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# **Thermosensory micromapping of warm and cold sensitivity across glabrous and hairy skin of male and female hands and feet**

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**Running title:** Warm and cold thermosensory mapping of human hands and feet

**Key words:** thermal sensation, skin, mapping

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## Abstract

The ability of human hands and feet to convey skin thermal sensations is an important contributor to our experience of the surrounding world. Surprisingly, the detailed topographical distribution of warm and cold thermosensitivity across hands and feet has not been mapped, although such sensitivity maps exist for touch and pain.

Using a recently developed quantitative sensory test, we mapped warm and cold thermosensitivity of 103 skin sites over glabrous and hairy skin of hands and feet in males ( $30.2 \pm 5.8$  y) and females ( $27.7 \pm 5.1$  y) adults matched for body surface area (M  $1.77 \pm 0.2$  m<sup>2</sup>; F  $1.64 \pm 0.1$  m<sup>2</sup>;  $p=0.155$ ).

Our findings indicated that warm and cold thermosensitivity varies by 5-fold across glabrous and hairy skin of hands and feet, and that hands are twice as sensitive as the feet. Opposite to what known for touch and pain sensitivity, we observed a characteristic distal-to-proximal increase in thermosensitivity over both hairy and glabrous skin (i.e. from fingers/toes to body of hands and feet), and found that hairy skin is more sensitive than glabrous. Finally, we show that body-surface-area-matched males and females presented small differences in thermosensitivity, and that these differences are constrained to glabrous skin only.

Our high-density thermosensory micromapping provides the most detailed thermosensitivity maps of hands and feet in healthy young adults available to date. These maps provide a window into the peripheral and central mechanisms of thermosensory integration in humans, and will help guiding future developments in smart skin and sensory neuroprostheses, in wearable energy-efficient personal comfort systems, and in sport and protective clothing.

## Key points

- Skin thermal sensations are key to our experience of the world, and often arise through humans' most important explorative organs, i.e. hands and feet
- The topographical distribution of warm and cold thermosensitivity across hands and feet has not been mapped, although such sensitivity maps exist for touch and pain
- We mapped warm and cold thermosensitivity of 103 skin sites over glabrous and hairy skin of hands and feet in males and females adults
- We found that: warm and cold thermosensitivity varies by 5-fold across hands and feet; distal regions (e.g. fingers, toes) are less sensitive than proximal (e.g. palm, sole); hands are twice as sensitive as the feet; males and females present small differences in thermosensitivity
- This work provides the most detailed thermosensitivity maps of hands and feet available to date, and will help guiding developments in sensory neuroprostheses, in wearable personal comfort systems, and in sport and protective clothing

## Introduction

Temperature sensing is a fundamental input in most animal species, including humans (McKemy, 2007; Filingeri, 2016). As homeothermic mammals, we rely on sensing the thermal state of our body and surroundings to regulate our body temperature (Romanovsky, 2007).

Yet temperature sensing in the form of skin thermal sensations is also a critical sensory attribute that enables our experience of the surrounding world (Filingeri, 2016). The warmth of a caress, or the coldness of dipping our toes in the sea, are common yet fundamental sensory experiences that accompany our life from its very first start, and that help shape our social and physical being (Craig, 2002; Ackerley *et al.*, 2014a; McGlone *et al.*, 2014). Such perceptual thermal experiences are often conveyed through humans' most important explorative and sensory organs, their hands and feet (Mountcastle, 2005).

While there is vast knowledge about hands and feet as *thermoregulatory* organs for providing heat and cold defence responses (i.e. cutaneous vasodilation / vasoconstriction) (Taylor *et al.*, 2014), their function and characteristics as *thermosensory* organs have rarely been investigated (Li *et al.*, 2008).

This is surprising, as detailed understanding of thermosensation in hands and feet has practical value in subjects such as helping restore naturalistic touch in amputees through sensory prosthesis and smart skin (Raspopovic *et al.*, 2014; Kim *et al.*, 2014; Chortos *et al.*, 2016; Shao *et al.*, 2016; Filingeri & Ackerley, 2017), and in designing effective personal comfort systems (Zhang *et al.*, 2015), thermal wearables (Smith *et al.*, 2017), and sport and protective clothing (Taylor *et al.*, 2014).

In humans and primates, skin temperature sensing is mediated by free nerve endings of the A $\delta$ - and C-type classes (i.e. thermoreceptors) (Darian-Smith, 1973; Konietzny & Hensel, 1975; Campero *et al.*, 2001, 2009), selectively conveying warm and cold afferent inputs via the anterolateral spino-thalamic tract, to neural centres located in the insular and somatosensory cortices (Davis *et al.*, 1998; Craig *et al.*, 2000; Rolls *et al.*, 2008).

Human temperature sensing is not homogenous across the body (Norrzell *et al.*, 1999), but in fact it varies significantly depending on the skin region (e.g. face and trunk are generally more sensitive than the limbs) (Ouzzahra *et al.*, 2012; Gerrett *et al.*, 2014; Filingeri *et al.*, 2014). While commonly observed in humans (Donaldson, 1885; Stevens, 1979; Nakamura *et al.*, 2008; Filingeri *et al.*, 2014; Gerrett *et al.*, 2015), this sensory feature has not been fully investigated in animal models of mammalian thermosensation (Vriens *et al.*, 2014;

Milenkovic *et al.*, 2014), leaving our understating of its underlying neurobiology somewhat speculative.

The presence of regional differences in temperature sensing in humans is in line with what has long been known about regional differences in touch sensitivity (Johansson & Vallbo, 1979a; Ackerley *et al.*, 2014b), and more recently, in pain acuity (Mancini *et al.*, 2014). Interestingly, large topographical differences in touch and pain sensitivity are present across relatively small body areas, such as the palm of the hand. This glabrous skin region exhibits a proximal-to-distal (i.e. palm to fingertips) increase in touch sensitivity (Johansson & Vallbo, 1979b; Johansson *et al.*, 1980), and in pain acuity (Mancini *et al.*, 2013).

Differences in touch and pain receptor densities across the hand (Johansson & Vallbo, 1979a; Hauer *et al.*, 2008; Mancini *et al.*, 2013), and in the size of the receptive fields of cortical neurons (Mancini *et al.*, 2012), contribute to the heterogeneous touch and pain sensitivity of our palms. This observation was first exemplified in the classic sensory homunculus developed by Penfield (Penfield & Boldrey, 1937).

In contrast to the knowledge above, it has not been fully elucidated yet whether thermosensitivity varies substantially across hands and feet, and whether the variation has a similar topography as touch and pain.

To date, only Li *et al.* (Li *et al.*, 2008) has attempted to characterize the topography of warm and cold sensitivity of the glabrous skin of the palm.

By mapping thermosensitivity with threshold detection methods across 23 locations of the palm in males and females, this study indicated that warm and cold sensitivity varies largely across this relatively small area, with proximal sites (e.g. base of the palm) showing higher sensitivity than the distal sites (e.g. fingers) (Li *et al.*, 2008).

It was also found that females are on average more thermosensitive than males (Li *et al.*, 2008), although differences in body surface area between genders could have contributed to this observation (i.e. the smaller females might have shown higher sensitivity due to the relatively larger proportion of their skin being stimulated).

While Li *et al.*' study (Li *et al.*, 2008) has provided initial evidence for the fact that the human palm could present a heterogeneous distribution of thermosensitivity, the study did not evaluate the entire hand (i.e. no assessment of the hairy skin of the dorsum), nor the foot. It also used a methodology (i.e. threshold detection, where the smallest perceivable temperature change is identified) that is unlikely to be representative of a real-life, supra-threshold thermal stimulus (e.g. when dipping a finger in the bath to check its temperature).

Finally, it assessed gender differences without matching groups for body size, which might create a potential bias in the context of thermal spatial summation (Defrin *et al.*, 2009). As a result, our knowledge on the thermosensitivity of hands and feet in humans, and of its topographical distribution across the hairy (i.e. dorsum) and glabrous portions (i.e. palm and sole) of these sensory organs, remains limited.

To fill this gap, we mapped topographical differences in warm and cold thermosensitivity across 103 locations of both hairy and glabrous skin of the hand and foot in young males and females, using an ecologically-valid magnitude estimation paradigm. We assessed gender differences by matching males and females for body surface area, in order to isolate the independent effect of gender on local thermosensitivity.

## Methods

### *Participants*

Sixteen age-matched healthy adults, eight females and eight males, volunteered to participate in the present study. All participants were college students and junior researchers without any neural or perceptual contraindications, non-smokers, moderately active (performing at least 5h of exercise a week) and had lived in the Berkeley area (California, USA) for at least 3 months prior to the test. Participants' characteristics are presented in Table 1.

**Table 1.** *Participants' characteristics*

	Age (yr)	Mass (kg)	Height (m)	BSA (m <sup>2</sup> )	Proportion of BSA stimulated by fixed-size (1.32cm <sup>2</sup> ) thermal probe (%)
<b>Men (n=8)</b>	30.2 ± 5.8	67.8 ± 13.4	1.69 ± 0.1	1.77 ± 0.2	0.0076 ± 0.0009
<b>Women (n=8)</b>	27.7 ± 5.1	58.0 ± 5.4	1.66 ± 0.1	1.64 ± 0.1	0.0081 ± 0.0005
<b>Probability</b>	0.381	0.076	0.546	0.155	0.184

Where: *n* = number of participants. BSA, body surface area. Statistical differences between groups for each characteristic were assessed by means of independent group *t*-tests, with cut-off probability value for significance set at *p*=0.05

The male and female groups comprised an almost identical proportion of Caucasian (4F/3M) and Asian ethnicities (4F/5M). Female participants were well spread across a typical 28-day menstrual cycle (mean day= 15.4; SD= 8.9), with 4 of them taking oral contraceptives. In addition to being age-matched, male and female participants were purposely matched for body surface area (see Tab. 1). Spatial summation is a well-known phenomenon in thermal sensitivity (Stevens *et al.*, 1974), where given the same thermal stimulus, increasing the area of skin being thermally stimulated increases the magnitude of the resulting thermal sensation (Darian-Smith, 1984).

Accordingly, matching males and females for body surface area ensured that a similar proportion of their body would be stimulated with our fixed-area thermal stimulus (i.e. a 1.32cm<sup>2</sup> thermal probe; see Table 1 column “*proportion of BSA stimulated*”), and that any confounding effect driven by gender differences in body size would be limited (Defrin *et al.*, 2009).

The project conformed to the Helsinki Declaration and was approved by the Institutional Committee for the Protection of Human Subjects of the University of California at Berkeley. Participants were naïve as to the purpose of the experiments and they each gave written informed consent.

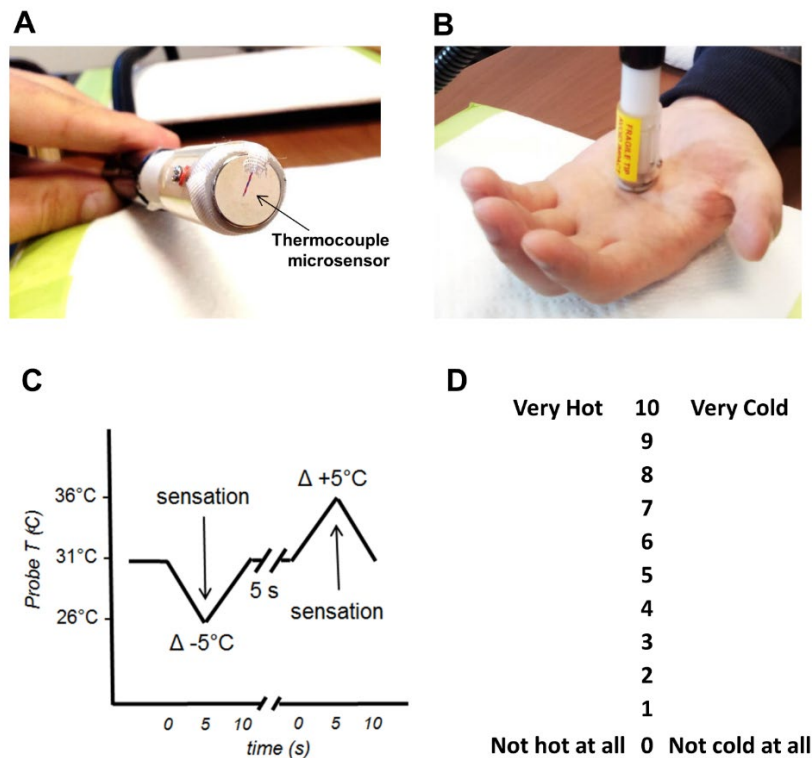
All testing occurred during the months of March and April.

### *Experimental design*

All participants took part in one experimental session, during which they underwent a standardized quantitative thermosensory test (duration ~1h) in a climatic chamber under thermo-neutral environmental conditions (air temperature= 23°C; relative humidity= 50%). This quantitative test was adapted from the one we recently developed and tested in both healthy individuals (Filingeri *et al.*, 2014, 2017b) and in neurological patients undergoing thermal stress (Filingeri *et al.*, 2017a).

The thermosensory test was designed to quantify local thermosensitivity of 103 skin sites across the hairy and glabrous skin of hands and feet in response to locally applied skin warming and cooling stimuli (i.e.  $\pm 5^{\circ}\text{C}$  from a baseline temperature of 31°C; duration of stimulation: 5s), whose temperature is within the range for maximal activation of both cutaneous cold (i.e. 27 – 22°C) and warm (i.e. 36 – 42°C) thermoreceptors (Filingeri, 2016). A schematic representation of the experimental design is presented in Fig. 1. Figure 2 presents the topographical distribution of the 103 skin sites mapped.

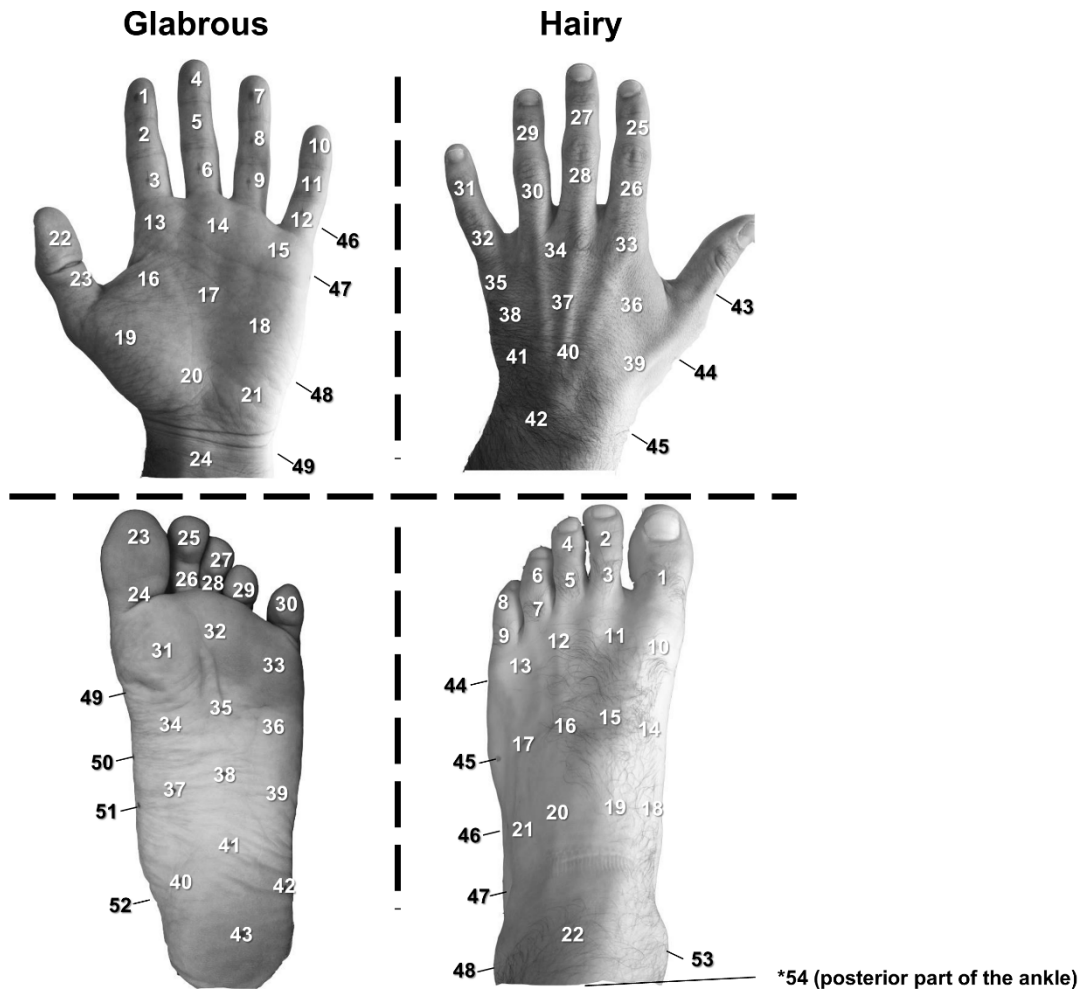




**Figure 1.** Schematic representation of the experimental design and protocol. Panel A shows the combination of thermal probe and thermocouple microsensor used to deliver thermal stimuli and record changes in probe-skin interface temperature, respectively. Panel B shows application of the probe on a representative skin site of the palm. Panel C presents an overview of the stimulation protocol, where 5s-cooling and –warming pulses were delivered at the skin, in a counterbalanced order, and with 5s in between them. At the end of each 5s-stimulation, participants reported their local thermal sensation, using the numerical rating scale showed in panel D.

We assessed both hairy and glabrous skin as there is evidence that thermosensitivity varies across these types of skin (Stevens & Choo, 1998), owing to both physiological (e.g. density of sensory innervation; (Norrzell *et al.*, 1999)) and biophysical factors (e.g. differences in thickness of the epidermal layer and related thermal conductance; (Iannetti *et al.*, 2006)). Participants were trained to report on a 11-point Numerical Rating Scale (Fig. 1D) the magnitude of local thermal sensations elicited by the skin warming and cooling stimuli (Fig. 1C), which were delivered with a hand-held 1.32cm<sup>2</sup> thermal probe (Fig. 1A; NTE-2A, Physitemp Instruments Inc., USA; probe response rate: 2.43°C/s) to each skin site (Fig. 1B) in a randomised order.

The density and anatomical location of the 103 skin sites tested (Fig. 2) were chosen in order to map as much skin area as possible across hairy and glabrous skin of hands and feet, in relation to the size of the thermal probe.



**Figure 2.** Topographical distribution of the 103 skin sites tested over the glabrous and hairy skin of hands and feet.

All tested skin sites were on the left side of the body, assuming bi-lateral symmetry (Claus & Hilz, 1987).

Local skin temperature ( $T_{sk}$ ) variations at the contact site between the skin and thermal probe were monitored and recorded before, during, and after the application of each stimulus, using a fast-response thermocouple microsensors (Fig. 1A; time constant: 0.005s; tip diameter: 0.3mm; IT-1E, Physitemp Instruments Inc., USA), located on the probe's surface, and interfaced with a Microprobe Thermometer (accuracy:  $\pm 0.1^{\circ}\text{C}$  between 0-50 $^{\circ}\text{C}$ ; BAT-12, Physitemp Instruments Inc., USA).

A single-blind psychophysical design was used for the present study, with the same investigator performing all testing.

### *Experimental protocol*

Participants arrived to the laboratory on testing days, after having refrained from caffeine and alcohol in the 12h preceding the experiment. They changed into shorts and t-shirt (no shoes were worn), and moved into the climatic chamber.

Five wireless temperature sensors (iButtons, Maxim, USA) were taped to five skin sites on the right side of the body (i.e. cheek, upper arm, abdomen, lower back and back lower thigh) with medical tape (3M, USA) in order to record local  $T_{sk}$  (10-s intervals), to be used for the estimation of mean  $T_{sk}$  for the entire body according to the equation of Houdas and Ring (1982):

Whole body mean  $T_{sk}$

$$= (CheekT_{sk} \times 0.07) + (UpperArmT_{sk} \times 0.19) + (AbdomenT_{sk} \times 0.175) \\ + (LowerBackT_{sk} \times 0.175) + (ThighT_{sk} \times 0.39)$$

Five-minute averages were determined for mean  $T_{sk}$  data.

Once instrumented, participants sat on a stool where they rested for the entire test.

Thirty minutes were allowed for adaptation to the environmental conditions, and for baseline recordings. During this time, participants were familiarized with the quantitative thermosensory test. The detailed procedures for familiarization and execution of the quantitative thermosensory test are presented below, along with the methods for quantifying and mapping local thermosensitivity.

### *Quantitative thermosensory test: familiarization and calibration*

During the 30-min adaptation, participants were briefed about the general producers underlying the quantitative thermosensory test.

They were informed that non-painful warming and cooling stimuli would be delivered separately to each of 103 different sites across their hands and feet using a thermal probe.

To avoid any expectation bias, no information was given about the temperature of the stimuli, or whether the same stimuli would be applied to different skin areas.

The 103 skin sites targeted for stimulation were marked with a washable marker to assure consistency in the location of stimulation.

Participants were then instructed that, when requested by the investigator, they would be expected to report the magnitude of the very first local thermal sensation resulting from each stimulus application. They would use a 0-10 numerical rating scale whose anchor points 0 and 10 were respectively labelled as “Not hot/Not cold at all” and “Very Hot/Very Cold”. This scale is similar to the one used by Gerrett et al., (2014) and Ouzzahra et al. (2012) in similar studies, and its choice was based on extensive evidence supporting the applicability and reliability of numerical rating scales for somatic sensations in humans (Farrar *et al.*, 2001; Hjermstad *et al.*, 2011).

To ensure consistency in the use of the scale, participants were calibrated to its anchor points. This was achieved by delivering 3 separate stimuli with the thermal probe to a representative skin site, and by asking participants to associate the resulting thermal sensations to the specific anchor point.

The first stimulus corresponded to a temperature of 31°C, which was similar to that of the skin, and which induced neither a warm nor a cold thermal sensation. After confirming the absence of any thermal sensation, participants were informed that they should associate the anchor point 0 “Not hot/Not cold at all”, to this absence of thermal sensation.

The second and third stimuli corresponded to  $\pm 10^\circ\text{C}$  from a baseline temperature of 31°C. These cold and warm stimuli were twice as large as the warming and cooling stimuli that would be used for the quantitative thermosensory mapping (i.e.  $\pm 5^\circ\text{C}$  from a baseline temperature of 31°C), and were delivered to induce thermal sensations that participants were instructed to associate to the “Very Hot/Very Cold” anchor points of the scale.

Once the calibration was completed, participants underwent some practice trials where they were allowed to experience the actual testing stimuli (i.e.  $\pm 5^\circ\text{C}$  from a baseline temperature of 31°C) on a variety of skin sites, and were informed that these stimuli would be similar to the ones to be used during the thermosensory mapping. Participants were also encouraged to practice the use of the rating scale during these practice trials, and were informed that local sensations would have to correspond to their first sensation upon stimulation, and that this would be reported at the request of the investigator, within 5s of delivering the stimulus.

Pilot studies indicated 5s as a sufficient time for the set stimuli to reach their target absolute temperatures (i.e. 26 and 36°C).

The above described familiarization protocol ensured that all participants were calibrated to the scale and fully familiar with the testing procedures upon commencing the actual experiment.

### *Quantitative thermosensory test: execution*

Upon termination of the familiarization, the quantitative thermosensory test initiated. Participants rested on a stool, facing away from the skin area stimulated. They were instructed to only focus on the numerical rating scale positioned in front of them, and to report their local sensation upon request.

The hand or foot were then selected as the first extremity to be tested, according to a between-participants counterbalanced order.

Testing for both the hand and the foot was split between the hairy (i.e. dorsum of hands and foot) and glabrous parts (i.e. palm of the hand and foot sole), and mapping of all skin sites on one part (e.g. palm of the hand) was completed, before moving to the next part (e.g. dorsum of the hand). A 5-min break was allowed in between testing of hands and feet.

Whenever the hand was tested, participants placed it on a fabric cushion on a table, with the palm resting in a comfortable position, facing either upwards or downwards. Whenever the foot was tested, participants placed their lower leg on a fabric cushion on a lowered stool, with the foot freely suspended beyond the stool.

Once a comfortable position was achieved, the investigator began testing of the first skin site. First, the investigator set the thermal probe at 31°C (i.e. neutral temperature) and placed this gently on the skin site to be tested, with a pressure sufficient to ensure full contact with the skin. Five seconds were allowed for the local  $T_{sk}$  to stabilize. This was monitored via the surface thermocouple, and was recorded before delivery of the first stimulus.

Following on to the initial stabilization, the +5°C skin warming or the -5°C cooling stimulus was delivered, and after 5s from delivery, the participant was requested to report their local thermal sensation (Fig. 2C). Along with the local sensation, the local  $T_{sk}$  at the 5-s stimulation was also recorded, to determine the  $\Delta T_{sk}$  change from pre-stimulation.

At this point, the probe was re-set to 31°C, and after a 5-s break, the second stimulus (i.e. a warming stimulus in case of a previous cooling one and vice versa) was delivered (Fig. 1C). Pilot studies indicated 5-s as a sufficient time to ensure that baseline  $T_{sk}$  and neutral sensations would be re-established.

The order of delivery of warming and cooling stimuli was balanced within-participants. Once both warm and cold sensitivity was assessed on a skin site, the investigator moved the probe on the next skin site, and the same procedure as above, was performed until all skin sites were tested.

### *Quantifying local thermosensitivity*

We collected data on local changes in  $T_{sk}$ , and local thermal sensations, for each of the 103 skin site tested, as a result of both the skin warming and cooling stimuli.

$T_{sk}$  and local thermal sensations data were combined to calculate an index of local thermosensitivity as follow:

$$Thermosensitivity \left( \frac{vote}{^{\circ}C} \right) = \frac{thermal\ sensation\ (vote)}{\Delta\ local\ T_{sk}\ (^{\circ}C)}$$

This thermosensitivity index provided, for each skin site, a normalised indication of the sensation resulting from a unit change in local  $T_{sk}$ .

### *Thermosensitivity maps*

To aid with visualization of regional thermosensory patterns, the data collected were used to generate high-density thermosensitivity maps.

Maps were created separately for males and females, for hairy and glabrous skin, and for warming and cooling.

High-density thermosensory maps were generated using a custom written MatLab script (The MathWorks, Inc., USA).

Average data per group (n=8) were entered into a matrix composed of the coordinates (X;Y) of the skin site of interest (which were based on representative images of the palm/dorsum of the hands and sole/dorsum of the foot, see Fig.2), and the associated thermosensitivity value (Z).

MatLab interpolation and extrapolation functions were used to create HeatMap objects, which were then superimposed over images of the extremity of interest, and morphed accordingly with an imaging software (Photoshop; Adobe, USA).

### *Statistical analysis*

In order to evaluate changes in whole-body thermal state during the test in male and females, mean  $T_{sk}$  data were analysed by means of a two-way mixed-model ANOVA, with gender as independent factor, and time as repeated factor.

In order to determine whether sensitivity to skin warming and cooling varied across skin sites and between male and females, thermosensitivity data were analysed separately for warming and cooling stimuli, and for hairy and glabrous parts of hands and feet, by means of a two-way mixed-model ANOVA, with gender as independent factor and skin site as repeated factor.

In the event of statistically significant main effects or interactions, post-hoc analyses were conducted with Fisher's LSD tests.

Analysis for the glabrous part of the hand included data for skin sites 1 to 23. Analysis for the hairy part of the hand included data for skin sites 24 to 49. Analysis for the glabrous part of the foot included data for skin sites 23 to 43. Analysis for the hairy part of the foot included data for skin sites 1 to 22 and 44 to 54.

In order to explore inter-individual variability in local thermosensitivity, coefficient of variations [i.e. (SD/mean)\*100)] were calculated for each skin site tested for both warming and cooling stimuli, in both males and females. Mean differences in inter-individual variability between genders were assessed by means of unpaired t-tests. Data were then summarised into heat maps to display skin sites of high and low inter-individual variability in local thermosensitivity.

In order to determine overall thermosensitivity differences between the hand and the foot, thermosensitivity data from hairy and glabrous skin sites were grouped for warm and cold sensitivity and for males and females, and compared between hands and feet by means of paired t-tests. Similarly, to determine overall thermosensitivity differences between glabrous (palms and soles) versus hairy skin (back of hands and feet), data from hands and feet were grouped for warm and cold sensitivity and for males and females, and compared between hairy and glabrous skin by means of paired t-tests.

Finally, correlation analyses between warm and cold thermosensitivity across all skin site tested were performed separately for males and females.

Data are reported as means, SD, and 95% Confidence Intervals. Observed power was computed using  $\alpha=0.05$ . Statistical analysis was performed using GraphPad Prism (version 6.0; GraphPad Software, La Jolla, CA, USA).

## Results

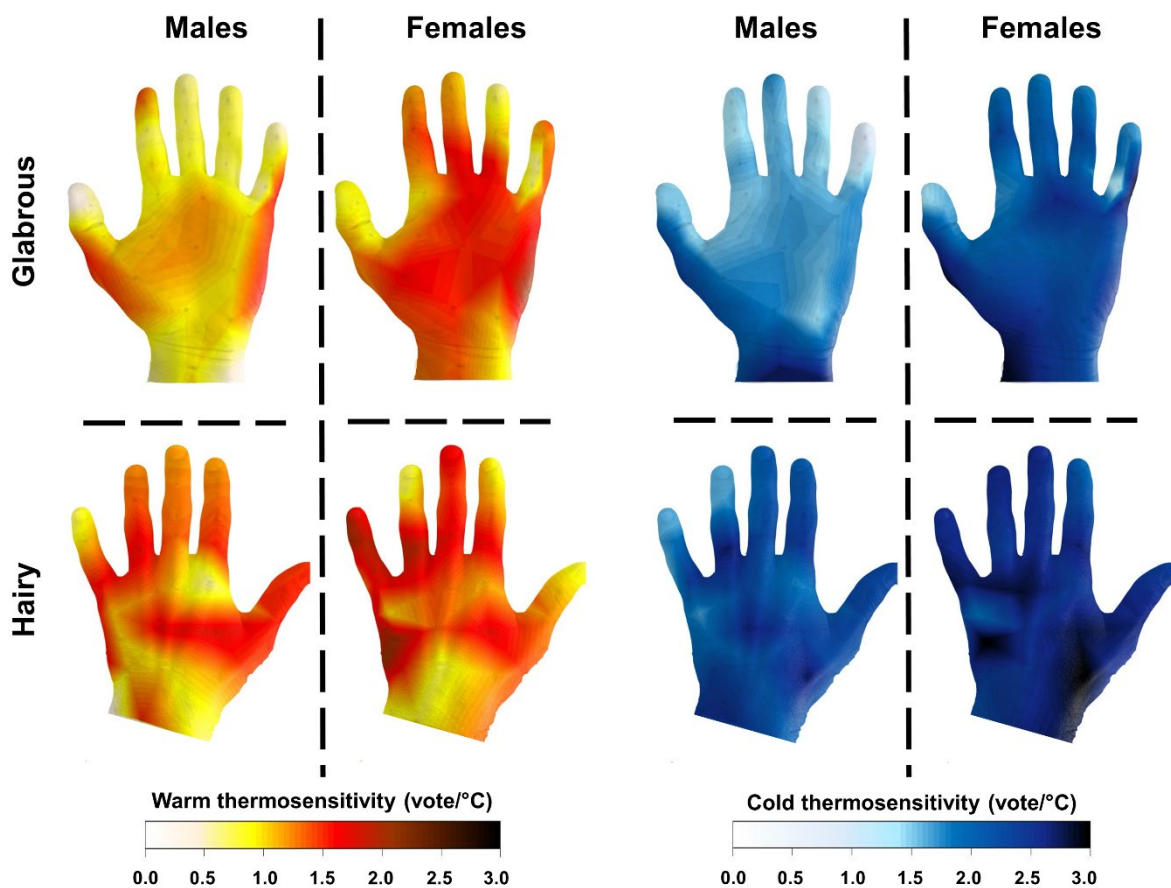
### *Whole body mean $T_{sk}$*

Average mean  $T_{sk}$  did not change over the course of the experiment ( $F_{(10, 40)}=0.6063$ ;  $p=0.799$ ) and was maintained within a neutral range (i.e. 31-34°C) (Filingeri *et al.*, 2017c), with no differences ( $F_{(1, 4)}=0.2124$ ;  $p=0.668$ ) between males (mean  $T_{sk}=32.14^{\circ}\text{C}$ ; SD 0.08) and females (mean  $T_{sk}=31.64^{\circ}\text{C}$ ; SD 0.18).

*Hand: glabrous skin warm thermosensitivity*

In the male group, mean warm thermosensitivity across glabrous skin (i.e. sites 1 to 23) was 0.89 vote/°C [95%CI= 0.80, 0.98], and varied between a minimum of 0.55 to a maximum of 1.22 vote/°C (Fig. 3). In the female group, mean warm thermosensitivity across the same skin sites was 1.23 vote/°C [95%CI= 1.09, 1.38], and varied between a minimum of 0.57 to a maximum of 1.68 vote/°C (Fig. 3).

Despite females presenting a slightly higher mean warm thermosensitivity than males, this difference did not reach statistical significance ( $F_{(1, 14)} = 1.97$ ;  $p = 0.181$ ).



**Figure 3.** Warm and cold thermosensitivity maps for glabrous and hairy skin of the hand in males and females. Maps shows mean data for each gender group ( $n=8$ ) and are based on the 49 sites tested over the hand.

While no clear gender differences were observed, warm thermosensitivity varied significantly across the palm of the hand ( $F_{(22, 308)} = 1.94$ ;  $p = 0.007$ ), with regional patterns that were similar between male and females ( $F_{(22, 308)} = 0.878$ ;  $p = 0.624$ ).



The centre of the palm (skin site 17), along with the area at the base of the thumb (skin site 19), presented some of the highest warm sensitivity in both males (site 17= 1.22 vote/°C; site 19= 1.16 vote/°C) and females (site 17= 1.54 vote/°C; site 19= 1.68 vote/°C). On the contrary, the thumb (skin site 22) and the intermediate portion of the fifth digit (skin site 11), presented some of the lowest warm sensitivity in both males (site 22= 0.55 vote/°C; site 11= 0.92 vote/°C) and females (site 22= 0.87 vote/°C; site 11= 0.57vote/°C).

Statistical significance values for multiple sites comparison are listed in *Supplementary Material 1*.

#### *Hand: glabrous skin cold thermosensitivity*

In the male group, mean cold thermosensitivity across glabrous skin (i.e. sites 1 to 23) was 1.49 vote/°C [95%CI= 1.40, 1.59], and varied between a minimum of 0.83 to a maximum of 1.81 vote/°C (Fig.). In the female group, mean cold thermosensitivity across the same skin sites was 1.99 vote/°C [95%CI= 1.86, 2.12], and varied between a minimum of 1.17 to a maximum of 2.56 vote/°C (Fig. 3).

Cold thermosensitivity varied largely across the palm of the hand in both males and females ( $F_{(22, 308)} = 1.93$ ;  $p=0.008$ ). However, and contrary to what observed for warm thermosensitivity, we observed a tendency for the female group to present an overall higher cold thermosensitivity than their male counterparts ( $F_{(1, 14)} = 3.29$ ;  $p=0.090$ ).

Similar regional patterns of cold sensitivity were observed across the palm in both groups ( $F_{(22, 308)} = 1.00$ ;  $p=0.459$ ), with the base of the palm (skin site 20) presenting high sensitivity in both males (site 20= 1.82 vote/°C) and females (site 20= 2.39 vote/°C).

In addition, females presented significantly higher cold sensitivity than males on specific skin sites, such as the intermediate portion of the second digit (skin site 2; mean difference=+ 0.95 vote/°C, [95%CI= 0.14, 1.75]), the distal portion of the fifth digit (skin site 10; mean difference=+ 0.90 vote/°C, [95%CI= 0.09, 1.70]), the middle part of the top of the palm (skin site 14; mean difference 0.86 vote/°C, [95%CI= 0.05, 1.67]), and the medial area at the base of the palm (skin site 21; mean difference 0.81 vote/°C, [95%CI= 0.01, 1.61]).

Statistical significance values for multiple sites comparison are listed in *Supplementary Material 1*.

#### *Hand: hairy skin warm thermosensitivity*

In the male group, mean warm thermosensitivity across hairy skin (i.e. sites 24 to 49) was 1.27 vote/°C [95%CI= 1.12, 1.42], and varied between a minimum of 0.28 to a maximum of

1.79 vote/°C (Fig. 3). In the female group, mean warm thermosensitivity across the same skin sites was 1.42 vote/°C [95%CI= 1.27, 1.58], and varied between a minimum of 0.78 to a maximum of 2.12 vote/°C (Fig. 3).

Despite females presenting a slightly higher mean warm thermosensitivity than males, this difference did not reach statistical significance ( $F_{(1, 14)} = 0.3409$ ;  $p = 0.568$ ).

While no clear gender differences were observed, warm thermosensitivity varied largely across the dorsum of the hand ( $F_{(25, 350)} = 2.72$ ;  $p < 0.0001$ ), with regional patterns that were similar between male and females ( $F_{(25, 350)} = 1.153$ ;  $p = 0.280$ ).

The proximal portion of the fourth digit (skin site 30), along with the area in between the metacarpophalangeal joint of the second digit and the base of the thumb (skin site 36), presented some of the highest warm sensitivity in both males (site 30= 1.74 vote/°C; site 36= 1.79 vote/°C) and females (site 30= 1.97 vote/°C; site 36= 1.76 vote/°C). On the contrary, the area over the metacarpophalangeal joint of the second digit (skin site 33) and the middle area at the base of the hand (skin site 40), presented some of the lowest warm sensitivity in both males (site 33= 0.59 vote/°C; site 40= 0.99 vote/°C) and females (site 33= 1.12 vote/°C; site 40= 0.79 vote/°C).

Statistical significance values for multiple sites comparison are listed in *Supplementary Material 1*.

#### *Hand: hairy skin cold thermosensitivity*

In the male group, mean cold thermosensitivity across hairy skin (i.e. sites 24 to 49) was 2.19 vote/°C [95%CI= 2.06, 2.32], and varied between a minimum of 1.63 to a maximum of 2.70 vote/°C (Fig.). In the female group, mean cold thermosensitivity across the same skin sites was 2.52 vote/°C [95%CI= 2.41, 2.63], and varied between a minimum of 1.82 to a maximum of 3.04 vote/°C (Fig. 3).

While no gender differences were observed, ( $F_{(1, 14)} = 1.566$ ;  $p = 0.231$ ), cold thermosensitivity varied significantly across the dorsum of the hand ( $F_{(25, 350)} = 1.98$ ;  $p = 0.003$ ), with regional patterns that were similar between male and females ( $F_{(25, 350)} = 1.38$ ;  $p = 0.103$ )

The area across the centre of the dorsum (skin sites 36 and 37) and the base of the thumb (skin site 39) presented some of the highest warm sensitivity in both males (site 36= 2.32 vote/°C; site 37= 2.63 vote/°C; site 39= 2.71 vote/°C) and females (site 36= 2.82 vote/°C; site 37= 2.46 vote/°C; site 39= 3.04 vote/°C). On the contrary, the area over the metacarpophalangeal joints of the second and fifth digits (skin sites 33 and 35), presented

some of the lowest cold sensitivity in both males (site 33= 1.76 vote/°C; site 35= 1.66 vote/°C) and females (site 33= 2.36 vote/°C; site 35= 1.82 vote/°C).

Statistical significance values for multiple sites comparison are listed in *Supplementary Material 1*.

*Hand: inter-individual variability in thermosensitivity*

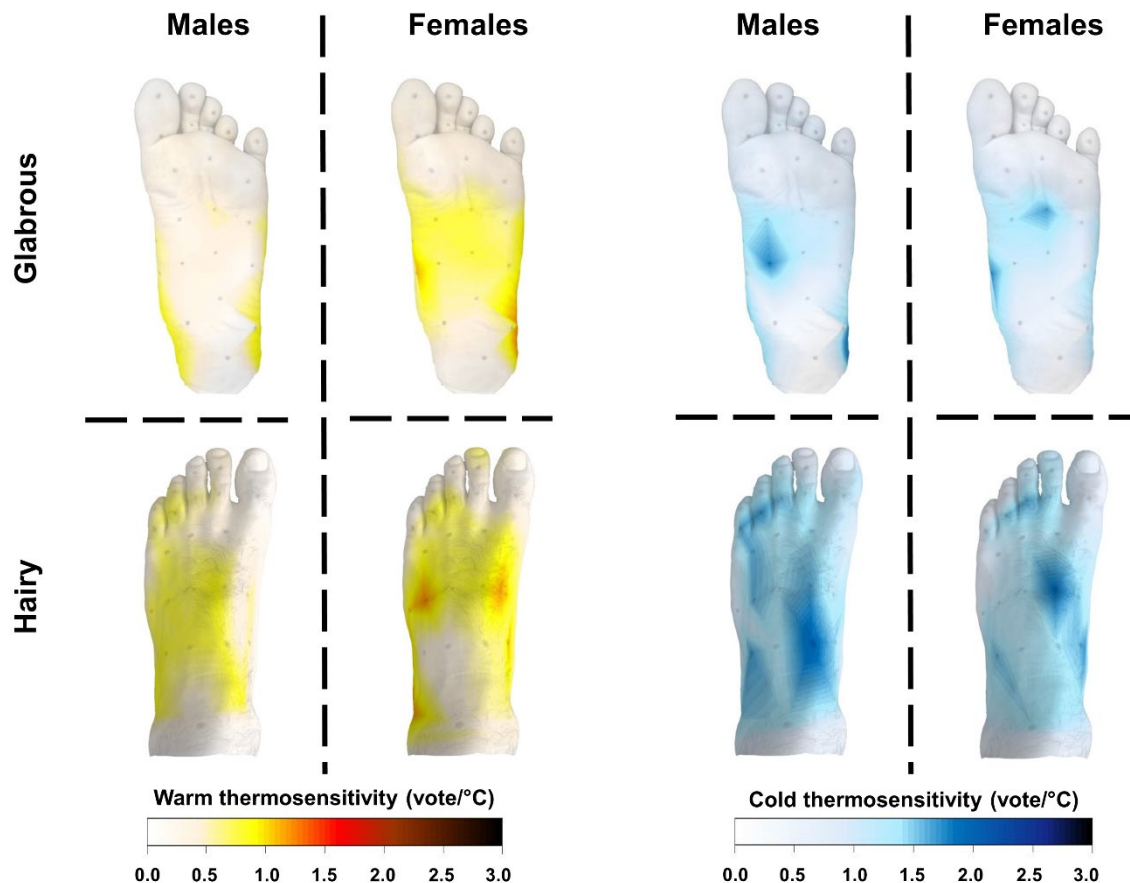
Inter-individual variability in warm thermosensitivity was greater in males than in females (mean difference= +10.5% [95% CI= 0.6, 20.4]; p=0.038), and ranged largely across the skin site tested, from a minimum of 39.2% (skin site 48) to a maximum of 186% (skin site 11) in males (mean= 79.1%), and from a minimum of 34.4% (skin site 32) to a maximum of 117.6% (skin site 42) in females (mean= 68.6%) (see Fig. 5).

Inter-individual variability in cold thermosensitivity was greater in males than in females (mean difference= +6.3% [95% CI= 1.2, 11.4]; p=0.016), and ranged largely across the skin site tested, from a minimum of 16.5% (skin site 26) to a maximum of 72.1% (skin site 11) in males (mean= 43.7%), and from a minimum of 31.1% (skin site 3) to a maximum of 81.1% (skin site 12) in females (mean= 37.37%) (Fig. 5).

All in all, it appeared that inter-individual variability in thermosensitivity was: 1) more pronounced in males than in females for both warm and cold; 2) greater in some specific skin sites across the glabrous and hairy skin of the hand; and 3) greater overall for warm than cold sensitivity.

*Foot: glabrous skin warm thermosensitivity*

In the male group, mean warm thermosensitivity across glabrous skin (i.e. sites 23 to 43) was 0.25 vote/°C [95%CI= 0.19, 0.31], and varied between a minimum of 0 to a maximum of 1.53 vote/°C (Fig. 4). In the female group, mean warm thermosensitivity across the same skin sites was 0.46 vote/°C [95%CI= 0.37, 0.55], and varied between a minimum of 0.21 to a maximum of 0.79 vote/°C (Fig. 4).



**Figure 4.** Warm and cold thermosensitivity maps for glabrous and hairy skin of the foot in males and females. Maps shows mean data for each gender group (n=8) and are based on the 54 sites tested over the foot.

Warm thermosensitivity varied largely across the sole of the foot in both males and females ( $F_{(20, 260)} = 2.17$ ;  $p = 0.003$ ).

The centre portion of the sole (skin sites 35 and 38) presented some of the highest warm sensitivity in both males (site 35 = 0.53 vote/°C; site 38 = 0.38 vote/°C) and females (site 35 = 0.75 vote/°C; site 38 = 0.79 vote/°C), while the distal part of the hallux (skin site 23) and the centre of the heel (skin site 43) presented some of the lowest warm sensitivity in males (site 23 = 0.13 vote/°C; site 43 = 0.08 vote/°C) and females (site 23 = 0.26 vote/°C; site 43 = 0.23 vote/°C).

Despite neither gender presenting an overall higher sensitivity *per se* ( $F_{(1, 13)} = 3.03$ ;  $p = 0.105$ ), there was a tendency for some specific skin sites to be more sensitive in females than in males ( $F_{(20, 260)} = 1.569$ ;  $p = 0.060$ ).

Specifically, females presented significantly higher warm sensitivity than males on the superior portion of the arch (skin site 34; mean difference=+ 0.55 vote/°C, [95%CI= 0.14, 0.96]), the centre (skin site 38; mean difference=+ 0.41 vote/°C, [95%CI= 0.01, 0.82]), and the lateral portion of the sole (skin site 39; mean difference +0.58 vote/°C, [95%CI= 0.17, 0.99]).

Statistical significance values for multiple sites comparison are listed in *Supplementary Material 1*.

#### *Foot: glabrous skin cold thermosensitivity*

In the male group, mean cold thermosensitivity across glabrous skin (i.e. sites 23 to 43) was 0.75 vote/°C [95%CI= 0.55, 0.94], and varied between a minimum of 0.04 to a maximum of 1.78 vote/°C (Fig.). In the female group, mean warm thermosensitivity across the same skin sites was 0.55 vote/°C [95%CI= 0.34, 0.75], and varied between a minimum of 0.04 to a maximum of 1.65 vote/°C (Fig. 4).

Cold thermosensitivity varied largely across the sole of the foot in both males and females ( $F_{(20, 260)} = 8.48$ ;  $p < 0.0001$ ).

The area over the arch (skin sites 34 and 37) presented some of the highest cold sensitivity in both males (site 34= 1.45 vote/°C; site 37= 1.78 vote/°C) and females (site 35= 1.35 vote/°C; site 38= 1.09 vote/°C), while the distal part of the hallux (skin site 23) and the centre of the heel (skin site 43) presented some of the lowest cold sensitivity in males (site 23= 0.47 vote/°C; site 43= 0.04 vote/°C) and females (site 23= 0.29 vote/°C; site 43= 0.25 vote/°C). Despite neither gender presenting an overall higher sensitivity *per se* ( $F_{(1, 13)} = 0.73$ ;  $p = 0.408$ ), there was a clear trend for some specific skin sites to be more sensitive in males than in females ( $F_{(20, 260)} = 2.04$ ;  $p = 0.006$ ).

Specifically, males presented significantly higher cold sensitivity than females on the proximal part of the second toe (skin site 26; mean difference=+ 0.74 vote/°C, [95%CI= 0.05, 1.43]), the distal part of the fourth toe (skin site 29; mean difference=+ 0.72 vote/°C, [95%CI= 0.03, 1.41]), and the centre portion of the arch (skin site 37; mean difference +0.69 vote/°C, [95%CI= 0.01, 1.38]).

Statistical significance values for multiple sites comparison are listed in *Supplementary Material 1*.

### *Foot: hairy skin warm thermosensitivity*

In the male group, mean warm thermosensitivity across hairy skin (i.e. sites 1 to 22 and 44 to 55) was 0.52 vote/°C [95%CI= 0.45, 0.60], and varied between a minimum of 0.16 to a maximum of 0.89 vote/°C (Fig.). In the female group, mean warm thermosensitivity across the same skin sites was 0.65 vote/°C [95%CI= 0.55, 0.75], and varied between a minimum of 0.16 to a maximum of 1.24 vote/°C (Fig. 4).

No gender differences in thermosensitivity were observed ( $F_{(1, 13)} = 1$ ;  $p = 0.335$ ), and warm thermosensitivity varied largely across the dorsum of the foot ( $F_{(33, 429)} = 2.117$ ;  $p < 0.001$ ), with regional patterns that were similar between male and females ( $F_{(33, 429)} = 0.93$ ;  $p = 0.574$ ). The central portion of the dorsum of the foot (skin sites 15, 16, 17), presented some of the highest warm sensitivity in both males (site 15= 0.89 vote/°C site; 16= 0.73 vote/°C; site 17= 0.77 vote/°C) and females (site 15= 0.83 vote/°C site; 16= 0.78 vote/°C; site 17= 1.24 vote/°C). In contrast, the proximal portion of the hallux (skin site 1) and the distal portion of the fifth toe (skin site 8), presented some of the lowest warm sensitivity in both males (site 1= 0.19 vote/°C; site 8= 0.45 vote/°C) and females (site 1= 0.32 vote/°C; site 8= 0.17 vote/°C). Statistical significance values for multiple sites comparison are listed in *Supplementary Material 1*.

### *Foot: hairy skin cold thermosensitivity*

In the male group, mean cold thermosensitivity across hairy skin (i.e. sites 1 to 22 and 44 to 55) was 1.23 vote/°C [95%CI= 1.09, 1.36], and varied between a minimum of 0.18 to a maximum of 2.01 vote/°C (Fig. 4). In the female group, mean cold thermosensitivity across the same skin sites was 1.18 vote/°C [95%CI= 1.07, 1.30], and varied between a minimum of 0.48 to a maximum of 1.87 vote/°C (Fig. 4).

No gender differences in thermosensitivity were observed ( $F_{(1, 13)} = 0.02$ ;  $p = 0.893$ ). Cold thermosensitivity varied largely across the dorsum of the foot ( $F_{(33, 429)} = 2.99$ ;  $p < 0.0001$ ) with regional patterns that were similar for males and females ( $F_{(33, 429)} = 1.19$ ;  $p = 0.213$ ).

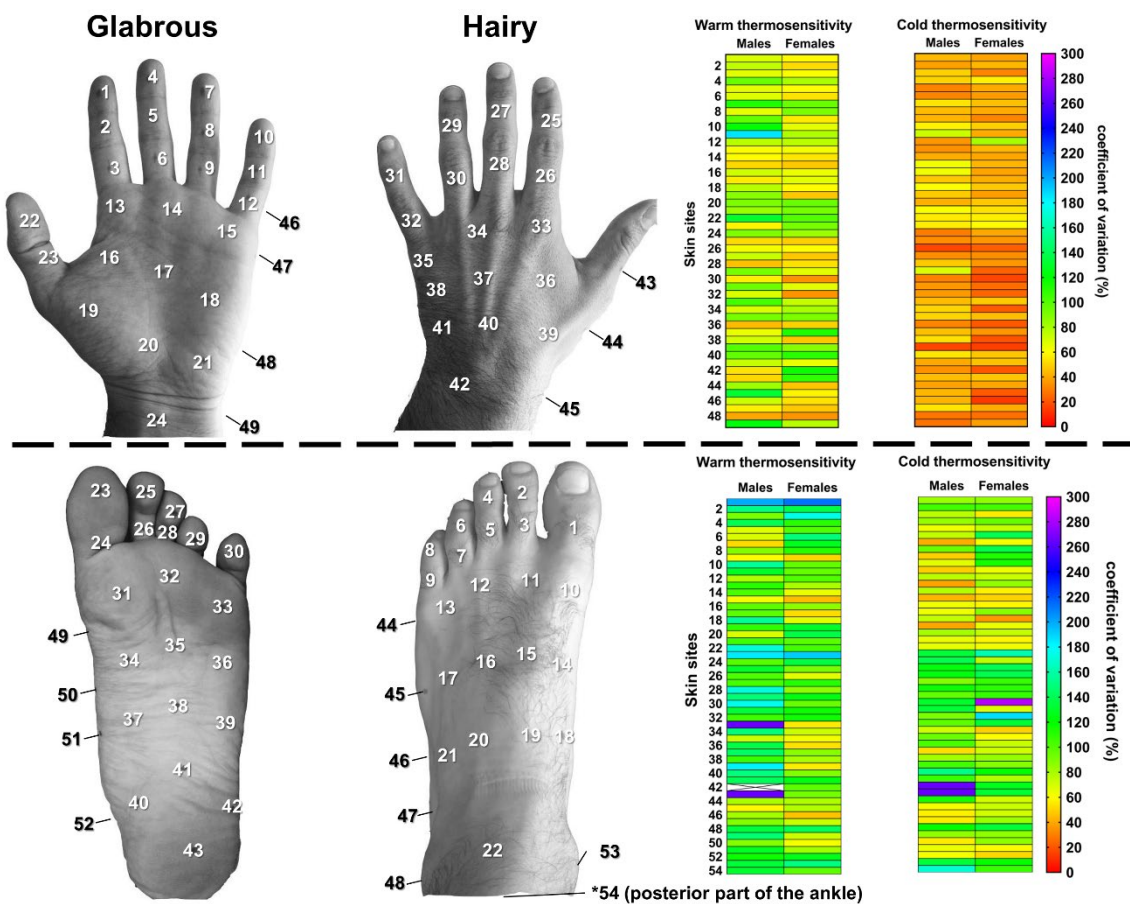
The central portion of the dorsum of the foot (skin sites 15), exhibited some of the highest cold sensitivity in both males (site 15= 1.62 vote/°C site) and females (site 15= 1.88 vote/°C site).

In contrast, the proximal portion of the hallux (skin site 1) and the distal portion of the fourth toe (skin site 6), exhibited some of the lowest cold sensitivity in both males (site 1= 1.17 vote/°C; site 6= 1.27 vote/°C) and females (site 1= 0.83 vote/°C; site 8= 0.67 vote/°C).

Statistical significance values for multiple sites comparison are listed in *Supplementary Material 1*.

*Foot: inter-individual variability in thermosensitivity*

Inter-individual variability in warm thermosensitivity was greater in males than in females (mean difference= +23.2% [95% CI= 7.4, 39.0]; p=0.004), and ranged largely across the skin site tested, from a minimum of 51.1% (skin site 7) to a maximum of 264.6% (skin site 43) in males (mean= 123.3%), and from a minimum of 44.7% (skin site 15) to a maximum of 213.3% (skin site 1) in females (mean= 100.1%) (Fig. 5).



**Figure 5.** Inter-individual variability in thermosensitivity for the hand (upper half panel) and the foot (lower half panel). Heat maps are presented and show coefficients of variation for warm and cold thermosensitivity, in males (n=8) and females (n=8), and for all 103 skin sites tested.

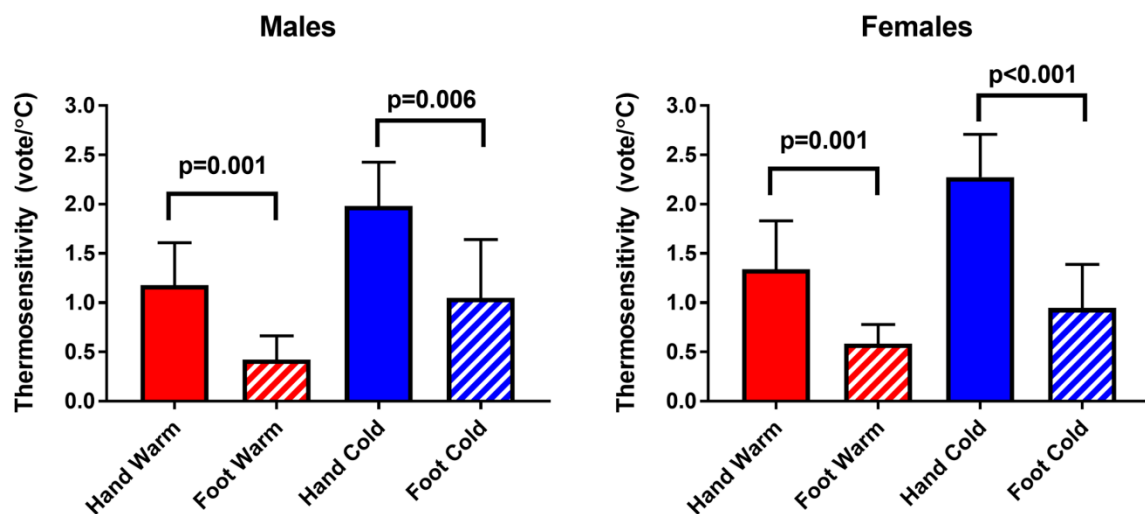
Inter-individual variability in cold thermosensitivity was similar between males and females (mean difference= +0.85% [95% CI= -16, 17.7]; p=0.920), yet ranged largely across the skin

site tested, from a minimum of 37.8% (skin site 13) to a maximum of 264.6% (skin sites 42 and 43) in males (mean= 94.9%), and from a minimum of 35.6% (skin site 18) to a maximum of 282.8% (skin site 30) in females (mean= 94%) (Fig. 5).

In sum, it appeared that inter-individual variability in thermosensitivity: 1) was more pronounced in males than in females with regards to warm sensitivity only; 2) was greater in some specific skin sites across the glabrous and hairy skin of the foot; 3) was overall greater for warm than cold sensitivity.

#### *Hand vs. Foot overall thermosensitivity*

Comparison between overall thermosensitivity of the hand versus the foot indicated the hand to be twice as warm sensitive (male hand vs. foot mean difference= 0.75 vote/°C [95%CI=0.46, 1.04], p=0.001; female hand vs. foot mean difference= 0.75 vote/°C [95%CI=0.45, 1.05], p=0.001), and as cold sensitive (male hand vs. foot mean difference= 0.93 vote/°C [95%CI=0.38, 1.47], p=0.006; female hand vs. foot mean difference= 1.32 vote/°C [95%CI=0.90, 1.75], p<0.001) as the foot, in both males and females (Fig. 6).

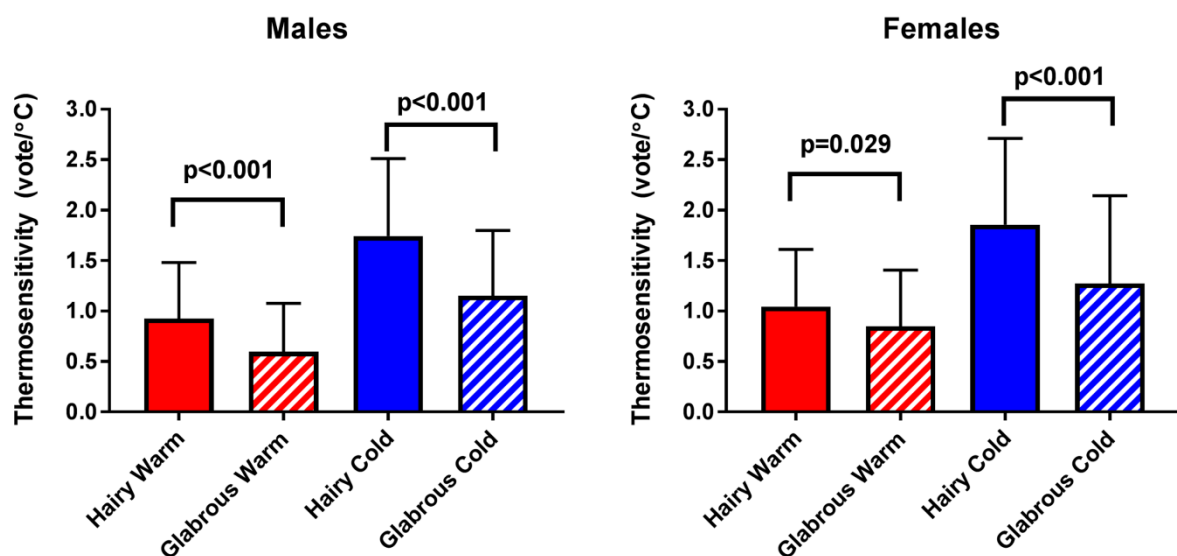


**Figure 6.** Hand and foot overall thermosensitivity in males and females. Each graph presents a comparison of the overall warm and cold thermosensitivity of the hand (49 sites) versus the foot (54 sites) for males (n=8) and females (n=8). It can be observed that the hand is significantly more sensitive than the foot for both warming and cooling, and in both males and females. Probability values for statistical comparisons between hands and feet thermosensitivity are shown.



### *Glabrous vs. Hairy skin overall thermosensitivity*

Comparison between overall thermosensitivity of glabrous (palms and soles) versus hairy skin (back of hands and feet) indicated the glabrous skin to be more warm sensitive (male glabrous vs. hairy mean difference= 0.34 vote/°C [95%CI=0.20, 0.45],  $p<0.001$ ; female glabrous vs. hairy mean difference= 0.19 vote/°C [95%CI=0.02, 0.36],  $p=0.029$ ), and more cold sensitive (male glabrous vs. hairy mean difference= 0.59 vote/°C [95%CI=0.41, 0.77],  $p<0.001$ ; female glabrous vs. hairy mean difference= 0.58 vote/°C [95%CI=0.31, 0.85],  $p<0.001$ ) than the hairy skin, in both males and females (Fig. 7).

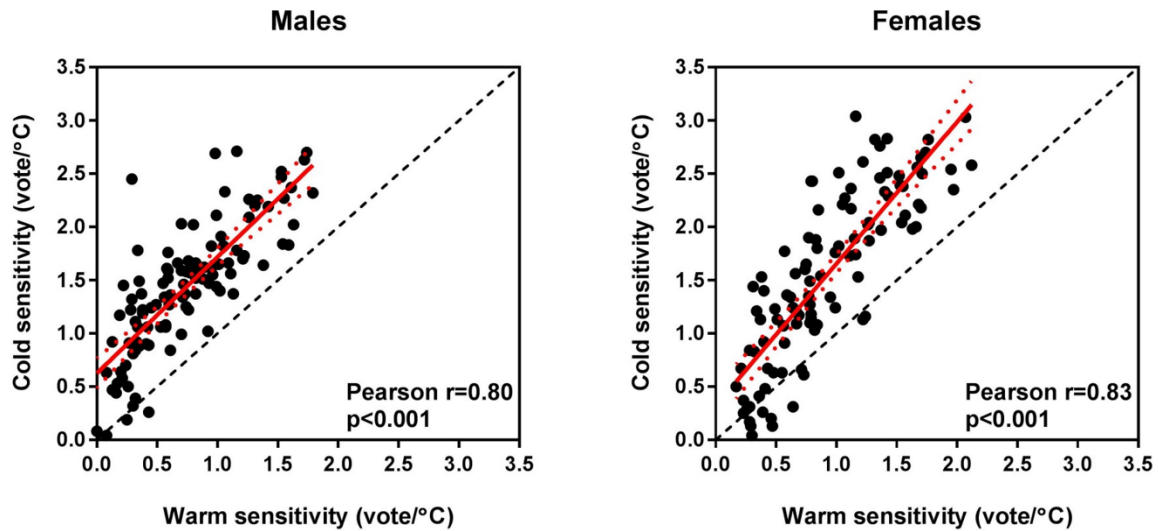


**Figure 7.** Glabrous and hairy skin overall thermosensitivity in males and females. Each graph presents a comparison of the overall warm and cold thermosensitivity of the glabrous skin of both (includes all skin sites over palms and soles) versus the hairy skin (includes all skin sites over back of hands and feet) for males ( $n=8$ ) and females ( $n=8$ ). It can be observed that the hairy skin is significantly more sensitive than the glabrous skin for both warming and cooling, and in both males and females. Probability values for statistical comparisons between hairy and glabrous skin thermosensitivity are shown.

### *Association between overall warm and cold thermosensitivity*

Correlation analyses performed on data from all skin sites tested across hand and feet showed a significant association between warm and cold sensitivity in both males (Pearson  $r=0.80$  [95%CI= 0.71, 0.86];  $R^2=0.64$ ;  $p<0.0001$ ) and females (Pearson  $r=0.83$  [95%CI= 0.76, 0.88];  $R^2=0.69$ ;  $p<0.0001$ ) (Fig. 8), with a tendency for cold to be greater than warm sensitivity.

The significant association between warm and cold sensitivity indicated that hands and feet contained areas that were highly sensitive to temperature changes *per se*, irrespective of their direction (i.e. warming or cooling).



**Figure 8.** Association between overall warm and cold thermosensitivity in males and females. Each graph presents the association between the warm and cold thermosensitivity of all 103 skin sites tested across hands and feet in males (n=8) and females (n=8). Pearson correlation coefficients and probability values for statistical significance are shown.

## Discussion

Our high-density thermosensory micromapping resulted in the development of the most detailed thermosensitivity maps of hands and feet in healthy young adults available to date.

Overall, our findings indicate that:

1. Thermosensitivity to warm and cold varies largely by up to 5-fold across the glabrous and hairy portions of both hands and feet (Fig. 3, 4), with a distal-to-proximal organisation, and with hairy skin being more thermosensitive than glabrous (Fig. 7);
2. The hand is twice as thermosensitive as the foot (compare Fig. 3 and 4; see Fig. 6);

3. Body-surface-area-matched males and females present small differences in thermosensitivity of hands and feet, and that these differences are constrained to glabrous skin only;

*Thermosensitivity varies largely across hands and feet, and between skin types*

The heterogeneous topography of thermosensitivity we observed here presents a distal-to-proximal organisation on both the hand and the foot, with the palm and dorsum being more sensitive than the fingers (e.g. palm was twice as warm sensitive as the thumb; Fig. 3), and with the sole and dorsum being more sensitive than the toes (e.g. the area over the arch was three times as cold sensitive as the hallux; Fig. 4).

As this observation extends across both hairy and glabrous portions of both hands and feet, in both males and females, we suggest that the distal-to-proximal increase in thermosensitivity is likely to be a specific topographical feature of hands and feet thermosensitivity in humans. This finding is novel and surprising, particularly, as one would expect that due to their primary role in manipulation and gripping (Witney *et al.*, 2004; Changizi *et al.*, 2011), fingers and toes would be more sensitive than the rest of the hand and foot, as it is indeed the case for touch (Johansson & Vallbo, 1979b, 1979a) and pain sensitivity (Mancini *et al.*, 2013) of the palm.

A potential explanation to this surprising finding might relate to the fact that the glabrous skin of the fingers and toes could have developed more to provide a thermoregulatory, rather than thermosensory, function.

This area of the fingers and toes indeed provides an enormous capacity for fast vasodilation and vasoconstriction, and it is heavily involved in releasing/retaining heat under thermal challenges (Taylor *et al.*, 2014).

Thermosensory function could have instead developed more in skin regions other than fingers and toes (e.g. palms and soles), and particularly on hairy skin sites (e.g. dorsum of hands and feet) (Filingeri, 2016).

This hypothesis is supported by our current findings, as we observed that hairy skin (i.e. dorsum of hand and foot) was more sensitive than glabrous skin (i.e. palm and sole) (see Fig. 7).

Previous psychophysical evidence has found a higher density of cold and warm sensitive spots on the hand/foot dorsum as opposed to the palm/sole, suggesting higher peripheral innervation of this type of skin (Hensel, 1981).

Accordingly, the hairy skin covering hands and feet could play a more specific thermosensory role than the glabrous skin, where the latter is likely to be more of a specialized area for thermoregulatory responses.

As hairy skin covers the majority of our body, and as small changes over a large proportion of the body are likely to result in higher rates of heat transfer to the environment (Darian-Smith & Johnson, 1977), the development of a higher sensitivity of the hairy skin would be biologically useful to help maintaining thermal homeostasis (Cabanac, 2011).

It could therefore be proposed that thermosensitivity differences within and between the hairy and glabrous skin of hands and feet observed here could be dependent on differences between the thermoregulatory and thermosensory specialization of different skin areas.

It cannot be excluded that differences in skin thickness between fingers/toes and palm/soles, as well as between hairy and glabrous skin, and related changes in heat diffusion/extraction to/from the epidermal layers where thermoreceptors are positioned, could at least partly explain the observed distal to proximal organization in thermosensitivity (Iannetti *et al.*, 2006).

Evidence is available indicating that hairy skin presents higher sensitivity than glabrous skin to heat pain, but only when thermal stimuli are delivered via conductive heating (Iannetti *et al.*, 2006). When radiant heat (e.g. laser pulses) stimulates the skin, regional differences between hairy and glabrous skin are eliminated (Iannetti *et al.*, 2006), supporting the impact of thickness-depend mechanisms of heat transfer on stimulation of thermoreceptors.

However, correlation between epidermal thickness and local thermosensitivity has been previously shown to be low across the palm (Li *et al.*, 2008).

Furthermore, in the present study we observed the distal-to-proximal topographical trend to also extend across hairy skin, where differences in epidermal thickness between fingers/toes and the body of hands/feet are likely to be smaller than across glabrous skin.

It is therefore likely that a combination of neurophysiological (e.g. peripheral innervation and central cortical representation) as well as biophysical factors (e.g. skin anatomy) could underlie the heterogeneous thermosensitivity we observed across hands and feet, as much as it is the case for touch and pain sensitivity of the palm (Penfield & Boldrey, 1937; Johansson & Vallbo, 1979b; Mancini *et al.*, 2013).

Irrespective of whether our observed differences within and between the hairy and glabrous skin of hands and feet are neurally- or anatomically-driven, it is remarkable to note that humans seem to be well aware of them, as reflected in some of our most common and instinctive thermal behaviours.

For example, it is common practice in many cultures to check whether one's baby has a fever by placing the dorsum of our hands (and not the palm nor fingers) on their forehead. On the contrary, we instinctively expose our palms (and not the dorsum) to the warming heat of a glowing fire.

These examples illustrate the thermosensory nature of hairy skin, as opposed to the thermoregulatory nature of glabrous skin, and could support the intriguing hypothesis for which some of our most important adaptive thermal behaviours could be rooted in the topographical differences in our hands and feet thermosensitivity shown in our thermosensitivity maps.

### *Hands are twice as thermosensitive as feet*

It is remarkable to note that the hand was on average twice as thermosensitive as the foot, in both males and females (Fig. 6).

The higher thermosensitivity of hands than feet has been previously reported by our group (Filingeri *et al.*, 2017b) and by others (Stevens & Choo, 1998), although such comparisons were based on a limited number of representative skin sites (e.g. the sole vs. the palm) (Filingeri *et al.*, 2017b).

In expanding to thermosensory processing, these results are in line with evidence indicating that the presence of a greater cortical representation of hands as compared to feet in the human brain (Penfield & Boldrey, 1937) is likely to underlie the greater sensitivity of the upper extremity to cutaneous stimulation.

In the context of thermosensitivity, it could be therefore speculated that the higher thermosensitivity of the hands is likely to be more dependent on central (i.e. size of the central representation of target skin area), than on peripheral factors (i.e. skin receptors density), as it is the case for pain (Mancini *et al.*, 2013).

It also interesting to note that, cold and warm sensitivities were highly associated across both hands and feet in both males and females (Fig. 8), although cold was overall higher than warm sensitivity.

That highly sensitive skin regions present higher sensitivity to both warm and cold has been repeatedly shown (Stevens & Choo, 1998; Li *et al.*, 2008), and our findings provide further evidence for the presence of “skin spots” that are highly sensitive to temperature changes *per se*, irrespective of their direction (i.e. warming or cooling), on both hands and feet.

Finally, our inter-individual variability analysis clearly showed modality- and region-dependent differences in individual variability in thermosensitivity, with variability being lower for cold than warm sensitivity, and for the hand as opposed to the foot (Fig. 5). The lower variability for cold is likely to be dependent on the higher cold than warm sensitivity of the skin, which was confirmed in this (Fig. 5) as well as in previous studies (Hensel, 1981; Green, 2004; Filingeri, 2016; Filingeri *et al.*, 2017c). Interestingly, our finding of higher inter-individual variability for the foot than hand is novel, and could be dependent on the lower thermosensitivity of this region (see Fig. 6), which is likely to result in less homogenous thermal responses between individuals.

#### *Males and females present small thermosensitivity differences*

A further major advance of this study is that we observed small gender differences in overall cold and warm thermosensitivity in our age- and body surface area-matched male and female groups.

A slight trend was present, with females presenting a slightly higher sensitivity on glabrous (i.e. palms and soles), but not hairy (i.e. hand/foot dorsum), skin.

Numerous studies have analysed gender-differences in thermosensitivity across the body, yet findings have been often contradictory, with females being alternatively reported as more sensitive (Gerrett *et al.*, 2014, 2015) or no different to males (Stevens & Choo, 1998).

Such contradictory evidence has often arisen from studies not matching gender groups for body surface area and relative stimulus size (Li *et al.*, 2008; Gerrett *et al.*, 2014), with this resulting in the inability to ascribe potential thermosensitivity differences to gender differences *per se* (Greenspan & Kenshalo, 1985), as opposed to size differences.

To overcome such limitations, in this study we matched our male and female groups for age and body surface area; we found that gender differences were small and only constrained to glabrous and not hairy skin.

That gender differences in thermophysiological responses of hands and feet are reduced when male and female groups are matched body surface area has been previously shown (Jay & Havenith, 2004; Lunt & Tipton, 2014).

Our analysis is the first to show that previously reported thermosensory differences between genders could be biased by gender differences in relative stimulus size.

By matching groups for relative stimulus size, gender differences can be remarkably reduced, and in the case of hands and feet, being present only over glabrous skin.

Glabrous skin covers a minimal portion of total body surface area, whose majority is covered by hairy skin.

Accordingly, we suggest that gender-related differences in thermosensitivity might be dependent on size than on gender *per se*, although further thermosensitivity analyses between body-surface-area matched groups, including other body regions, are warranted to confirm these findings.

## Conclusions

Our high-density thermosensory micromapping resulted in the development of the most detailed thermosensitivity maps of hands and feet in healthy young adults available to date. We found that thermosensitivity to warm and cold varied largely by up to 5-fold across the glabrous and hairy portions of human hands and feet, with hands being twice as sensitive as the feet.

We observed a characteristic distal to proximal increase in thermosensitivity over both hairy and glabrous skin (i.e. from fingers/toes to body of hands and feet), and found that hairy is more sensitive than glabrous skin.

We therefore argue that distal to proximal organization is a specific topographical feature of hand and feet thermosensitivity in humans, and that thermosensitivity differences between skin sites highlight the thermosensory role of hairy skin, as opposed to the thermoregulatory role of glabrous skin.

Finally, we determined that body-surface-area matched males and females, present small differences in thermosensitivity, and that these are constrained to glabrous skin only.

Our novel findings fill a knowledge gap on the sensory function of human hands and feet. Also, by complementing the available evidence on the topography of touch and pain sensitivity, these findings provides a more comprehensive picture on the sensory function of two of our most important sensory and exploratory organs, i.e. our hands and feet.

As well as providing a window into the peripheral and central mechanisms of thermosensory integration in humans (Filingeri *et al.*, 2017c), these maps will be valuable to guide future developments in smart skin and prosthesis, in wearable energy-efficient personal comfort systems, and in protective clothing.

## **Competing interests**

The authors declare no competing interests.

## **Author contributions**

DF, HZ, EA contributed to the conception and design of the work; DF performed the experiments and data analysis; DF, HZ, EA contributed to the interpretation of the results; DF drafted the work; DF, HZ, EA revised the work critically for important intellectual content.

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## **Author profile**

Davide Filingeri is an Assistant Professor/Vice-Chancellor's Lecturer at Loughborough University. Davide's research programme focuses on understanding how our brain senses the external world through our skin, how this influences body temperature regulation and thermal behavior, and how this integrated system fails when neurodegeneration (e.g. Multiple Sclerosis) takes place.

After completing a BSc and MSc in exercise physiology (University of Palermo), Davide went on obtaining a PhD in Environmental Physiology and Sensory Neuroscience (Loughborough University). He then performed post-doctoral research at the University of Sydney and at the University of California Berkeley, before returning to Loughborough to set up the THERMOSENSELAB.

## **References**

Ackerley R, Backlund Wasling H, Liljencrantz J, Olausson H, Johnson RD & Wessberg J

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pgs. 723–736

<https://doi.org/10.1152/jappphysiol.00158.2018>  
<https://escholarship.org/uc/item/0bs743x8>



- (2014a). Human C-Tactile Afferents Are Tuned to the Temperature of a Skin-Stroking Caress. *J Neurosci* 34, 2879–2883.
- Ackerley R, Carlsson I, Wester H, Olausson H & Backlund Wasling H (2014b). Touch perceptions across skin sites: differences between sensitivity, direction discrimination and pleasantness. *Front Behav Neurosci* 8, 54.
- Cabanac M (2011). Heat Stress and Behavior. *Compr Physiol* 2011, Supplement 14: *Handbook of Physiology, Environmental Physiology: 261-278. First published in print 1996. doi: 10.1002/cphy.cp040113.*
- Campero M, Baumann TK, Bostock H & Ochoa JL (2009). Human cutaneous C fibres activated by cooling, heating and menthol. *J Physiol* 587, 5633–5652.
- Campero M, Serra J, Bostock H & Ochoa JL (2001). Slowly conducting afferents activated by innocuous low temperature in human skin. *J Physiol* 535, 855–865.
- Changizi M, Weber R, Kotecha R & Palazzo J (2011). Are wet-induced wrinkled fingers primate rain treads? *Brain Behav Evol* 77, 286–290.
- Chortos A, Liu J & Bao Z (2016). Pursuing prosthetic electronic skin. *Nat Mater* 15, 937-950.
- Claus D & Hilz M (1987). Methods of measurement of thermal thresholds. *Acta Neurol Scand* 76, 288-296.
- Craig A (2002). How do you feel? Interoception: the sense of the physiological condition of the body. *Nat Rev Neurosci* 3, 655–666.
- Craig A, Chen K, Bandy D & Reiman E (2000). Thermosensory activation of insular cortex. *Nat Neurosci* 3, 184–190.
- Darian-Smith I (1973). “ Cold” fiber population innervating palmar and digital skin of the monkey: responses to cooling pulses. *J Neurophysiol* 36, 325-346.
- Darian-Smith I (1984). Thermal sensibility. *Compr Physiol* 2011, Supplement 3: *Handbook of Physiology, The Nervous System, Sensory Processes: 879-913. First published in print 1984. doi: 10.1002/cphy.cp010319*
- Darian-Smith I & Johnson K (1977). Thermal sensibility and thermoreceptors. *J Invest Dermatol* 69, 146-153.
- Davis KD, Kwan CL, Crawley AP & Mikulis DJ (1998). Functional MRI study of thalamic and cortical activations evoked by cutaneous heat, cold, and tactile stimuli. *J Neurophysiol* 80, 1533–1546.
- Defrin R, Petrini L & Arendt-Nielsen L (2009). Spatial summation of thermal sensations depends on skin type and skin sensitivity. *Exp brain Res* 198, 29–36.

- Donaldson H (1885). On the temperature-sense. *Mind* 10-X, 398–416.
- Farrar JT, Young JP, LaMoreaux L, Werth JL & Poole RM (2001). Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain* 94, 149–158.
- Filingieri D (2016). Neurophysiology of skin thermal sensations. *Compr Physiol* 6, 1429–1491.
- Filingieri D & Ackerley R (2017). The biology of skin wetness perception and its implications in manual function and for reproducing complex somatosensory signals in neuroprosthetics. *J Neurophysiol* 117, 1761–1775.
- Filingieri D, Chaseling G, Hoang P, Barnett M, Davis SL & Jay O (2017a). Afferent thermosensory function in relapsing-remitting Multiple Sclerosis following exercise-induced increases in body temperature. *Exp Physiol* 102, 887–893.
- Filingieri D, Fournet D, Hodder S & Havenith G (2014). Body mapping of cutaneous wetness perception across the human torso during thermo-neutral and warm environmental exposures. *J Appl Physiol* 117, 887–897.
- Filingieri D, Morris NB & Jay O (2017b). Warm hands, cold heart: progressive whole-body cooling increases warm thermosensitivity of human hands and feet in a dose-dependent fashion. *Exp Physiol* 102, 100–112.
- Filingieri D, Zhang H & Arens EA (2017c). Characteristics of the local cutaneous sensory thermo-neutral zone. *J Neurophysiol* 117, 1797–1806.
- Gerrett N, Ouzzahra Y, Coleby S, Hobbs S, Redortier B, Voelcker T & Havenith G (2014). Thermal sensitivity to warmth during rest and exercise: a sex comparison. *Eur J Appl Physiol* 114, 1451–1462.
- Gerrett N, Ouzzahra Y, Redortier B, Voelcker T & Havenith G (2015). Female thermal sensitivity to hot and cold during rest and exercise. *Physiol Behav* 152, 11–19.
- Green BG (2004). Temperature perception and nociception. *J Neurobiol* 61, 13–29.
- Greenspan JD & Kenshalo D (1985). The primate as a model for the human temperature-sensing system: 2 area of skin receiving thermal stimulation (spatial summation). *Somatosens Mot Res* 2, 315–324.
- Hauer P, Stocks A, McArthur JC, Cornblath DR & Griffin JW (2008). Epidermal Nerve Fiber Density. *Arch Neurol* 65, 1513–1520.
- Hensel H (1981). *Thermoreception and temperature regulation*, Issue 38 o. Academic Press.
- Hjermstad MJ, Fayers PM, Haugen DF, Caraceni A, Hanks GW, Loge JH, Fainsinger R, Aass N & Kaasa S (2011). Studies comparing numerical rating scales, verbal rating

- scales, and visual analogue scales for assessment of pain intensity in adults: A systematic literature review. *J Pain Symptom Manage* 41, 1073–1093.
- Houdas Y & Ring E (1982). *Human body temperature-Its measurement and regulation*. Plenum Press, New York, NY.
- Iannetti GD, Zambreanu L & Tracey I (2006). Similar nociceptive afferents mediate psychophysical and electrophysiological responses to heat stimulation of glabrous and hairy skin in humans. *J Physiol* 577, 235–248.
- Jay O & Havenith G (2004). Finger skin cooling on contact with cold materials: an investigation of male and female responses during short-term exposures with a view on hand and finger size. *Eur J Appl Physiol* 93, 1–8.
- Johansson RS & Vallbo AB (1979a). Detection of tactile stimuli. Thresholds of afferent units related to psychophysical thresholds in the human hand. *J Physiol* 297, 405–422.
- Johansson RS & Vallbo AB (1979b). Tactile sensibility in the human hand: relative and absolute densities of four types of mechanoreceptive units in glabrous skin. *J Physiol* 286, 283–300.
- Johansson RS, Vallbo AB & Westling G (1980). Thresholds of mechanosensitive afferents in the human hand as measured with von Frey hairs. *Brain Res* 184, 343–351.
- Kim J, Lee M, Shim HJ, Ghaffari R, Cho HR, Son D, Jung YH, Soh M, Choi C, Jung S, Chu K, Jeon D, Lee S-T, Kim JH, Choi SH, Hyeon T & Kim D-H (2014). Stretchable silicon nanoribbon electronics for skin prosthesis. *Nat Commun* 5, 5747.
- Konietzny F & Hensel H (1975). Warm fiber activity in human skin nerves. *Pflügers Arch Eur J Physiol* 267, 265–267.
- Li X, Petrini L, Defrin R, Madeleine P & Arendt-Nielsen L (2008). High resolution topographical mapping of warm and cold sensitivities. *Clin Neurophysiol* 119, 2641–2646.
- Lunt H & Tipton M (2014). Differences in conductive foot cooling: a comparison between males and females. *Eur J Appl Physiol* 114, 2635–2644.
- Mancini F, Bauleo A, Cole J, Lui F, Porro C a., Haggard P & Iannetti GD (2014). Whole-body mapping of spatial acuity for pain and touch. *Ann Neurol* 75, 917–924.
- Mancini F, Haggard P, Iannetti GD, Longo MR & Sereno MI (2012). Fine-grained nociceptive maps in primary somatosensory cortex. *J Neurosci* 32, 17155–17162.
- Mancini F, Sambo CF, Ramirez JD, Bennett DLH, Haggard P & Iannetti GD (2013). A fovea for pain at the fingertips. *Curr Biol* 23, 496–500.
- McGlone F, Wessberg J & Olausson H (2014). Discriminative and Affective Touch: Sensing

- and Feeling. *Neuron* 82, 737–755.
- McKemy DD (2007). Temperature sensing across species. *Pflügers Arch* 454, 777–791.
- Milenkovic N, Zhao W-J, Walcher J, Albert T, Siemens J, Lewin GR & Poulet JFA (2014). A somatosensory circuit for cooling perception in mice. *Nat Neurosci* 17, 1560–1566.
- Mountcastle VB (2005). *The Sensory Hand: Neural Mechanisms of Somatic Sensation*. Harvard University Press.
- Nakamura M, Yoda T, Crawshaw L, Yasuhara S, Saito Y, Kasuga M, Nagashima K & Kanosue K (2008). Regional differences in temperature sensation and thermal comfort in humans. *J Appl Physiol* 105, 1897–1906.
- Norrzell U, Finger S & Lajonchere C (1999). Cutaneous sensory spots and the “law of specific nerve energies”: history and development of ideas. *Brain Res Bull* 48, 457–465.
- Ouzzahra Y, Havenith G & Redortier B (2012). Regional distribution of thermal sensitivity to cold at rest and during mild exercise in males. *J Therm Biol* 37, 517–523.
- Penfield W & Boldrey E (1937). Somatic Motor and Sensory Representation in Man. *Brain* 4, 389–443.
- Raspopovic S et al. (2014). Restoring Natural Sensory Feedback in Real-Time Bidirectional Hand Prostheses. *Sci Transl Med* 6, 222ra19-222ra19.
- Rolls ET, Grabenhorst F & Parris B a (2008). Warm pleasant feelings in the brain. *Neuroimage* 41, 1504–1513.
- Romanovsky A (2007). Thermoregulation: some concepts have changed. Functional architecture of the thermoregulatory system. *Am J Physiol Regul Integr Comp Physiol* 292, R37-R46.
- Shao Y, Hayward V & Visell Y (2016). Spatial patterns of cutaneous vibration during whole-hand haptic interactions. *Proc Natl Acad Sci U S A* 113, 201520866.
- Smith M, Warren K, Cohen-Taguchi D, Shames S, Sprehn K, Schwartz J, Zhang H, Arens E. (2017) Augmenting smart buildings and autonomous vehicles with wearable thermal technology. *Proceedings of HCI International*, July, Boston: 550-561.  
<https://escholarship.org/uc/item/9q24x8p3>
- Stevens J (1979). Variation of cold sensitivity over the body surface. *Sens Processes* 3, 317.
- Stevens J & Choo K (1998). Temperature sensitivity of the body surface over the life span. *Somatosens Mot Res* 15,13-28.
- Stevens J, Marks L & Simonson D (1974). Regional sensitivity and spatial summation in the warmth sense. *Physiol Behav* 13, 825–836.
- Taylor NAS, Machado-Moreira CA, van den Heuvel AMJ & Caldwell JN (2014). Hands and

feet: physiological insulators, radiators and evaporators. *Eur J Appl Physiol* 114, 2037–2060.

Vriens J, Nilius B & Voets T (2014). Peripheral thermosensation in mammals. *Nat Rev Neurosci* 15, 573–589.

Witney AG, Wing A, Thonnard J-L & Smith AM (2004). The cutaneous contribution to adaptive precision grip. *Trends Neurosci* 27, 637–643.

Zhang H, Arens E & Zhai Y (2015). A review of the corrective power of personal comfort systems in non-neutral ambient environments. *Build Environ* 91, 15–41.