, 11% larger, and with twice the number of tubes, thus increasing patch size and optimizing the skin–patch interface.

Body temperatures. Core temperatures were measured from the oesophagus (40.0 ± 2.1 cm from the naves; after Mekjaviæ & Rempel, 1990), the auditory canal (19 mm from the skin surface, passively insulated) and the rectum (11 cm from the anus) using flexible thermistors (Edale Instruments Ltd, Cambridge, UK, and YSI type-401, Yellow Springs Instruments, Yellow Springs, OH, USA). Mean core temperature was calculated as the unweighted mean of these temperatures. Skin temperature was measured at the forehead, right abdomen and bilaterally on the chest, arm, forearm, dorsal hand, anterior thigh, lateral leg and dorsal foot using thermistors fastened either beneath perfusion patches (YSI type-EU, Yellow Springs Instruments, U.S.A), or using one layer of adhesive tape. Mean skin temperature was calculated from these sites (excluding the treated site) using area weightings (Hardy & DuBois, 1938). Mean body temperature was calculated from the mean core and skin temperatures, using a ratio of 0.8 : 0.2. An unweighted average T_{skl} for the site being treated was measured using five thermistors positioned beneath each treatment patch (YSI type-EU, Yellow Springs Instruments). All temperatures were logged at 0.2 Hz (1206 Series Squirrel, Grant Instruments Ltd, Shepreth, Cambridgeshire, UK). Thermistors were calibrated against a certified reference mercury thermometer in a stirred water bath (±0.05°C: Dobros total immersion thermometer, Dobbie Instruments, Sydney, Australia).

Sweating. Sweat rates ($\dot{m}_{sw}$) were sampled simultaneously (1 Hz) from the treatment site and seven other skin surfaces using two 4-channel ventilated capsule systems (Sweat Monitor 1.1, Clinical Engineering Solutions, Sydney, Australia). Reference sweat capsules ($3.16\,cm^2$) were glued to the anterolateral surface of each leg and the dorsal surface of each hand during every treatment, so that sweat rate was always measured from the four limbs. The remaining four capsules were distributed such that sweat rate was always measured within the treatment perfusion patch, with contralateral measurements recorded when testing the foot, thigh, abdomen and forearm (and leg and hand). Low-humidity airflow (~12%, $0.2\,l\,min^{-1}$) was generated for each capsule by pumping room air across a saturated solution of lithium chloride. Differences between pre- and postcapsular air were sampled for humidity (Minicap 2 capacitance hygrometer, Panametrics Pty. Ltd, Sydney, Australia) and temperature (AD 590, Analog Devices, Norwood, MA, USA), permitting the real-time derivation of $\dot{m}_{sw}$.

The configuration of sweat capsules allowed us to investigate three aspects of sudomotor function during these T_{skl} treatments. First, the generalized (overall) sweating response was obtained by averaging data collected from each of the capsules positioned at the untreated sites.

Second, local sweating responses could be evaluated from capsules positioned wholly within each treatment patch, and took two forms. The gross local sweating response was simply the sweat rate recorded within each treatment patch. Since local sweating responses are invariably greater than the generalized responses, we

subtracted the generalized sweat rates from local sweat rate to derive the nett local sweating response. Each treated site acted as its own control in deriving the nett local response. For example, the nett local sweating response of the right forearm, when it was warmed, was calculated as:

([right forearm $\Delta\dot{m}_{sw}$] − [mean $\Delta\dot{m}_{sw}$ of untreated sites]) − (mean [right forearm $\Delta\dot{m}_{sw}$ − mean $\Delta\dot{m}_{sw}$ of untreated sites] during warming of hand, arm and face).

This calculation was performed within subjects for all 10 treated sites, before averaging across those sites for each treatment type. Data from the tenth minute of the mild warming and cooling treatments were used to optimize ΔT_{skl} uniformity beneath the intrapatch sweat capsule and treatment patch.

Third, the sweat response occurring contralaterally to the ΔT_{skl} treatment was calculated in a similar manner (with each site used as its own control). This calculation was performed using the five sites for which a limb treatment also had a contralateral sweat capsule, and data from the full treatment period were used because T_{skl} was stable within these contralateral sites throughout these treatments.

Cutaneous sudomotor thermosensitivity was quantified from the $\dot{m}_{sw}$ changes during each treatment, relative to T_{skl} changes, averaged across the four reference sweat capsules. When T_{skl} stimuli were applied to a limb site that also contained a reference sweat capsule, the nett local effects of T_{skl} on $\dot{m}_{sw}$ were calculated, as described above, and subtracted from the local $\dot{m}_{sw}$ response. Baseline and treatment $\dot{m}_{sw}$ were taken as an average over the 3.5 min preceding, and the 4 min (C_{-11}) or 10 min (C_{-4} and W_{+4}) following subject-reported stimulus detection. A single index of thermosensitivity was also estimated for each treated skin site, within subjects, from the change in sweat rate ($\Delta\dot{m}_{sw}$) relative to the ΔT_{skl}, across the three stimuli. This analysis was performed since a linear relationship between $\Delta\dot{m}_{sw}$ and ΔT_{skl} was evident across stimuli, when averaged across the first 4 min of treatments. The first 4 min of the sweat response was chosen because this duration was common to all treatments, and it was least affected by non-thermal influences (especially discomfort votes obtained at 4 min; see below). The index was not specific to the direction or the nature of the stimulus, but provided an estimation of local, absolute thermosensitivity under conditions of mild, resting heat stress.

Thermal discomfort. Whole-body thermal discomfort was reported 1 min before, and 4 min after, initiating each local stimulus. Discomfort votes were obtained using a five-point continuous scale (Gagge *et al.* 1967), in response to the question, 'How comfortable do you feel with the temperature of your whole body?'. Cutaneous thermosensitivity for this variable was quantified by subtraction of the baseline discomfort, and normalizing for the ΔT_{skl}.

Statistical analysis

Data from the 10 treated skin sites were analysed separately, and also following grouping into body segments, to provide intersite and intersegmental assessments of cutaneous thermosensitivity. The local and segmental nature of cutaneous thermosensitivity was analysed using one- and two-way repeated-measures ANOVA, with differences isolated using Tukey's *HSD* statistic ($\alpha = 0.05$). Statistical power (φ) was calculated for non-significant differences. Studentised scores were used to assess whether or not responses to the three stimuli differed from zero. The Pearson Product Moment correlation was used to evaluate the relation between the local sensitivity distributions for $\dot{m}_{sw}$ and thermal discomfort. Parametric analysis was considered acceptable since, across the three treatment conditions, the responses were linearly related to the independent variable (ΔT_{skl}), and therefore approximated a scalar quantity. Unless stated otherwise, temperatures are means with standard deviations (± S.D.; $n = 13$), whereas the $\dot{m}_{sw}$ ($n = 13$) and thermal discomfort ($n = 12$) responses are means. with standard errors of the means (S.E.M.).

Results

Temperatures

Across all trials, mean body temperature remained clamped (36.79 ± 0.15°C) during localized skin warming ($\Delta = 0.02 \pm 0.01$°C), equivalent local cooling ($\Delta = 0.00 \pm 0.01$°C) and more intense skin cooling ($\Delta = 0.01 \pm 0.01$°C). The ΔT_{skl} stimuli were of equivalent magnitude among sites for warming (W_{+4}; 3.55 ± 0.15°C when averaged across first 4 min; $P = 0.28$) and mild cooling (C_{-4}; -3.30 ± 0.11°C; $P = 0.22$), but were less powerful at the face (-7.40 ± 0.60°C) than at each of the other sites, except the back (-7.54 ± 0.69°C), during the C_{-11} treatment (-8.09 ± 0.27°C; $P = 0.01$). Furthermore, the ΔT_{skl} during the last minute of each treatment was 4.07 ± 0.39°C (W_{+4}), -4.07 ± 0.13°C (C_{-4}) and -10.90 ± 0.42°C (C_{-11}). Because we successfully clamped mean body temperature, normalized both sweating and discomfort responses with respect to the ΔT_{skl} and applied a relatively uniform ΔT_{skl}, we consider that our methods conformed to open-loop experimental conditions. In addition, we believe that the thermoregulatory responses reported below were primarily due to the effects of T_{skl} stimuli upon primed sweat glands, and represent valid assessments of local cutaneous thermosensitivities.

Sweating responses

The average, generalized steady-state $\dot{m}_{sw}$ between treatment periods was 0.48 ± 0.13 mg cm^{-2} min^{-1},

which generally, but not universally, increased and decreased in accordance with the direction of T_{skl} stimuli (Fig. 1). When considered across subjects and stimulated sites, $\dot{m}_{sw}$ increased by 16% (0.08 ± 0.01 mg cm^{-2} min^{-1}; $P < 0.01$) with W_{+4}, then decreased by 26% (-0.12 ± 0.02 mg cm^{-2} min^{-1}; $P < 0.01$) from this slightly elevated, precooling baseline, with the immediate application of the moderate cooling stimulus (C_{-11}). Conversely, the mild cooling stimulus (C_{-4}) elicited a sweat decrease from baseline of only 7% (-0.03 ± 0.01 mg cm^{-2} min^{-1}; $P = 0.01$; Fig. 1). Of the 10 sites treated, only the face showed a consistently high thermosensitivity. For example, warming the face by 4°C increased $\dot{m}_{sw}$ by ~50%, and cooling it by 4°C elicited the only clear and consistent suppression of $\dot{m}_{sw}$.

In this study, our focus was to evaluate local cutaneous thermosensitivities from a generalized sweating response. However, because all treatment sites also contained sweat capsules, we were able to differentiate between generalized, gross local, nett local and contralateral sweating responses. The following response patterns were evident. First, the gross local sweating response was always larger than the generalized sweating response ($P < 0.01$), as would be expected. Second, the generalized sweating response was

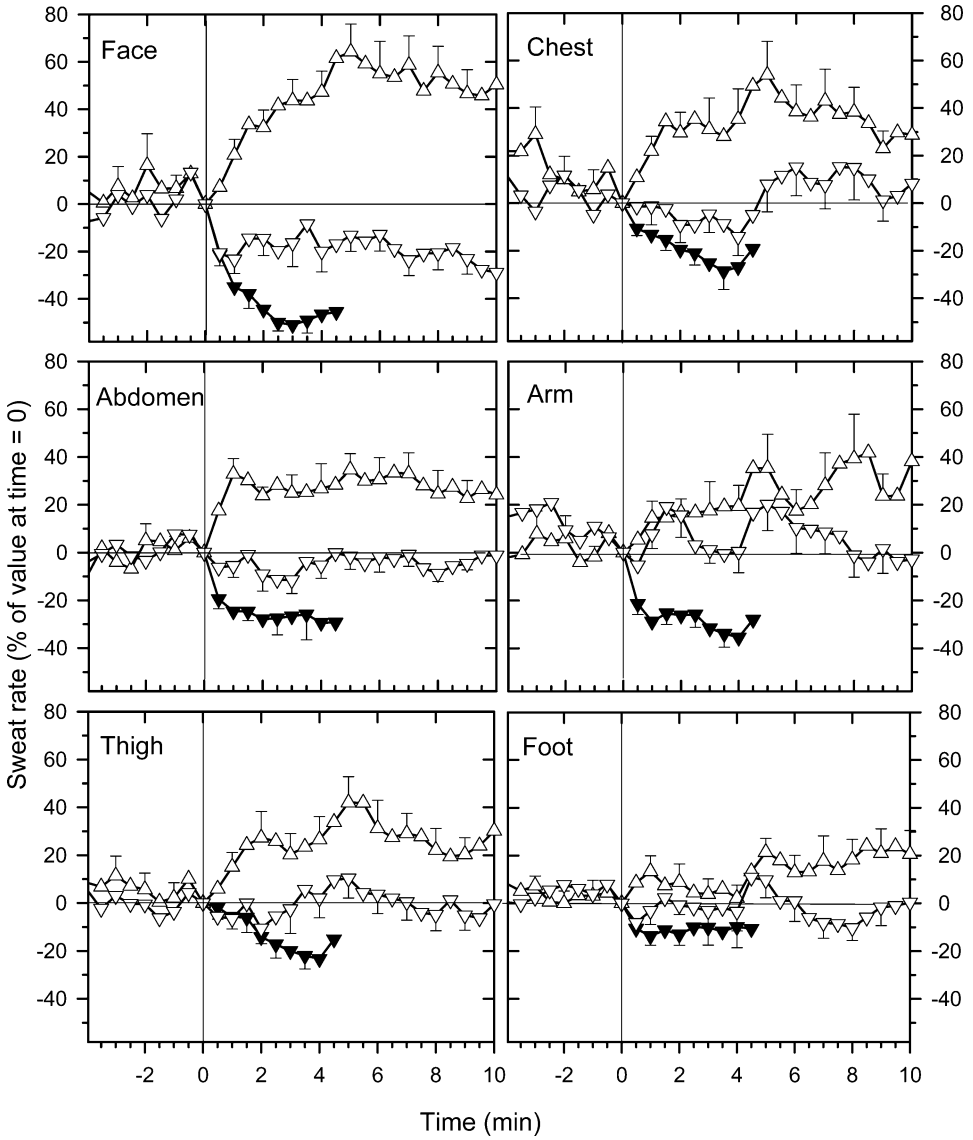

Figure 1. Limb sweat rates during warming and cooling of six discrete skin sites
Data are means (± S.E.M.), averaged across all limbs, during mild warming (4°C; Δ), mild cooling (−4°C; ∇) or moderate cooling treatments (−11°C; ▼) applied to local skin sites. Moderate cooling was applied immediately after mild warming, so the baseline was elevated relative to the other treatments. Sweat rates are percentages of the value observed when the thermal stimulus was first perceived (time = 0).

2.5 times more sensitive to heating than to equivalent cooling ($P < 0.01$). Third, and in contrast, the nett local sweating response was of equivalent magnitude for these two stimuli (0.022 ± 0.002 mg cm^{-2} min^{-1} °C^{-1} for both treatments), and accounted for approximately half (48%) of the gross local sweating response to warming, and for three-quarters (73%) of the gross local response to mild cooling. The relatively high contribution of local (e.g. physicochemical) *versus* generalized (neural) effects on sweat inhibition within the patch was presumably due, in part, to the small area of stimulation and the fact that these sweating responses were examined over a period of stable ΔT_{skl}, when additional dynamic thermoreceptor influences were minimized. Fourth, the sweating response within the contralateral site was more pronounced than at other untreated sites during the strong cooling stimulus (C_{-11}; $P < 0.01$). This was not attributed to local skin temperature shifts, since ΔT_{skl} at these sites was clamped ($\Delta T_{skl} = 0.01 \pm 0.02$°C; $P = 0.99$). Fifth, while the sweating response varied among the sampling sites, this variation was neither systematic nor asymmetric for warming ($P = 0.88$) or cooling ($P = 0.40$).

Local thermosensitivities. Localized, temperature-dependent differences in cutaneous thermosensitivity were observed ($F_{29,360} = 1.52$; $P = 0.04$; Fig. 2). The face showed the strongest cold sensitivity, with moderate facial cooling (C_{-11}) suppressing sweating more powerfully than equivalent cooling of the forearm, thigh, leg or foot ($F_{9,120} = 2.65$; $P = 0.01$; Fig. 2). Whilst the face was the only treated site to clearly suppress sweating during C_{-4}, between-site differences were not significant ($P = 0.56$; $\varphi = 0.05$; Fig. 2). Similarly, the warm thermosensitivities of the face and abdomen were 4–5 times greater than those of the forearm, hand and foot, but significant differences were not evident ($F_{9,120} = 2.37$; $P = 0.02$; Fig. 2).

Segmental thermosensitivity. When thermosensitivity comparisons were made among body segments, the face was 2–3 times more sensitive than any other segment during the C_{-11} treatments ($P < 0.01$; Fig. 3). That is, rapid cooling of the face consistently elicited the most powerful suppression of generalized sweating. During mild cooling (C_{-4}), the face was more sensitive than the upper limb ($P = 0.03$; Fig. 3). During local warming (W_{+4}), the face was 2, 3 and 5 times more thermosensitive than the lower limb, upper limb and limb extremity segments, respectively ($P < 0.01$). Only one site differed significantly from the sensitivity of the torso, with the limb extremities being 4 times less sensitive ($P < 0.01$; Fig. 3).

Thermal discomfort

During the pretreatment steady state (baseline), whole-body thermal discomfort (alliesthesia) ranged between 'comfortable' and 'slightly uncomfortable' (1.42 ± 0.10; $n = 12$). This mild discomfort was heightened during mild warming (0.16 ± 0.04; $P = 0.01$) and reduced, but not eliminated, during moderate cooling (C_{-11}: -0.22 ± 0.06; $P = 0.01$). However, the C_{-4} treatment had minimal alliesthesial affect (-0.01 ± 0.01; $P = 0.53$).

Local thermosensitivities. We have previously reported the effects of these local thermal stimuli on thermal discomfort (Cotter *et al.* 1996). Our principal observation was that the face generally displayed the highest thermosensitivity across the three thermal stimuli, but was only significantly greater than that of the forearm, hand, leg and foot during C_{-11} treatments ($P = 0.01$). To these observations, we now add segmental data.

Segmental thermosensitivities. The pattern for the intersegmental cutaneous sensitivities for whole-body thermal discomfort was similar to that observed for sweating. That is, intersegmental differences were not apparent for the C_{-4} treatment ($P = 0.23$; $\varphi = 0.14$), whereas the face was 2–5 times more sensitive than any

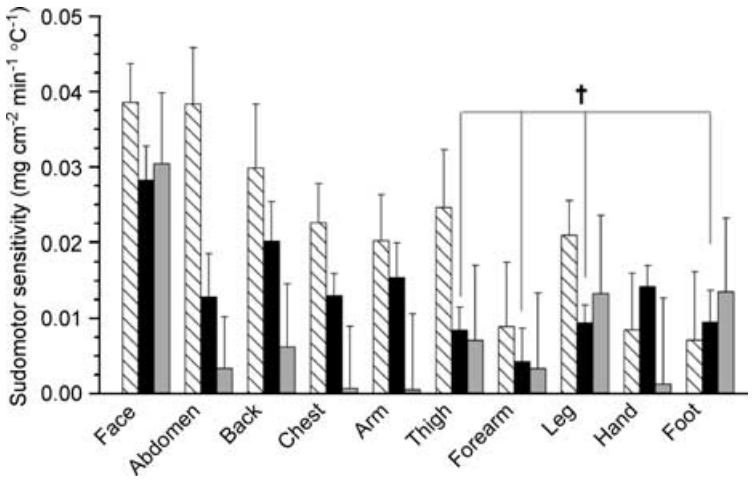

Figure 2. Local cutaneous thermosensitivities for sudomotor control
Data are mean (± S.E.M.) sweat rate changes, averaged across all limbs, relative to local skin temperature change, during mild warming (4°C; hatched bars), mild cooling (−4°C; grey bars) and moderate cooling (−11°C; black bars) of 10 discrete skin sites. Significant differences ($P < 0.05$) between local sites were only apparent with respect to the face (†).

other segment during moderate cooling (C_{-11}; $P < 0.01$), and 2–3 times more sensitive than the lower limb, proximal limb and limb extremities during warming (W_{+4}; $P = 0.01$; Fig. 4).

Thermosensitivity indices

Indices of cutaneous sudomotor thermosensitivity and thermal discomfort (alliesthesial thermosensitivity) were estimated for each treated skin site within subjects, across the three treatments (Fig. 5). Sensitivities (gains) were computed as the ratio of the change in sweat rate (first 4 min only) and thermal discomfort to the change in T_{skl} (ΔT_{skl}; linear regression), as illustrated in Fig. 5*B*. The resultant sensitivity coefficients were averaged across subjects, but within skin sites, to provide site-specific sensitivity indices, across the T_{skl} range 30–40°C (Fig. 5*A*). Facial thermosensitivity dominated both indices, revealing significantly higher thermosensitivity for sudomotor control than the forearm, hand, thigh, leg and foot (Fig. 5*A*; $P = 0.01$), and significantly higher alliesthesial thermosensitivity than the hand, leg and foot ($P = 0.01$). The abdomen and back also had relatively high sudomotor, but not alliesthesial sensitivities, which were approximately 3 times greater than that of the forearm (Fig. 5*A*).

Sudomotor *versus* alliesthesial thermosensitivity. Analysis of the mean site-specific sensitivity indices for sweating and thermal discomfort revealed moderately high, positive correlations across the 10 skin sites ($r = 0.84$; $P = 0.01$). Thus, approximately 70% of the local variance in sudomotor sensitivity was common to the alliesthesial sensitivity. A similar correlation was observed when sensitivity indices were compared for the body segments (distal limbs, proximal limbs, torso and face; $r = 0.95$; $P = 0.04$). These relations emphasize the consistently high thermosensitivity of the face, and a general reduction in thermosensitivity for more distal sites and segments (Fig. 5*A*).

Discussion

Previous studies of local cutaneous thermosensitivities in humans have not yielded any statistically supported evidence for regional differentiation of either warm or cool thermosensitivity for the control of sweating, and suffered substantial methodological limitations. We have minimized those limitations, and used an open-loop experimental model to provide a comprehensive assessment of intersite cutaneous thermosensitivities for humans, unbiased by thermoafferent flow from untreated thermosensitive tissues. This was achieved using whole-body thermal clamping, by standardizing the magnitude of the ΔT_{skl} and the size of the skin surface area being stimulated, and by applying both warming and cooling stimuli to 10 skin sites, over the T_{skl} range from approximately 30 to 40°C. This experimental design has resulted in four novel findings regarding cutaneous thermosensitivity in resting humans during mild heat stress.

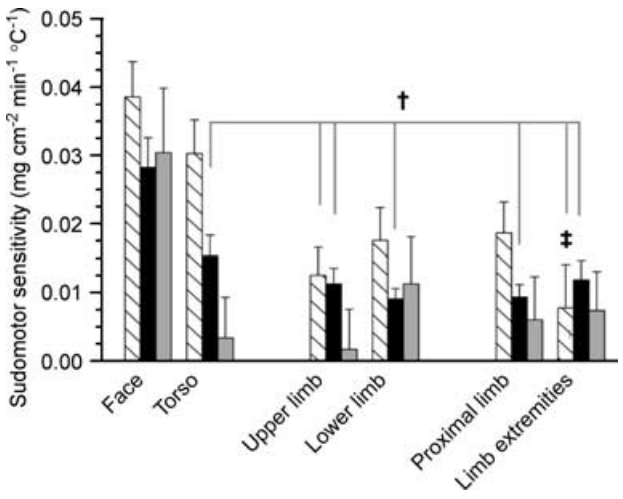

Figure 3. Segmental cutaneous thermosensitivities for sudomotor control
Segments are groups of locally treated skin sites: face; torso (chest, abdomen and lower back); upper limb (arm, forearm and hand); lower limb (thigh, leg and foot); proximal limb (arm, forearm, thigh and leg); and limb extremities (hand and foot). Data are mean (± S.E.M.) sweat rate changes, averaged across all limbs, relative to local skin temperature changes, during mild warming (4°C; hatched bars), mild cooling (−4°C; grey bars) and moderate cooling (−11°C; black bars) of 10 discrete skin sites. Significant differences ($P < 0.05$) between body segments were only apparent with respect to the face (†) and torso (‡).

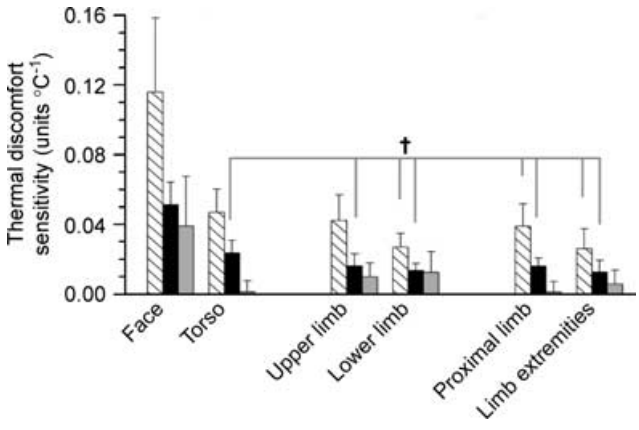

Figure 4. Segmental cutaneous thermosensitivities for alliesthesia
Segments are groups of locally treated skin sites. Data are mean (± S.E.M.) whole-body thermal discomfort changes, relative to local skin temperature changes, during mild warming (4°C; hatched bars), mild cooling (−4°C; grey bars) and moderate cooling (−11°C; black bars) of 10 discrete skin sites. Significant differences ($P < 0.05$) between sites were only apparent with respect to the face (†).

First, the facial surfaces displayed greater sudomotor and alliesthesial thermosensitivity than did other sites to cooling and, to a lesser extent, warming. Thus, cooling the face resulted in a two- to five-fold more powerful suppression of sweating and thermal discomfort than did cooling an equivalent area within any other skin segment. Second, the torso displayed high warmth sensitivity for sudomotor control, but not thermal discomfort, with no differences apparent during skin cooling. Third, the pattern of cutaneous thermosensitivity was similar for sudomotor control and thermal discomfort. Fourth, by simultaneously analysing data across the three treatments, relative to ΔT_{skl}, we have derived estimates of the absolute thermosensitivity for each of the 10 local skin sites studied. This unified thermosensitivity index, obtained across T_{skl} from 30 to 40°C, relates to both autonomic and behavioural thermoregulation, if we assume that thermal discomfort drives behaviour.

A greater facial thermosensitivity has previously been reported for autonomic function (Nadel *et al.* 1973; Crawshaw *et al.* 1975) and temperature sensation (Hardy & Oppel, 1938; Kenshalo *et al.* 1967; Stevens *et al.* 1974; Crawshaw *et al.* 1975) under closed-loop conditions. Nevertheless, this apparent consensus is neither universally supported (Attia & Engel, 1981; Libert *et al.* 1984; Patterson *et al.* 1998) nor is it convincing with regard to autonomic or behavioural thermoregulation. For instance, in neither of the two most cited investigations were the core or untreated skin temperatures clamped (Nadel *et al.* 1973; Crawshaw *et al.* 1975). These groups also stimulated variable skin surface areas and reported only descriptive data from one to three subjects, screened according to cutaneous thermosensitivity. Although Libert *et al.* (1984) used a servo-feedback control of mean skin temperature in evaluating steady-state thermosensitivities, they did not treat the face separately, and, as with earlier studies, sampled sweating responses only from a single limb. Furthermore, most psychophysical thermosensitivity data are relevant only to dynamic stimuli and detection thresholds for the perception of local temperature, and we have shown that local temperature perception sensitivity may not reflect thermoregulatory sensitivity (Cotter *et al.* 1996). Notwithstanding these experimental limitations, data from the present study generally conform to previous observations of a greater facial thermosensitivity. However, we submit that, under the present open-loop conditions, this differential cutaneous thermosensitivity has now unequivocally been established.

A higher facial thermosensitivity might result from a greater thermoreceptor density, or minimal thermoafferent convergence. High facial cold receptor densities have been reported in non-primates (Dostrovsky & Hellon, 1978; Dickenson *et al.* 1979), but, to our knowledge, thermoreceptor density distributions are unavailable for humans. However, a high density of facial cold receptors is indicated by evidence of a high cold spot density (M. Cabanac, personal communication; Hensel, 1981). Animal studies also reveal minimal convergent processing of facial thermoafferent signals (Poulos & Molt, 1976; Hellon & Dawson, 1979), in contrast to the extensive convergence of afferents arising from the trunk and limbs (Hellon & Mitchell, 1975; Iggo & Ramsey, 1976; Taylor & Gayton, 1986). Thus, a neurological basis exists for a greater facial thermosensitivity, which we suggest is important for both autonomic (sudomotor) and behavioural (whole-body discomfort) thermoregulation in humans.

Whilst the limb extremities were the least warm-sensitive segment for both sweat rate and whole-body

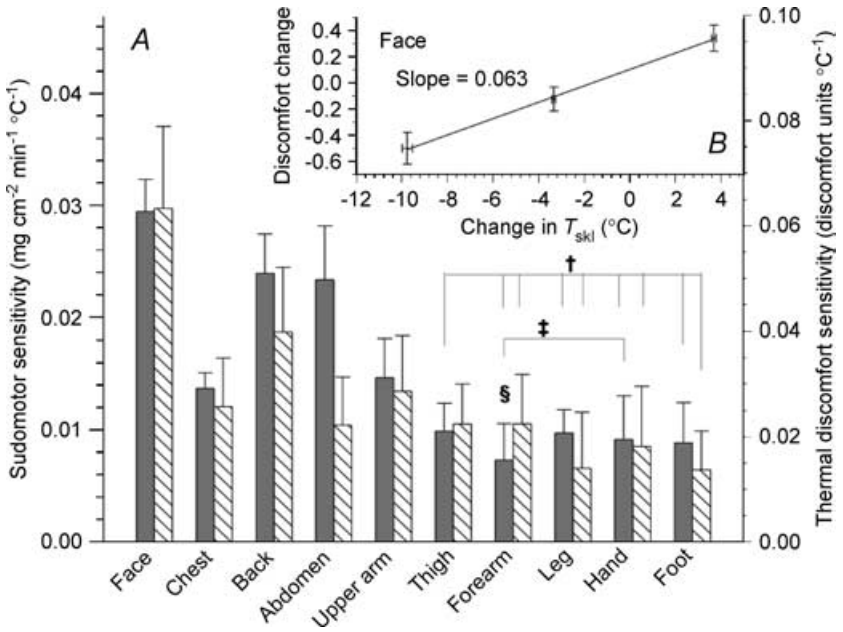

Figure 5. Local cutaneous thermosensitivities for sudomotor control and whole-body thermal discomfort (alliesthesia)
A, data are site-specific, mean sudomotor (grey bars) and alliesthesial (hatched bars) thermosensitivities (± S.E.M.) derived across three localized thermal treatments ($n = 12$): mild warming (4°C), mild cooling (−4°C) and moderate cooling (−11°C). Significant differences ($P < 0.05$) between local sites were only apparent with respect to the face (†), abdomen (‡) and back (§). The inset (*B*) displays the relation between changes in whole-body thermal discomfort and local skin temperature (T_{skl}), and represents the alliesthesial thermosensitivity for these treatments at the face.

thermal discomfort, they simultaneously elicited a high sensitivity for local warmth perception, matched only by that of the face (Cotter *et al.* 1996). This indicates that local thermal perception sensitivity does not match general thermoregulatory sensitivities elicited from the same local treatment. This finding may reflect different patterns of afferent flow from the hand to the cortex compared with the hypothalamus, due, perhaps, to activation of thermal nociceptors or slowly adapting mechanoreceptors, which are densely distributed in human hands and become active above 35–40°C (Iggo & Ramsey, 1976; Konietzny & Hensel, 1979). Irrespective of the mechanism, such a separation in sensitivity distributions is of teleological appeal, since the limb extremities undergo far greater temperature fluctuations than facial skin, and superior local temperature discrimination would be beneficial in providing conscious perception of the thermal environment, while simultaneously providing minimal feedback for autonomic control (Benzinger, 1976). Thus, the more sensitive face and the less sensitive distal limb surfaces appear well suited for driving autonomic thermoeffectors.

One practical implication from the present cutaneous thermosensitivity indices (Fig. 5) is the derivation of provisional skin temperature weightings for use when deriving mean skin temperature ($\bar{T}_{sk}$) to reflect cutaneous thermoafferent flow. Notwithstanding the limitations of these sensitivity indices, they do provide a comprehensive whole-body assessment of sudomotor and alliesthesial thermosensitivity for resting humans during mild heat stress. In general, our data indicate that area-weighted estimations adequately reflect cutaneous thermosensitivities for most limb sites, but the face, and possibly the torso, require larger weightings to better align with local sudomotor, and perhaps alliesthesial, thermosensitivities (Fig. 5). To derive these weightings, we have simply used the product of each local area weighting (Hardy & DuBois, 1938) and the respective mean local thermosensitivity (Fig. 5). The following equations are offered as a first-level approximation of such sensitivity weightings, and as a basis for future experimental evaluation:

$$\text{Sudomotor}: \bar{T}_{sk} = 0.14\,T_{face} + 0.08\,T_{chest} + 0.13\,T_{abdomen} + 0.28\,T_{back} + 0.07\,T_{arm} + 0.04\,T_{forearm} + 0.02\,T_{hand} + 0.12\,T_{thigh} + 0.10\,T_{leg} + 0.02\,T_{foot}.$$

$$\text{Alliesthesial}: \bar{T}_{sk} = 0.16\,T_{face} + 0.08\,T_{chest} + 0.07\,T_{abdomen} + 0.26\,T_{back} + 0.07\,T_{arm} + 0.06\,T_{forearm} + 0.03\,T_{hand} + 0.16\,T_{thigh} + 0.08\,T_{leg} + 0.03\,T_{foot}.$$

A second implication of the present observations is that they provide a basis upon which physiologically sound recommendations can be made concerning the use of local cooling to extract heat. If the present thermosensitivities are indicative of the wider population and other levels of heat stress, then the face appears to be the site that provides the greatest alliesthesial impact. Thus, facial cooling can be used to optimally reduce thermal discomfort, as suggested previously (Nunneley *et al.* 1971, 1982; Brown & Williams, 1982). However, since the face also has a high sensitivity for sudomotor control, local cooling will appreciably reduce general sweating and may exacerbate heat storage, as previously demonstrated (Kissen *et al.* 1971). Conversely, the distal limb surfaces may be well suited to alleviating heat storage using external cooling. For instance, the hands, when compared with other sites, possess three key attributes: (a) a high surface area:volume ratio; (b) large reserves for skin blood flow (Tenland *et al.* 1983; Hirata *et al.* 1993) and sweating (Kuno, 1956; Cotter *et al.* 1997); and (c) generally lower thermosensitivities (Figs 2, 3 and 5). Accordingly, localized hand (Livingstone *et al.* 1989; House *et al.* 1997) and feet cooling (House, 1998; Livingstone *et al.* 1995) is an effective means for alleviating heat storage, perhaps with minimal negative feedback. Thus, it is possible that cooling the face reduces the affective heat load, but may exacerbate the actual heat load, whereas cooling distal limb surfaces may have little impact on the affective thermal load, yet more effectively reduce the actual thermal load.

In conclusion, this experiment has provided a comprehensive, open-loop assessment of cutaneous warm and cool sensitivities for sudomotor control and alliesthesia in resting humans during mild heat stress. The facial surfaces were 2–5 times more thermosensitive than any other segment for both sudomotor and discomfort responses during moderate cooling, and 2–5 times more thermosensitive than the upper limb, lower limb and limb extremities for these responses during warming. The limb extremities were also less warm sensitive than the torso for sweating. The patterns of thermosensitivity for sudomotor control and discomfort were closely related.

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