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Thermosensory mapping of skin wetness sensitivity across the body of young males and females at rest and following maximal incremental running

Alessandro Valenza[1,2], Antonino Bianco[2] and Davide Filingeri[1]

[1] *THERMOSENSELAB, Environmental Ergonomics Research Centre, Loughborough University, Loughborough, UK*
[2] *Sport and Exercise Sciences Research Unit, SPPF Department, University of Palermo, Palermo, Italy*

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Key points

- Humans lack skin receptors for wetness (i.e. hygroreceptors), yet we present a remarkable wetness sensitivity.
- Afferent inputs from skin cold-sensitive thermoreceptors are key for sensing wetness; yet, it is unknown whether males and females differ in their wetness sensitivity across their body and whether high intensity exercise modulates this sensitivity.
- We mapped sensitivity to cold, neutral and warm wetness across five body regions and show that females are more sensitive to skin wetness than males, and that this difference is greater for cold than warm wetness sensitivity.
- We also show that a single bout of maximal exercise reduced the sensitivity to skin wetness (i.e. hygro-hypoesthesia) of both sexes as a result of concurrent decreases in thermal sensitivity.
- These novel findings clarify the physiological mechanisms underpinning this fundamental human sensory experience. In addition, they indicate sex differences in thermoregulatory responses and will inform the design of more effective sport and protective clothing, as well as thermoregulatory models.

Abstract Humans lack skin hygroreceptors and we rely on integrating cold and tactile inputs from A-type skin nerve fibres to sense wetness. Yet, it is unknown whether sex and exercise independently modulate skin wetness sensitivity across the body. We mapped local sensitivity to cold, neutral and warm wetness of the forehead, neck, underarm, lower back and dorsal foot in 10 males (27.8 ± 2.7 years; 1.92 ± 0.1 m^2 body surface area) and 10 females (25.4 ± 3.9 years; 1.68 ± 0.1 m^2 body surface area), at rest and post maximal incremental running. Participants underwent our quantitative sensory test where they reported the magnitude of thermal and wetness perceptions (visual analogue scale) resulting from the application of a cold (5°C below

Alessandro Valenza recently completed an MSc in sciences and techniques of preventive and adapted sports activities at the University of Palermo (Thesis: Monitoring of the Young Soccer Player via GPS: Comparison of Exercises). In 2015, he qualified as 'Professional Athletic Trainer' (Thesis: Aerobic power: the intermittent race as a method of development and evaluation methods) and, in 2018, as a 'Basic Football Technician: UEFA B'. Alessandro joined the THERMOSENSELAB as a visiting researcher in April 2018, and his research now focuses on the impact of maximal exercise on thermoregulation and local thermosensitivity in males and females.

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skin temperature) wet (0.8 mL of water), neutral wet and warm wet (5°C above skin temperature) thermal probe (1.32 cm^2) to five skin sites. We found that: (i) females were ∼14% to ∼17% more sensitive to cold-wetness than males, yet both sexes were as sensitive to neutral- and warm-wetness; (ii) regional differences were present for cold-wetness only, and these followed a craniocaudal increase that was more pronounced in males (i.e. the foot was ∼31% more sensitive than the forehead); and (iii) maximal exercise reduced cold-wetness sensitivity over specific regions in males (i.e. ∼40% decrease in foot sensitivity), and also induced a generalized reduction in warm-wetness sensitivity in both sexes (i.e. ∼4% to ∼6%). For the first time, we show that females are more sensitive to cold wetness than males and that maximal exercise induce hygro-hypoesthesia. These novel findings expand our knowledge on sex differences in thermoregulatory physiology.

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Corresponding author D. Filingeri: THERMOSENSELAB, Environmental Ergonomics Research Centre, Loughborough University, Loughborough LE11 3TU, UK. Email: d.filingeri3@lboro.ac.uk

Introduction

The perception of skin wetness is a fundamental sensory experience for humans (Filingeri & Havenith, 2015) and a key contributor to our thermoregulatory behaviours (Vargas *et al.* 2018). Sensing when and where we get wet on the skin as a result of sweating or contact with a wet surface (e.g. a wet t-shirt) (i.e. hygrosensation) contributes to the awareness of our own thermal state (Filingeri *et al.* 2015*a*) and of that of our surrounding environments (Filingeri, 2015). For example, the experience of exercise- and sweat-induced skin wetness is a well-known trigger of thermal discomfort (Gagge *et al.* 1967) and this provides a drive for thermal behaviours (e.g. active body cooling) (Vargas *et al.* 2019*a*).

As humans, we present a very well developed skin wetness sensitivity (i.e. we can discriminate wetness levels differing by as little as of 0.04 mL) (Ackerley *et al.* 2012), yet our skin is not provided with a specific hygro-receptor (Clark & Edholm, 1985). In the absence of a skin hygroreceptor, humans have developed alternative sensory integration mechanisms to sense skin wetness (Filingeri *et al.* 2014*a*), which appear to be shared by other hygroreceptor-lacking species (e.g. nematodes) (Russell *et al.* 2014; Filingeri, 2015).

In the past 6 years, we have repeatedly shown that humans make inferences about the presence of physical wetness on their skin using thermal and skin cooling-related sensory cues triggered by conductive and evaporative heat transfer in the presence of moisture on the skin (Filingeri *et al.* 2013, 2014*a*, 2014*b*, 2014*e*, 2015*c*), in combination with mechanical and skin deformation-related cues arising from the movement of moisture across the skin (Filingeri *et al.* 2014*a*, 2014*e*, 2015*a*). The role of thermal cues in sensing wetness is so pronounced that an illusion of skin wetness can be induced in blindfolded participants by cooling their skin with a dry–cold stimulus inducing skin cooling at a rate (i.e. 0.14–0.41°C s^{-1}) equivalent to that resulting from actual moisture evaporation (Filingeri *et al.* 2013; Filingeri, 2014). Furthermore, regional differences in cold sensitivity across the torso positively correlate with regional differences in wetness sensitivity (Filingeri *et al.* 2014*b*). Similarly, sweat-induced skin wetness perceptions can be significantly reduced independently of the level of physical skin wetness by limiting the extent of intermittent, sweat-induced mechanical stimulation of the skin arising from wearing wet clothes (Filingeri *et al.* 2015*a*).

Our findings have contributed to the empirical demonstration that afferent inputs from peripheral A-type afferent nerve fibres innervating the skin and subserving cold and touch sensing play a fundamental role in the conscious experience of skin wetness (Filingeri *et al.* 2014*a*; Filingeri & Havenith, 2018). However, although our understanding of the physiology of human skin wetness sensing has undoubtedly expanded (Filingeri & Havenith, 2018), our knowledge on the mechanisms and modulators of skin wetness perception remain somewhat fragmentary.

First, there is a lack of empirical data on whether sex independently modifies wetness sensitivity in humans. Females are generally more thermally sensitive than males (Gerrett *et al.* 2014; Filingeri *et al.* 2018) and present more sensitive thermal behaviours during exercise (Vargas *et al.* 2019*b*), yet male and female skin wetness sensitivity has never been formally compared. Given the critical role that thermal (cold) sensitivity plays in sensing wetness (Filingeri *et al.* 2013), as well as the importance of thermal afferents for the regulation of thermal behaviour (Schlader *et al.* 2011), it would be reasonable to expect that females show greater wetness sensitivity than males.

Second, there is limited evidence regarding the presence of regional differences in wetness sensitivity over body regions (e.g. forehead, neck, underarm, lower back, foot) that experience high-levels of sweat-induced wetness following high intensity exercise (Smith & Havenith, 2011, 2012). Our previous data (Filingeri *et al.* 2014*b*, 2015*a*), as well as that of others (Ackerley *et al.* 2012), indicate that regional differences in wetness sensing exist and that these are highly dependent on regional patterns of cold sensitivity. Given that regional patterns of perceptual sensitivity often correlate with regional thermoeffector sensitivity (e.g. decreases in local skin temperature of the forehead produce more intense cold sensations and greater decreases in local sweating than similar changes over the abdomen) (Crawshaw *et al.* 1975), it might be expected that regions with high local sweat rates, such as the forehead, neck, underarm, lower back and foot, present high wetness sensitivity (Smith & Havenith, 2012).

Third, there is a paucity of data regarding the independent effect of maximal exercise on local skin wetness sensitivity. Acute bouts of submaximal exercise are known to induce transient reductions in thermal sensitivity (i.e. exercise-induced thermo-hypoethesia) (Gerrett *et al.* 2014; Ouzzahra *et al.* 2014) via potential changes in circulating stress hormones (Koltyn, 2000). Furthermore, exercise-induced hypoalgesia is more consistently observed following high-intensity exercise (Koltyn, 2002). Hence, it might be expected that maximal exercise probably reduces wetness sensitivity via large changes in local sensitivity to thermal stimuli.

Increasing our fundamental understanding on the independent and interactive effects of sex, regional differences and maximal exercise, on human skin wetness sensitivity has important implications for better clarifying the drivers of sex differences in human thermoregulatory behaviour at rest and during exercise (Vargas *et al.* 2019*b*), for optimizing the design of sport and protective clothing (Filingeri *et al.* 2014*b*), and for further developing individualized thermoregulatory models (Havenith, 2001).

The present study aimed to determine: (i) whether healthy males and females differ in their ability to sense wetness on their skin; (ii) whether the forehead, neck, underarm, lower back and foot present different levels of wetness sensitivity; and (iii) whether wetness sensitivity decreases following maximal exercise. We hypothesized that females present greater wetness sensitivity than males, that regional differences in sensitivity are present for both sexes, and that maximal exercise similarly reduces wetness sensitivity in both sexes.

Methods

Ethical approval

The testing procedure and the conditions were explained to each participant and they all gave written informed consent for participation. The study was approved by the Loughborough University Ethics Sub-Committee for Human Participants (#R18-P083) and testing procedures were in accordance with the tenets of the *Declaration of Helsinki* (note: the study was not registered in a database). All testing took place at Loughborough (UK) between June and September 2018.

Participants

We performed an *a priori* sample size calculation using an effect size corresponding to a 15 ± 8% (mean ± SD) difference in wetness perception between sexes. This value derived from pilot data and from the experimental assumption that this mean difference [equivalent to 1.5 cm on the visual analogue scale (VAS) scale] would be the minimum required to infer the presence of meaningful differences in wetness perception between sexes. The resulting effect size $f = 0.93$, combined with an $\alpha = 0.05$ and a β (power) = 0.8, determined a minimum sample of eight participants per group. We recruited 10 participants per group.

Twenty non-smoking, recreationally active (i.e. ≥3 exercise sessions per week) participants (i.e. 10 males and 10 females), with no history of cardiovascular, neurological and skin-related conditions (e.g. eczema), who were familiar with treadmill running, were recruited from the student population of Loughborough University to take part in the present study. Participants characteristics are presented in Table 1. Males and female participants were matched for age. Male participants presented a greater body surface area (BSA) than females, which resulted in a smaller proportion of their body being stimulated by thermal probe (surface area: 1.32cm^2) that we used to deliver the wet stimuli (see Experimental design below). Female participants were spread across a typical 28 day menstrual cycle (day of cycle: 16.3 ± 8.1) and only two of them were taking oral contraceptives at the time of the study. Participants were instructed to refrain from: (i) performing strenuous exercise in the 48 h preceding testing; (ii) consuming caffeine or alcohol in the 24 h preceding testing; and (iii) consuming food in the 3 h preceding testing.

Experimental design

We used a single-blind psychophysical approach based on a well-established quantitative sensory test of skin wetness sensing that we have developed (Filingeri *et al.* 2014*a*) to map sex differences in regional wetness sensitivity at rest and following a maximal incremental running test performed in a thermoneutral environment (ambient temperature: 25°C; relative humidity: 45%).

All participants took part in one experimental session, during which we performed the same quantitative sensory test prior to and following a maximal running test. We opted for a maximal exercise protocol to induce the greatest systemic perturbation achievable within a

Table 1. Participant characteristics, including age, mass, height, BSA, proportion of BSA stimulated by the fixed-size (i.e. 1.32 cm^2) thermal probe used, are reported for male and female groups

	Age (years)	Mass (kg)	Height (m)	BSA (m^2)	Proportion of BSA stimulated (%)	Self-reported day of menstrual cycle	Oral contra-ceptive Yes (No)
Males (n = 10)	27.8 ± 2.7	76.4 ± 10.2	1.77 ± 0.1	1.92 ± 0.1	0.0069 ± 0.0005		
Females (n = 10)	25.4 ± 3.9	62.7 ± 8.0	1.65 ± 0.1	1.68 ± 0.1	0.0079 ± 0.0006	16.3 ± 8.1	2 (8)
Probability	0.130	0.004	<0.001	0.001	0.001		

Menstrual cycle and oral contraceptive information are also reported for the female group only. Statistical differences between groups for each characteristic were assessed by means of independent group t tests, with the cut-off probability value for significance set at $P = 0.05$.

single bout of acute exercise [e.g. large changes in heart rate (HR), core temperature (T_{core}), mean and local skin temperatures (T_{sk})]. Furthermore, evidence indicates that exercise-induced hypoalgesia is consistently observed following high-intensity exercise (Koltyn, 2002). Previous investigations on exercise-induce thermo-hypoesthesia have utilized submaximal exercise intensities (Ouzzahra *et al.* 2012; Gerrett *et al.* 2015) and so no study has determined the impact of maximal exercise on local non-noxious thermo- and wetness sensitivity.

The quantitative sensory test that we used was based on our established protocol (Filingeri *et al.* 2014*a*) and consisted of participants having to report the perceived magnitude of local thermal and wetness perceptions arising from the short-duration (i.e. 5 s) static application of a cold-wet (i.e. 5°C below local T_{sk}), neutral-wet (i.e. equal temperature as local T_{sk}) and warm-wet (i.e. 5°C above local T_{sk}) hand-held temperature-controllable probe (surface area: 1.32cm^2, water content: 0.8 mL). Participants reported the magnitude of their local perceptions on two digital VAS for thermal sensation (length 200 mm; anchor points: 0, very cold; 100, neutral; 200, very hot) and wetness perception (length: 100 mm; anchor points: 0, dry; 100, completely wet). We used stimuli whose temperatures were relative to the local T_{sk} pre-stimulation (i.e. ± 5°C or equal to local T_{sk}) to account for the expected exercise-induced changes in local T_{sk}. In this way, we ensured that the same relative thermal stimulus would be applied pre and post exercise because the difference between the temperature of a stimulus and that of the skin is an important determinant of the magnitude of a resulting thermal sensation (i.e. the greater the difference, the more intense the sensation) (Darian-Smith, 1984).

We mapped thermal and wetness sensitivity at five different locations over the body: the centre of the forehead (i.e. 5 cm above the pupillary line), the posterior neck (i.e. over the process spinous of cervical 4), the centre of the underarm (i.e. over the midaxillary line, 10 cm above the nipple line), the lower lateral back (i.e. over the posterior superior iliac crest) and the dorsal foot (i.e. midpoint between the second and third metatarsal joints). We chose those body regions because: (i) they present high exercise-induced local sweat rates (e.g. forehead and lower back) (Smith & Havenith, 2012); (ii) they are generally reported to trigger wet-induced thermal discomfort (e.g. underarm and lower back) (Fukazawa & Havenith, 2009); and (iii) there is limited evidence of their intrinsic wetness sensitivity in males and females.

In accordance with previous studies (Filingeri *et al.* 2014*a*, 2014*b*, 2018), all participants were blinded to the nature and application of the stimuli to limit expectation biases, and they were only informed about the location of the stimulation. Furthermore, participants underwent a systematic familiarization and calibration to the testing procedures and perceptual scales prior to testing (Filingeri *et al.* 2014*a*, 2018). The same investigator performed all testing, to limit any inter-individual variability arising from the procedures carried out.

Experimental protocol

Participants arrived at the laboratory on testing days and underwent preliminary measurements and preparation. They changed into running shorts (and sport-bra) before we assessed their semi-nude body mass on a precision scale (Model 874; Seca GmbH, Hamburg, Germany) and their height on a wall stadiometer. Six skin thermistors (Grant, Cambridge, UK) were taped to six location on the left side of the body (i.e. cheek, upper chest, outer mid lower arm, hand dorsum, anterior thigh and lower lateral back) to record local T_{sk} for the estimation of mean T_{sk} according to the equation (Lund & Gisolfi, 1974):

$$\begin{aligned}\text{mean } T_{sk} = {} & (\textit{cheek } T_{sk} \times 0.14) + \left(\textit{upper chest } T_{sk} \times 0.19\right) \\ & + (\textit{outer mid lower arm } T_{sk} \times 0.11) \\ & + (\textit{hand dorsum } T_{sk} \times 0.05) \\ & + \left(\textit{anterior tigh } T_{sk} \times 0.32\right) \\ & + (\textit{lower lateral back } T_{sk} \times 0.19)\end{aligned}$$

Local T_{sk} was recorded at 2 Hz via a dedicated data acquisition system (USB-Temp; MCCdaq, Norton, MA, USA) and custom-written software (DASYLab; MCCdaq). Participants then wore a HR monitor and chest strap (Ambit 3 sport; Suunto, Vantaa, Finland). We used a washable marker to mark the skin sites to be stimulated, and we gently shaved each site to limit any insulative effect of hairiness on heat transfer during the application of the stimuli.

Following on this preparation, participants underwent 20 min of resting on a chair to adjust to the environmental conditions. During this time, participants were familiarized with the experimental procedures, and calibrated to the VAS. Calibration procedures consisted of the following. Six stimuli varying in temperature and wetness (i.e. 0.8 mL of water, or dry) were applied to the volar surface of both forearms (i.e. midpoint between wrist and antecubital fossa) in a randomized order, and participants were instructed to associate each stimulus to a specific descriptor on the thermal scale. The stimuli and related descriptors were: (i) wet stimulus, 10°C above local skin temperature – scale descriptor: Very hot; (ii) wet stimulus, 5°C above local skin temperature – scale descriptor: midpoint between Neutral and Very hot; (iii) wet stimulus, equal temperature as local skin temperature – scale descriptor: Neutral; (iv) dry stimulus, equal temperature as local skin temperature – scale descriptor: Neutral; (v) wet stimulus, 5°C below local skin temperature – scale descriptor: midpoint between Neutral and Very cold; and (vi) wet stimulus, 10°C below local skin temperature – scale descriptor: Very cold. During each of the six stimuli applications, participants were instructed to freely determine the level of wetness experienced on the wetness VAS. This procedure ensured that all participants had comparable experiences of the different stimuli and related perceptual anchor points to be used during testing. The forearm was chosen as a 'neutral' calibration site to avoid any priming, given that this region was not going to be tested during the mapping protocol.

Upon termination of calibration, recordings of local T_{sk} and HR were started and continued throughout the testing session. Furthermore, spot measurements of tympanic temperature (ThermoScan IRT 6520; Braun, Kronberg, Germany) were taken at this stage and every 3 min thereafter and until completion of the testing session and used as an indicator of T_{core}.

At this point, the pre-exercise quantitative sensory test commenced, which lasted 20 min. Depending on the body region to be tested, we first recorded the local T_{sk} of the testing site with an infrared thermometer (Spot IR Thermometer TG54; FLIR Systems, Wilsonville, OR, USA). We then determined the temperature of the first wet stimulus (e.g. cold wet, 5°C below local skin temperature) and applied a 100% cotton fabric on the hand-held, round thermal probe (surface area: 1.32 cm^2; NTE-2A; Physitemp Instruments LLC, Clifton, NJ, USA), that was then wetted with a pipettor with 0.8 mL of water to ensure its full saturation. Following a verbal warning, the wet stimulus was applied statically on the participant' skin for 5 s, during which the participant was encouraged to rate their very first thermal and wetness perception. Application pressure was not measured but was controlled to be sufficient to ensure full contact, at the same time not resulting in pronounced skin indention. Upon acquisition of the perceptual rating, we removed the stimulus, gently dried the skin, and then repeated the same procedure for the other stimuli (e.g. neutral and warm wet) on the same skin site, before proceeding to the next skin region. The order of testing region was counter-balanced between participants and the order of stimuli (e.g. warm *vs.* neutral *vs.* cold wet) was counter-balanced between and within participants. Immediately after completion of the quantitative sensory test for all five regions, participants moved to a motorized treadmill (Jet 200; Reebok, Boston, MA, USA) to start the maximal incremental running testing.

The incremental test comprised seven steps, consisting of a combination of increases in speed and inclination at 3 min intervals (i.e. step 1: 6.5 km h^{-1}, 0%; step 2: 8.5 km h^{-1}, 0%; step 3: 8.5 km h^{-1}, 5%; step 4: 8.5 km h^{-1}, 10%; step 5: 8.5 km h^{-1}, 15%; step 6: 10.5 km h^{-1}, 15%; step 7: 12 km h^{-1}, 15%). This was carried out until participants reached their age-predicted maximum HR (i.e. calculated as 220 – age), or until they verbally signalled the obtainment of volitional fatigue.

Upon termination of the running test, participants returned to their seated position where any sweating was dried off with a towel, and the same quantitative sensory test, as described above, was immediately performed (note: we continued to dry off any sweat before any stimulus application as the test continued).

Statistical analysis

We analysed HR, mean T_{sk}, and T_{core} for the independent and interactive effect of sex (two levels: male *vs.* female) and exercise (two levels: pre- *vs.* post maximal tests) by means of two-way mixed ANOVAs. We assessed the independent and interactive effect of sex (two levels: male *vs.* female), body region (five levels) and exercise (two levels: pre- *vs.* post maximal tests) on baseline local T_{sk} (i.e. prior to application of wet stimuli) by means of a three-way mixed ANOVA.

We evaluated the independent and interactive effect of sex (two levels: male *vs.* female), body region (five levels) and exercise (two levels: pre- *vs.* post maximal tests), separately for thermal and wetness perceptions and for each stimulus (i.e. cold-wet, neutral-wet and warm-wet), by means of three-way mixed ANOVAs.

Also, we evaluated the independent effect of the temperature of the stimuli (three levels: cold-wet, neutral-wet and warm-wet) on wetness perceptions collapsed over body region (i.e. cumulative mean perception of the five regions tested for each participant), separately for males and females and for rest and post exercise, by means of a one-way repeated measure ANOVA. In the event of statistically significant main effects or interactions, *post hoc* analyses were conducted with Tukey's tests.

Finally, we assessed the relationship between cold-wet-, neutral-wet- and warm-wet induced wetness perceptions and thermal sensations, separately for males and females, as well as for rest and post exercise, by means of regression analyses. First, we assessed the relationship between thermal and wetness sensations for each individual participant, and separately for males *vs.* females, and for rest *vs.* post exercise. Individual data sets were plotted, visually inspected and then analysed. We first compared which one between a linear model (simpler) and a quadratic polynomial (more complex) would best fit the data by means of an extra-sum-of-squares F test. Depending on the test results, a linear or quadratic model would be fitted, and we calculated related r^2 values. Individual r^2 values arising from best fitting model (i.e. linear *vs.* quadratic) were analysed by means of a two-way mixed ANOVA for the independent effects of sex and maximal exercise. Following on the individual analyses, we went on developing group models that could provide a generalizable relationship between thermal and wetness perceptions, which accounted for the inter-individual variability observed in the individual models. Mean and SD data, along with sample size (n = 10), for thermal and wetness perceptions in males and females at rest and post exercise entered four separate regression models. Accounting for mean and SD, along with sample size, ensured that our group models provided a better representation of the relationship between thermal and wetness perception for our entire sample.

Normality testing using Shapiro–Wilk test was performed for all datasets. Data are reported as the means, SD and 95% confidence intervals (CI). Observed power was computed using α = 0.05. Statistical analysis was performed using Prism, version 8.0 (GraphPad Software Inc., La Jolla, CA, USA).

Results

Physiological responses at rest and post maximal exercise

The maximal incremental running test lasted 16.7 ± 1.4 min for males and 14.2 ± 1.7 min for females (p = 0.002). Exercise elevated HR (main effect of exercise: $F_{1,18}$ = 1706; P < 0.001) similarly (main effect of sex: $F_{1,18}$ = 0.925; p = 0.348) in males (pre-exercise = 58 ± 9 beats min^{-1}; post-exercise = 197 ± 11 beats min^{-1}) and females (pre-exercise = 63 ± 8 beats min^{-1}; post-exercise = 195 ± 7 beats min^{-1}) (Table 2). When expressed as a percentage of the age-predicted maximal HR, the post-exercise HR corresponded to 102 ± 6% in males and to 100 ± 4% in females.

Table 2. Physiological responses to the maximal exercise test

	Males (n = 10)	Females (n = 10)
Δ HR (beats min^{-1})	+113.6 (+104.7, +122.5)*	+100.6 (+91.6, +109.5)*
Δ Tympanic T_{core} (°C)	+0.81 (+0.54, +1.07)*	+0.56 (+0.29, +0.82)*
Δ Mean T_{sk} (°C)	−0.81 (−1.22, −0.39)*	−0.93 (−1.34, −0.51)*

Data are reported as means with 95% confidence intervals.
*Statistical difference between rest and exercise with the cut-off probability value for significance set at p = 0.05.

Participants tympanic T_{core} was significantly elevated following the maximal test (main effect of exercise: $F_{1,18}$ = 79.9; P < 0.001) and similarly (main effect of sex: $F_{1,18}$ = 0.043; p = 0.837) in males (pre-exercise = 36.9 ± 0.3°C; post-exercise = 37.7 ± 0.3°C) and females (pre-exercise = 37.1 ± 0.3°C; post-exercise = 37.6 ± 0.3 beats min^{-1}) (Table 2). By contrast, the maximal test reduced mean T_{sk} (main effect of exercise: $F_{1,18}$ = 52.3; P < 0.001), which tended to be lower in females than in males (main effect of sex: $F_{1,18}$ = 7.06; p = 0.016), prior to (males: 32.95 ± 0.76°C; females: 32.22 ± 0.53°C) and following exercise (males: 32.13 ± 0.90°C; females: 31.31 ± 0.63°C) (Table 2).

Baseline local T_{sk} (i.e. prior to the wet stimuli application) varied significantly across body regions (main effect of body region: $F_{4,72}$ = 67.1; P < 0.001) and similarly for males and females (main effect of sex: $F_{1,18}$ = 3.51; p = 0.077). Specifically, we observed a clear craniocaudal pattern of decrease in local skin temperature from the forehead to the foot in both sexes (Fig. 1*A*). Exercise resulted in a decrease in local T_{sk} in all skin regions except the dorsal foot (interaction body region with exercise: $F_{4,72}$ = 62.5; P < 0.001), which, in contrast, showed a significant increase in local T_{sk} in both males (mean change in foot T_{sk}: +3.49°C; 95% CI = 2.65–4.32; P < 0.001) and females (mean change in foot T_{sk}: +3.47°C; 95% CI = 2.63–4.30; P < 0.001) (Fig. 1*B*).

Pre and post exercise thermal and wetness perception: cold wet stimulus

Thermal sensations resulting from the application of the cold wet stimulus varied significantly as a function of sex (main effect: $F_{1,18}$ = 12.1; p = 0.009) and of body region (main effect: $F_{2.9,52.9}$ = 4.3; p = 0.003) (Fig. 2*A*

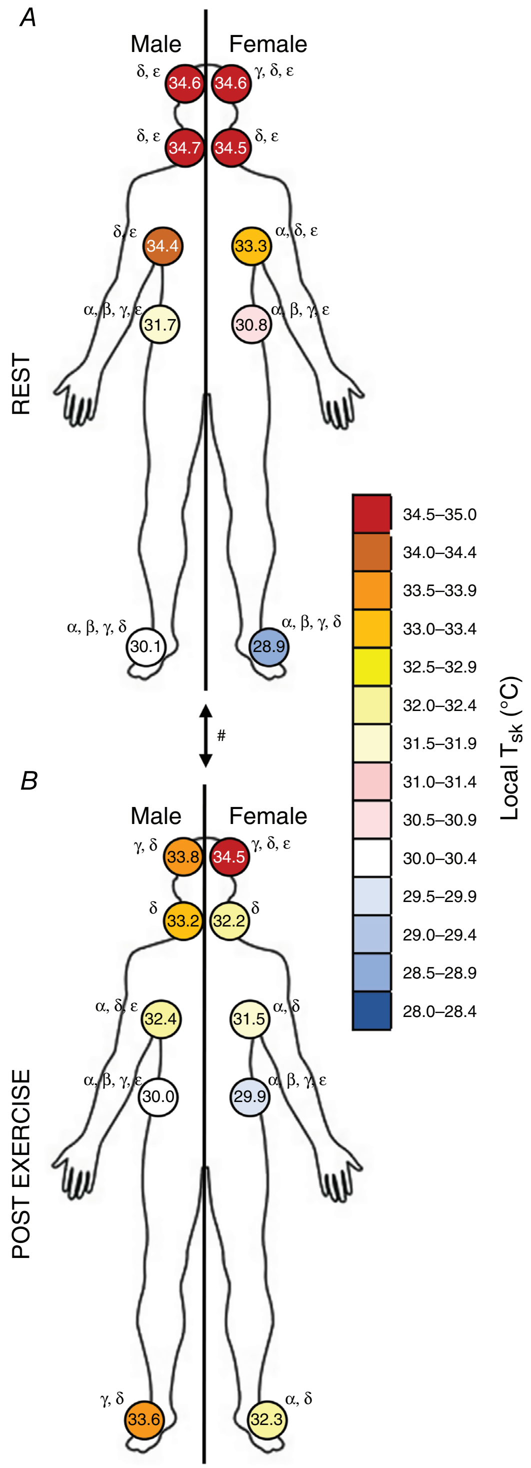

Figure 1. Local skin temperature body maps
Body maps of pre-stimulation local T_{sk} in males ($n = 10$) and females ($n = 10$) at rest (*A*) and following maximal incremental running (*B*). Numerical data represent group means. Symbols denote statistical differences at $P < 0.05$, where α = different from forehead; β = different from neck; γ = different from underarm; δ = different from lower lateral back; ε = different from dorsal foot; # = interaction body region with exercise. [Colour figure can be viewed at wileyonlinelibrary.com]

and *D*). Irrespective of body region, females generally perceived the same cold wet stimulus as colder compared to males (compare males and females in Fig. 2*A* and *D*), both at rest (female mean thermal sensation collapsed over body region: 38.2 ± 18.1 mm; male mean thermal sensation collapsed over body region: 53.5 ± 15.2 mm) and following exercise (female mean thermal sensation collapsed over body region: 33.6 ± 10.6 mm; male mean thermal sensation collapsed over body region: 61.4 ± 10.8 mm). When expressed as percentage of the thermal VAS scale used, those sex differences corresponded to females being ∼8% and 14% more cold sensitive than males at rest and post exercise, respectively.

Irrespective of sex, we observed a craniocaudal increase in the magnitude of cold sensations resulting from the application of the same cold wet stimulus at rest (Fig. 2*A*), with the forehead presenting some of the less intense cold sensations, whereas the foot presented some of the most intense, in both males (mean difference forehead *vs.* foot: 26.5 mm; 95% CI = 8.0–45.0; $p = 0.010$; corresponding to a ∼13% difference) and females (mean difference forehead *vs.* foot: 39.5 mm; 95% CI = 17.6–61.4; $p = 0.003$; corresponding to a ∼20% difference). The only exception to this trend concerned the underarm, which presented responses similar to those of the forehead, in both males (underarm at rest: 73.3 ± 27.7 mm; forehead at rest: 57.5 ± 18.3 mm) and females (underarm at rest: 56.7 ± 30.2 mm; forehead at rest: 52.6 ± 8.6 mm) (Fig. 2*A*).

Exercise modulated thermal sensations to the cold wet stimulus, although this only occurred for some specific regions (interaction body region with exercise: $F_{3,62} = 5.4$; $p = 0.001$) (Fig. 2*D*). The most pronounced of such exercise-induced changes occurred for the dorsal foot in males, where a large reduction in cold sensation arising from stimulation of this region took place following exercise (mean difference: 47.5 mm; 95% CI = 15.8–79.1; $p = 0.008$) (Fig. 2*A* and *D*). When expressed as percentage of the thermal VAS scale used, this region-specific difference corresponded to the foot being ∼24% less cold sensitive post exercise.

Wetness perceptions resulting from the application of the cold wet stimulus varied significantly as a function of sex (main effect: $F_{1,18} = 5.6$; $p = 0.029$), with females generally reporting greater wetness sensations than males (Fig. 3*A* and *D*), both at rest (female mean wetness perception collapsed over body region: 69.0 ± 7.6 mm; male mean thermal sensation collapsed over body region: 51.7 ± 18.6 mm) and following exercise (female mean wetness perception collapsed over body region: 64.4 ± 8.3 mm; male mean thermal sensation collapsed over body region: 50.6 ± 13.1 mm). When expressed as percentage of the wetness VAS scale, these sex differences corresponded to females being ∼17% and 14% more wetness sensitive than males at rest and post exercise, respectively.

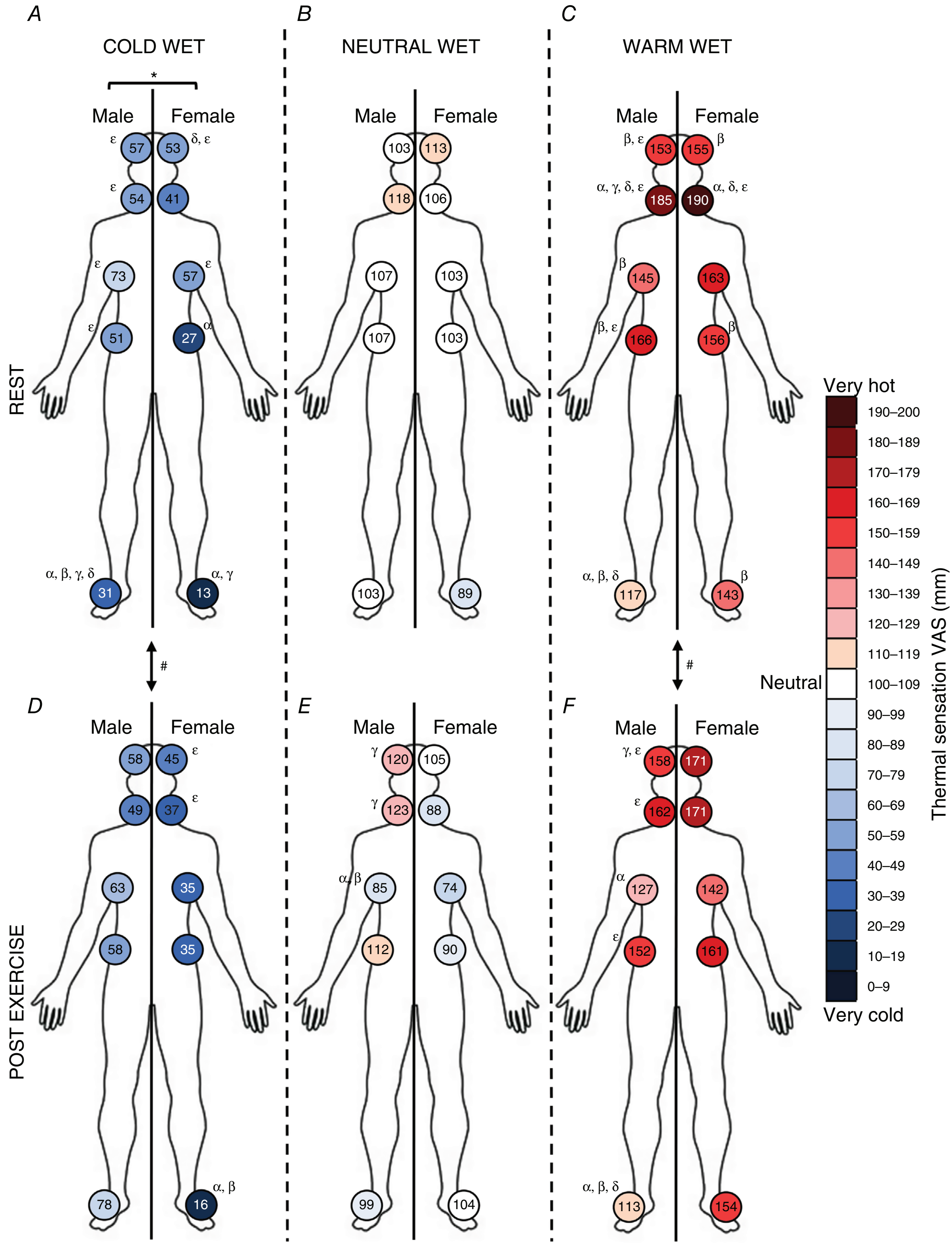

Figure 2. Thermosensory body maps
Body maps of thermal sensations in males ($n = 10$) and females ($n = 10$) resulting from the application of the cold wet (*A* and *D*), neutral wet (*B* and *E*) and warm wet stimulus (*C* and *F*), at rest and following maximal incremental running. Numerical data represent group means. Symbols denote statistical differences at $P < 0.05$, where α = different from forehead; β = different from neck; γ = different from underarm; δ = different from lower lateral back; ε = different from dorsal foot; * = main effect of sex; # = interaction body region with exercise. [Colour figure can be viewed at wileyonlinelibrary.com]

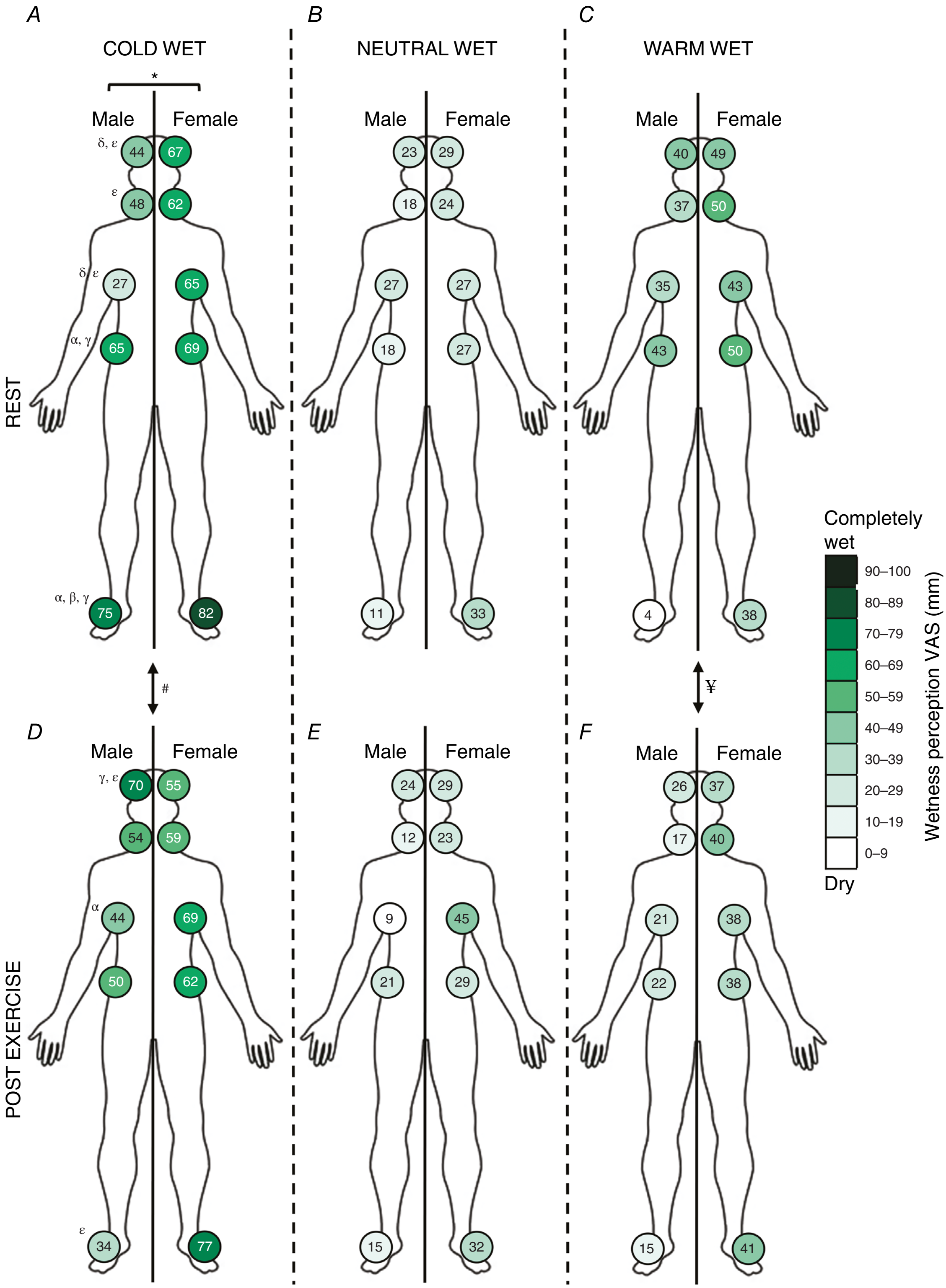

Figure 3. Hygrosensory body maps

Body maps of wetness perceptions in males (n = 10) and females (n = 10) resulting from the application of the cold wet (*A* and *D*), neutral wet (*B* and *E*) and warm wet stimulus (*C* and *F*), at rest and following maximal incremental running. Numerical data represent group means. Symbols denote statistical differences at $P < 0.05$, where α = different from forehead; β = different from neck; γ = different from underarm; δ = different from lower lateral back; ε = different from dorsal foot; * = main effect of sex; # = interaction body region with exercise; ¥ = main effect of exercise. [Colour figure can be viewed at wileyonlinelibrary.com]

We observed a significant interaction for sex, body region and exercise (interaction: $F_{4,72} = 4.6$; $p = 0.002$), indicating that certain regional differences in wetness perception were present in one sex, and that these regional patterns changed as a result of exercise. For example, similar to that observed for thermal sensations, males showed a clear craniocaudal increase in wetness perception at rest, with the forehead presenting lower sensitivity than the foot (mean difference: 30.6 mm; 95% CI = 8.6–52.6; $p = 0.012$; corresponding to a ~31% difference), with the only exception to this trend being the underarm, which presented the lowest wetness sensitivity (Fig. 3*A*). By contrast to what seen for thermal sensation, the craniocaudal trend was not as pronounced in females (mean difference forehead *vs.* foot: 15.2 mm; 95% CI = –2.8 to 33.2; $p = 0.089$) (Fig. 3*A*). Of note, exercise induced a clear inversion in the craniocaudal trend observed in males at rest, with the male forehead showing an increase in wetness sensitivity to the extent that this became the most sensitive region (mean difference pre- *vs.* post-exercise: 25.9 mm; 95% CI = 9.2–42.6; $p = 0.007$; corresponding to a ~26% difference), and with the male foot showing a decrease in wetness sensitivity to the extent that this became the least sensitive region (mean difference pre- *vs.* post-exercise: 40.2 mm; 95% CI = 18.1–62.3; $p = 0.003$; corresponding to a ~40% difference), following the maximal incremental running test (Fig. 3*A* and *D*). We did not observe any clear change in wetness sensitivity over any region in females following exercise (Fig. 3*D*).

In sum, these findings indicated that females were generally more sensitive to coldness (i.e. ~8% rest; ~14% post exercise) and cold wetness (i.e. ~17% rest; ~14% post exercise) than males; that a craniocaudal increase (i.e. 31%) in cold wetness sensitivity was present in males only (despite both sexes showed a craniocaudal increase in cold sensitivity, i.e. ~13% males; ~20% females); and that exercise contributed to reductions in local cold sensitivity (i.e. ~24%) and in cold wetness sensitivity (i.e. ~40%) over the male dorsal foot only.

Pre and post exercise thermal and wetness perception: neutral wet stimulus

Thermal sensations resulting from the application of the neutral wet stimulus did not vary either as a function of sex (main effect: $F_{1,18} = 4.3$; $p = 0.052$) or as a function of body region (main effect: $F_{3.6,65.3} = 2$; $p = 0.109$) (Fig. 2*B* and *E*). Although there was a trend for women to present slightly lower thermal sensations than males, average thermal sensations (collapsed over body region) in both sexes generally aligned to the 'Neutral' descriptor located at the 100th mm of the 200 mm VAS, both at rest (female: 102.5 ± 8.7 mm; male: 107.6 ± 6.3 mm) and following exercise (female: 92.0 ± 12.3 mm; male: 107.8 ± 15.9 mm). This confirmed that the neutral wet stimulus triggered minimal thermosensory cues, and that the stimulus was generally perceived as neither warm, nor cold (Fig. 2*B* and *E*). Of note, following exercise, there was a greater heterogeneity in the thermal sensations reported across body regions (interaction body region with exercise: $F_{3.3,59.1} = 2.9$; $p = 0.036$) (Fig. 2*B* and *E*). For example, the male underarm presented a lower thermal sensation (i.e. more on the cold side of the scale, mean: 84.9 ± 28.0 mm) than the forehead (i.e. more on the warm side, mean: 119.9 ± 28.8 mm) as a result of the neutral wet stimulus following exercise (Fig. 2*E*).

Wetness perceptions resulting from the application of the neutral wet stimulus did not vary either as a function of sex (main effect: $F_{1,18} = 8.9$; $p = 0.105$) or body region (main effect: $F_{3.4,60.8} = 4.3$; $p = 0.615$), nor exercise (main effect: $F_{1,18} < 0.001$; $p = 0.983$) (Fig. 3*B* and *E*). Average wetness perceptions (collapsed over body region) corresponded to 19.6 ± 6.2 mm and 28.14 ± 3.6 mm in males and females at rest, respectively; and to 16.1 ± 6.1 mm and 31.6 ± 8.1 mm in males and females following exercise, respectively.

In sum, these findings indicated that the neutral wet stimulus did not trigger either cold or warm sensations, and that this induced minimal wetness sensations (e.g. compared to the cold wet stimulus) in males and females that did not differ either as a function of the region stimulated or following exercise.

Pre and post exercise thermal and wetness perception: warm wet stimulus

Thermal sensations resulting from the application of the warm wet stimulus varied significantly as a function of body region (main effect: $F_{3.3,59.7} = 10.2$; $P < 0.001$) but not of sex (main effect: $F_{1,18} = 3.5$; $p = 0.079$) (Fig. 2*C* and *F*). Irrespective of sex, we observed a craniocaudal decrease in the magnitude of warm sensations experienced as a result of the same warm wet stimulus at rest (Fig. 2*C*), with the neck presenting the most intense warm sensations, whereas the foot presented the least intense, in both males (mean difference neck *vs.* foot: 68.3 mm; 95% CI = 46.6–90.3; $P < 0.001$; corresponding to a ~34% difference) and females (mean difference forehead *vs.* foot: 46.6 mm; 95% CI = 35.9–57.3; $P < 0.001$; corresponding to a ~23% difference). Exercise induced decreases in warm sensations to the same warm wet stimulus (main effect: $F_{1,18} = 5.4$; $p = 0.032$), with this effect being more pronounced for certain regions (interaction body region and exercise: $F_{2.4,43.5} = 3.5$; $p = 0.030$), such as the male neck (mean difference pre- *vs.* post-exercise: 23.1 mm; 95% CI = 9.2–37.0; $p = 0.004$; corresponding to a ~11% difference) (Fig. 2*C* and *F*).

Wetness perceptions resulting from the application of the warm wet stimulus did not vary either as a function of sex (main effect: $F_{1,18} = 2.6$; $p = 0.123$) or body region (main effect: $F_{2.7,48.8} = 2.2$; $p = 0.107$) (Fig. 3*C* and *F*). Irrespective of sex and body region, exercise induced a general reduction in wetness sensations arising from the warm wet stimulus (main effect: $F_{1,18} = 7.3$; $p = 0.015$) in both males (pre-exercise mean wetness perception collapsed over body region: 31.9 ± 15.8 mm; post exercise: 20.3 ± 4.6 mm) and females (pre-exercise mean wetness perception collapsed over body region: 46.0 ± 5.4 mm; post exercise: 38.7 ± 1.6 mm) (Fig. 3*C* and *F*). When expressed as percentage of the wetness VAS scale used, those exercise-induced differences corresponded to males and females being ∼6% and 4% less warm sensitive than males at rest and post exercise, respectively.

In sum, the findings indicated that the warm wet stimulus induced similar warm sensations in both males and females, with both sexes showing a similar pattern of craniocaudal decrease in warm sensitivity (i.e. ∼34% males; ∼23% females); they also indicated that the warm wet stimulus induced wetness sensations that did not differ between sexes or across different body regions, and that these wet sensations generally decreased in intensity following exercise (i.e. ∼6% males; ∼4% females).

Comparison of cold-wetness, neutral-wetness and warm-wetness perceptions

When comparing the overall level of wetness (i.e. collapsed over body region) experienced as a result of the cold-wet, neutral-wet and warm-wet stimulus, we observed that the cold-wet stimulus induced consistently greater wetness perceptions than the neutral- and warm-wet stimuli (Fig. 4), despite all stimuli presenting the same level of wetness (i.e. 0.8 mL of water). At rest, males perceived the cold-wet stimulus as wetter ($F_{1.5,13.3} = 19.7$; $P < 0.001$) than both neutral-wet (mean difference: 32.1 mm; 95% CI = 20.9–43.3; $P < 0.001$; corresponding to a ∼32% difference) and warm-wet (mean difference: 19.8 mm; 95% CI = 1.8–37.9; $p = 0.033$; corresponding to a ∼20% difference), with no differences between neutral- and warm-wet (mean difference: –12.3 mm; 95% CI = –25.3 to 0.7; $p = 0.064$) (Fig. 4*A*). Similarly, at rest, females perceived the cold-wet stimulus as wetter ($F_{1.6,14.8} = 39.8$; $P < 0.001$) than both neutral-wet (mean difference: 40.8 mm; 95% CI = 29.7–51.9; $P < 0.001$; corresponding to a ∼41% difference) and warm-wet (mean difference: 23.0 mm; 95% CI = 7.5–38.5; $p = 0.006$; corresponding to a ∼23% difference); they also perceived the warm-wet as wetter than the neutral-wet (mean difference: 17.9 mm; 95% CI = 6.6–29.2; $p = 0.004$; corresponding to a ∼18% difference) (Fig. 4*B*).

Post exercise, males perceived the cold-wet stimulus as wetter ($F_{1.4,12.7} = 31.5$; $P < 0.001$) than both neutral-wet (mean difference: 34.5 mm; 95% CI = 25.1–43.8; $P < 0.001$; corresponding to a ∼34% difference) and warm-wet (mean difference: 30.3 mm; 95% CI = 13.6–47.1; $p = 0.002$; corresponding to a ∼30% difference), with no differences between neutral- and warm-wet (mean difference: –4.2 mm; 95% CI = –16.7 to 8.4; $p = 0.636$) (Fig. 4*C*). Similarly, post exercise, females perceived the cold-wet stimulus as wetter ($F_{1.6,14.8} = 19.9$; $P < 0.001$) than both neutral-wet (mean difference: 32.8 mm; 95% CI = 20.6–45.0; $P < 0.001$; corresponding to a ∼33% difference) and warm-wet (mean difference: 25.7 mm; 95% CI = 7.4–43.9; $p = 0.009$; corresponding to a ∼26% difference), with no differences between neutral- and warm-wet (mean difference: –7.1 mm; 95% CI = –21.8 to 7.6; $p = 0.403$) (Fig. 4*D*).

Relationship between wetness perception and thermal sensations

In males at rest, a quadratic model best fitted the data in seven out 10 individual datasets (*F* test $P < 0.05$). In males post exercise and females at rest, a quadratic model best fitted the data (*F* test $P < 0.05$) in five out 10 individual datasets. In females post exercise, a quadratic model best fitted) the data (*F* test $P < 0.05$) in four out 10 individual datasets. Individual r^2 values arising from best fitting individual model (i.e. linear *vs.* quadratic) are reported in Table 3. Analysis of individual r^2 values indicated that: (i) changes in the magnitude of thermal sensations explained an average 44% (±29%) and 42% (±40%) of changes in wetness perception in males at rest and post exercise, respectively, and (ii) changes in the magnitude of thermal sensation explained an average 33% (±32%) and 29% (±30%) of changes in wetness perception in females at rest and post exercise, respectively. Neither sex ($F_{1,18} = 0.95$; $p = 0.342$), nor exercise ($F_{1,18} = 0.09$; $p = 0.769$) had an independent effect on the variance in wetness perception explained by thermal sensations.

Following on the individual analyses, we went on developing group models that could provide a generalizable relationship between thermal and wetness perceptions that accounted for the inter-individual variability observed in the individual models. Visual inspection and comparison between r^2 values resulting from linear *vs.* quadratic polynomial group model fitting indicated that second order (quadratic) polynomial regression models best fitted group data for the relationship between wetness perceptions and thermal sensations. This observation applied to both male and female data for both the rest and post exercise components of the test. Models parameters with 95% CIs and related r^2 values are summarized in Fig. 5. Based on the fitted group models, thermal and wetness perceptions presented a U-shaped relationship across the thermal sensation continuum (i.e. from very cold to very hot), with thermal sensations explaining 41% and 36% of the variability in wetness perceptions at rest in males (Fig. 5*A*) and females (Fig. 5*B*), respectively. Post exercise group models indicated a reduction in variance explained by thermal sensations in both males (i.e. 17%) (Fig. 5*C*) and females (i.e. 20%) (Fig. 5*D*) and they also showed a 'downward' shift and a 'shrinkage' over the horizontal axis in both sexes (Fig. 5*C* and *D*), probably as a result of the exercise-induced reductions in thermal and wetness sensitivity as described above.

Discussion

The present study aimed to determine the independent and interactive effect of sex, body region and maximal

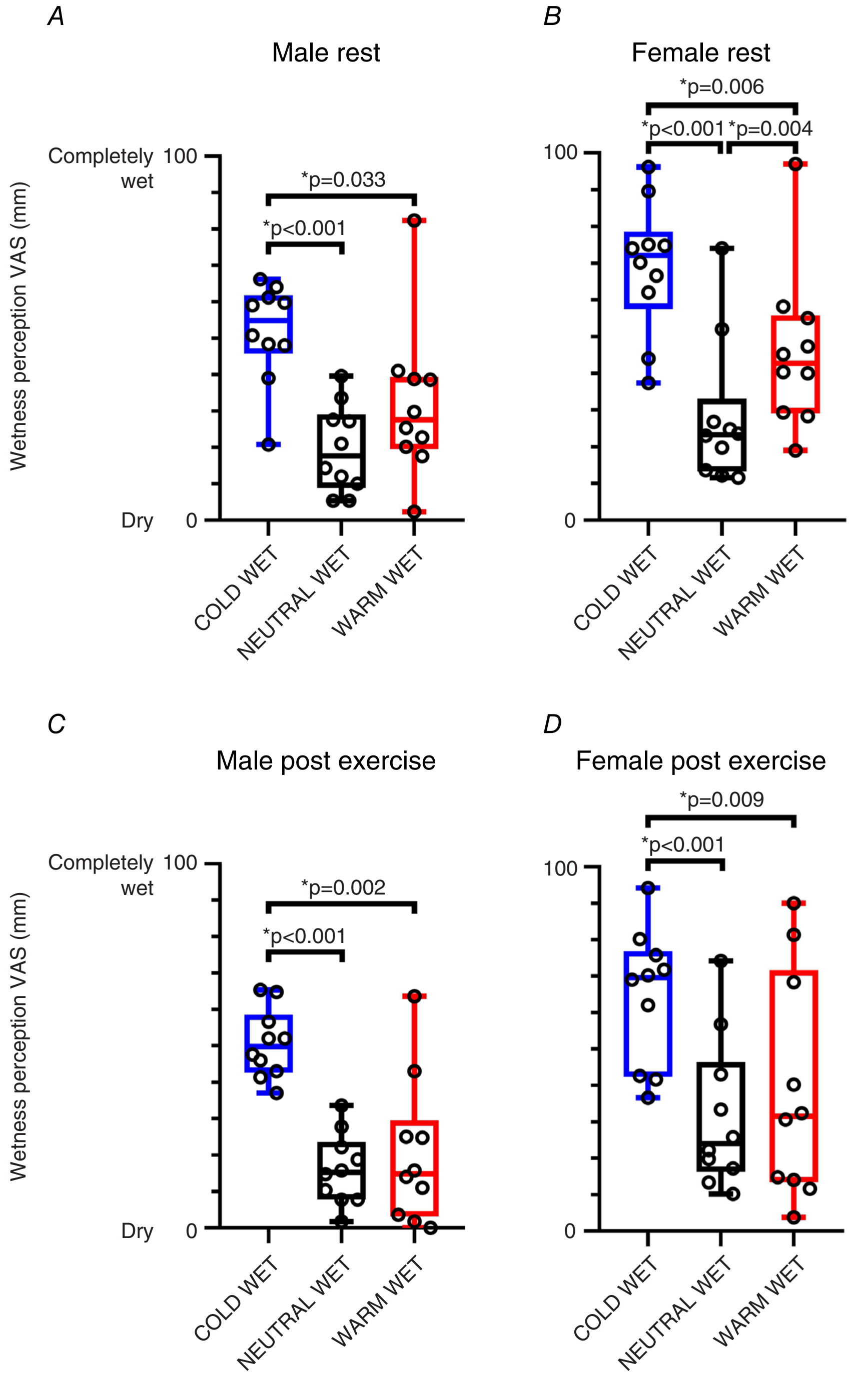

Figure 4. Hygrosensing as a function of stimulus temperature
Box and whisker plots and individual data ($n = 10$ per group) for wetness perceptions arising from the application of the cold wet, neutral wet and warm wet stimulus, at rest and following maximal incremental running in males (*A* and *C*) and females (*B* and *D*). Wetness perception data are collapsed over body region for each data point (i.e. participant). *Statistical significance at $P < 0.05$. [Colour figure can be viewed at wileyonlinelibrary.com]

Table 3. Summary data for individual model fitting for the relationship between thermal sensations and wetness perceptions for each participant, at rest and post exercise

Participant	Model (polynomial = 1; linear = 0)	r^2	Probability (polynomial best fitting *vs*. linear)	Participant	Model (polynomial = 1; linear = 0)	r^2	Probability (polynomial best fitting *vs*. linear)
	Male rest				Female rest		
1	1	0.57	0.011*	1	1	0.87	0.001*
2	1	0.37	0.010*	2	0	0.27	0.368
3	1	0.68	0.001*	3	1	0.50	0.003*
4	0	0.10	0.387	4	0	−0.09	0.154
5	1	0.86	0.001*	5	1	0.61	0.032*
6	1	0.67	0.001*	6	1	0.44	0.018*
7	1	0.30	0.028*	7	0	−0.07	0.669
8	0	0.18	0.276	8	1	0.50	0.045*
9	1	0.63	0.001*	9	0	−0.07	0.070
10	0	0.01	0.311	10	0	0.34	0.287
Mean ± SD	0.70 ± 0.48	0.44 ± 0.29		Mean ± SD	0.50 ± 0.53	0.33 ± 0.32	
	Male post exercise				Female post exercise		
1	1	0.75	0.007*	1	1	0.91	0.001*
2	1	0.98	0.001*	2	1	0.42	0.004*
3	0	−0.06	0.119	3	1	0.24	0.025*
4	0	0.33	0.473	4	0	−0.03	0.728
5	1	0.81	0.004*	5	0	0.57	0.150
6	1	0.31	0.030*	6	0	0.23	0.060
7	0	0.08	0.257	7	1	0.33	0.027*
8	1	0.91	0.001*	8	0	0.33	0.987
9	0	−0.04	0.107	9	0	−0.03	0.502
10	0	0.15	0.059	10	0	−0.03	0.174
Mean ± SD	0.50 ± 0.53	0.42 ± 0.40		Mean ± SD	0.40 ± 0.52	0.29 ± 0.30	

A quadratic polynomial or linear model best fit was determined based on the outcome of an extra-sum-of-squares *F* test (probability values are reported).
*Statistical difference at $P < 0.05$. Variance in wetness perception explained by thermal sensation is reported in terms of r^2 values.

incremental running on humans' local sensitivity to cold, neutral and warm skin wetness.

In relation to our initial hypotheses, our findings indicated that: (i) females were ∼14 to 17% more sensitive to cold-wetness than males, yet they were as sensitive to neutral- and warm-wetness as their male counterparts; (ii) regional differences were present for cold-wetness only, and these followed a cranio-caudal pattern of increased sensitivity that was more pronounced in males (i.e. the foot was ∼31% more sensitive than the forehead); (iii) maximal exercise reduced cold-wetness sensitivity over specific regions in males only (i.e. ∼40% decrease in foot sensitivity) and also induced a generalized reduction in warm-wetness sensitivity in both sexes (i.e. ∼4 to 6%). Additionally, we observed a clear U-shaped relationship between thermal and wetness perceptions (Fig. 5), where greater thermal sensations (and particularly cold sensations) induced greater wetness perceptions, and where exercise-induced reductions in thermal sensitivity translated in reduction in wetness sensitivity.

To our knowledge, this is the first study to provide empirical evidence indicating that females are more sensitive to skin wetness than males, and that this difference in dependent on the thermal quality of the skin wetness experienced (i.e. there are greater sex differences for cold than warm wetness sensitivity). Importantly, our data provide clear evidence indicating that the independent role of sex is rooted in sex-related differences in thermal sensing (i.e. females were ∼8 to 14% more cold sensitive than males) and that the relationship between thermal and wetness sensing is one that strongly determines the extent of wetness that a stimulus will induce based on its thermal qualities (Fig. 5).

Finally, we show, for the first time, that a single bout of maximal exercise can reduce the sensitivity of both sexes to skin wetness to an extent that is dependent on the concurrent exercise-induced reduction in thermal sensation. Hence, our results provide novel evidence for the fact that the previously described exercise-induced thermo-hypoesthesia is accompanied by 'hygro-hypoesthesia' (i.e. a reduction in skin wetness sensitivity) in healthy young males and females.

The role of biological sex in human wetness sensing

The results of the present study indicate that females rely on integration mechanisms for skin wetness sensing similar to those described previously (and also observed in the present study) in males (Filingeri *et al.* 2014*a*). This is confirmed by the fact that, despite all the wet stimuli used in the present study presenting the same level of physical skin wetness (i.e. 0.8 mL of water), both male and female participants systematically perceived the cold-wet stimulus as largely wetter (i.e. ∼20 to 40%) than the neutral- and warm-wet stimuli, both at rest and post exercise (Fig. 4). This perceptual behaviour is well predicted by our neurophysiological model of skin wetness sensing, which has shown that irrespective of the physical presence of moisture on the skin, activations of cold-sensitive A-type skin thermoreceptors will trigger the neural representation of a typical wet stimulus (hence a perception of wetness), which is often associated with the cooling sensations arising from evaporative skin cooling (Filingeri *et al.* 2014*a*; Filingeri & Havenith, 2015, 2018). Humans are therefore more likely to perceive cold-wet (and cold-dry) (Filingeri *et al.* 2013, 2014*e*) stimuli as wetter than equally wet warm (Filingeri *et al.* 2015*c*) and neutral stimuli (Filingeri *et al.* 2014*a*). The fact that we often struggle to determine whether the washing hanging on the line is wet or just cold, as well the common experience of not immediately realising to have a nose bleed (note: blood is often warmer than the skin), are good real-life examples of how much we rely on coldness to infer about skin wetness (Filingeri, 2016). Finally, the fact that both sexes presented a clear U-shaped relationship between their thermal and wetness perceptions (Fig. 5), which was asymmetrical between the cold and warm portions of the thermal sensation continuum (i.e. given the same magnitude of thermal sensation, cold stimuli induced greater wetness sensations than warm stimuli), provided further evidence for the presence of similar sensory integration mechanisms for wetness sensing in males and females.

Although our male and female participants appeared to experience skin wetness according to similar thermo-sensory mechanisms, the extent of skin wetness experienced was different between sexes, with females being ∼14 to 17% more sensitive to cold wetness than males, despite both sexes being exposed to the same amount of physical moisture. Interestingly, the greater female sensitivity to cold-wetness correlated well with the fact that females were also ∼8 to 14% more cold sensitive than males. Once again, these findings fit well our neuro-physiological model of skin wetness (Filingeri *et al.* 2014*a*) and the fact that colder sensations are generally associated with wetter perceptions (Filingeri *et al.* 2014*b*). It would therefore appear probable that the greater sensitivity to coldness of females is at the root of their greater sensitivity

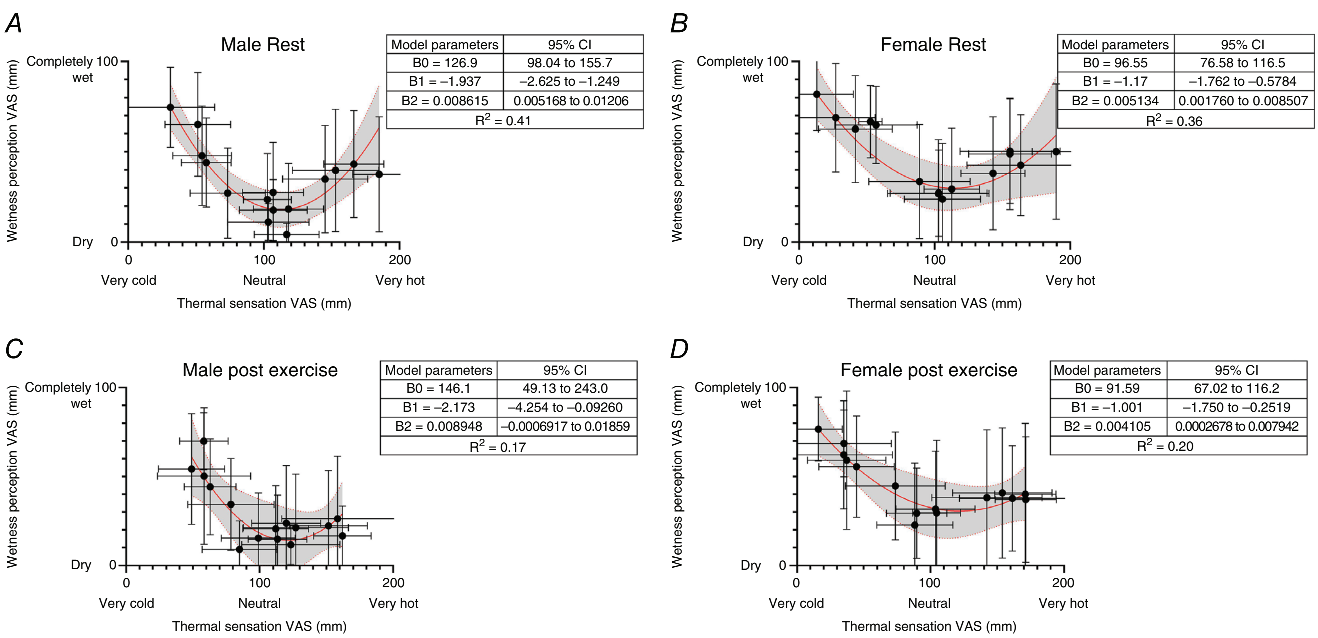

Figure 5. Thermo-hygro-sensory models
Quadratic regression models of the relationship between mean ± SD thermal sensations and wetness perceptions at rest and post exercise in males (*A* and *C*) and females (*B* and *D*). Dedicated tables present model parameters with 95% CI and r^2 values. Model fit lines are depicted in red with 95% CI grey bands. [Colour figure can be viewed at wileyonlinelibrary.com]

to cold wetness. Importantly, this observation is confirmed by the fact that males and females presented similar sensitivity to warmth and, consequently, they were equally sensitive to warm-wetness.

Females have been previously reported to be more thermally sensitive than males (Gerrett *et al.* 2014); yet sex differences in thermal sensitivity are often ambiguous (Stevens & Choo, 1996), and so it remains to be fully clarified whether sex has an independent physiological role in those difference (Filingeri *et al.* 2018).

Body morphology is an important factor in driving sex-related thermoregulatory differences, and this also applies to thermosensation. Spatial summation in the thermal sense exists and it explains why, given the same thermal stimulus, stimulating a larger portion of skin induces more intense thermal sensations (Stevens *et al.* 1974). In this respect, we have recently shown that BSA-size matched males and females present limited differences in warm and cold sensitivity across their hands and feet (Filingeri *et al.* 2018). It could be speculated that the greater female cold (and wetness) sensitivity observed here is driven by the fact that our female group had a smaller BSA than males (Table 1) and that this translated in a greater proportion of their skin being stimulated by the fixed size (1.32 cm^2) thermal probe used (Table 1). However, it should be noted that, had BSA driven sex differences in thermal sensations, we would have expected our female group to be also more warm sensitive than males, although this was not the case. Hence, it cannot be excluded that the sex differences in cold and cold-wetness sensitivity are dependent on either a greater density of cold sensitive afferents or in differently weighted central integration mechanisms for thermal sensations in females (Filingeri, 2016). The greater female sensitivity could be driven by the greater thermoprotective needs that females have when exposed to the cold, given that they generally present smaller body masses and lower resting metabolic rates than males (Gagnon *et al.* 2008).

Aside from their physiological purpose, it is worth nothing that our observed sex differences in skin wetness sensing complement recent reports demonstrating that females present more sensitive thermal behaviours than males during exercise (Vargas *et al.* 2019*b*). We consider that some of these recent behavioural observations could be explained by our observations indicating that females are more cold and wetness sensitive and that this could underlie their greater behavioural sensitivity to thermal discomfort and changes in body temperature (Vargas *et al.* 2019*b*).

The role of body region in human wetness sensing

The present study provides further evidence that skin wetness sensitivity does vary across the body, yet we show that these regional differences are dependent on the thermal quality of wetness, and that are indeed limited to cold-wet stimuli. Specifically, we observed a craniocaudal increase in cold wetness sensitivity in males (and to a lesser extent in females) (Fig. 3*A*). This pattern was in line with the observed craniocaudal increase in cold sensitivity in both sexes (Fig. 2*A*) and it therefore further supports the importance of cold sensing for discriminating wetness levels across the body (Filingeri *et al.* 2014*b*). Interestingly, we did not observe any regional difference in either neutral- or warm-wetness sensitivity (Fig. 3*B* and *C*), despite warm thermal sensitivity presenting a clear craniocaudal decrease, with the foot being less sensitive than the forehead, in both males and females (Fig. 2*C*). We consider that these thermal quality-dependent patterns of regional wetness sensitivity are driven by changes in the relative importance of thermal cues for wetness sensing when moving from colder to warmer wet stimuli. As we described previously (Filingeri *et al.* 2014*a*), when the key cold thermal cues that strongly underpin the neural representation of a typical wet stimulus are lacking (i.e. in the presence of neutral- and warm-wetness), humans increase their reliance on mechanosensory cues (i.e. movement of moisture across the skin, skin friction, stickiness and adhesion of wet skin with clothing), which are driven by the activation of Aβ skin mechanoreceptors (Bergmann Tiest *et al.* 2012; Filingeri *et al.* 2015*a*). Given that, in the present study, we only performed a static application of wet stimuli, it is probable that the lack of regional differences in neutral and warm wet sensitivity is a result of the insufficient stimulation of those mechanosensory afferents that play a greater role in neutral and warm wetness sensing. Further support for the reduced role of thermal afferents in neutral and warm wetness sensing is provided by the observation that both sexes experienced ~20 to 40% less wetness when the stimuli were neutral and warm than when they were cold (Fig. 4). Given that mechanosensory innervation varies greatly across the body (Johansson & Vallbo, 1979), that tactile sensitivity has been repeatedly shown to vary regionally (Ackerley *et al.* 2014) and that humans discriminate regional wetness levels during exercise-induced sweating (i.e. probably inducing warm-wet sensations) (Lee *et al.* 2011), it could be speculated that regional differences in warm wetness sensing could also exists in humans, although these might become apparent only under conditions of dynamic skin interactions with warm wet stimuli.

The role of exercise in human wetness sensing: hygro-hypoesthesia

By showing that maximal incremental running induced a localized reduction in cold wetness sensitivity in males (i.e. foot, ~40%), as well as a generalized reduction in warm wetness sensitivity in both sexes (~4 to 6%), our findings provide the first observation of exercise-induced hygro-hypoesthesia. It is noteworthy that the quality and extent of hygro-hypoesthesia observed in the present study correlated well with a reduction in our participants' thermal sensitivity (e.g. ~24% reduction in male foot cold sensitivity; ~10% reduction in warm sensitivity of both sexes). Exercise-induced changes in thermosensing therefore trigger equivalent changes in hygrosensing.

The exact mechanisms for exercise-induced thermo-hypoesthesia and consequent hygro-hypoesthesia cannot be fully determined in the present study and we can only speculate that an involvement of the endogenous opioid neural systems might have occurred as a result of high intensity running exercise, as previously showed for pain (Janal *et al.* 1984). Nevertheless, exercise-induced local T_{sk} changes could have also played a role in modulating some of the perceptual changes observed. Our quantitative sensory test did account for exercise-induced changes in local T_{sk} (Fig. 1) because we used stimuli temperatures that were relative to the local T_{sk} pre-stimulation. In this way, we ensured that the same relative thermal stimulus would be applied pre and post exercise. Yet, in doing so, we necessarily changed the absolute temperature of the stimuli applied pre and post exercise. For example, the absolute temperature of cold-wet stimulus applied to the foot of males was on average ~25.1°C pre exercise and ~28.6°C post exercise. Although both stimuli were well within the range of activation of cold-sensitive thermoreceptors (Filingeri *et al.* 2017*b*), it could be argued that the 'less cold' (in absolute terms) post exercise stimulus could have induced lower steady-state discharge of cold sensitive thermoreceptors, which are known to have a peak frequency sensitivity at steady state temperatures of ~27°C (Hensel & Iggo, 1971). A similar scenario might have occurred with regard to the application of warm wet stimuli.

Finally, we have recently demonstrated that changes in whole-body thermal state can modulate local thermal sensitivity (Filingeri *et al.* 2017*a*) and so it cannot be excluded that exercise-induced changes in mean T_{sk} and T_{core} could have also shifted local thermal sensitivity (Cabanac *et al.* 1972). The same considerations could apply to the differential changes in T_{core} occurring between males and females and their potential contribution to our observed sex-differences in wetness sensing.

Irrespective of whether exercise-induced neuro-endocrine or biophysical changes are the primary trigger of hygro-hypoesthesia, our observation of a reduced skin wetness sensitivity is particularly relevant in the context of better understanding how thermoregulatory behaviours during and following exercise are modulated by changes in local sensitivity to temperature and skin wetness. Physical skin wetness has been recently shown to describe 52% of the variance in thermoregulatory behaviours during and following exercise, thereby proving to be the most significant drive to exercise-induced thermal behaviours (Vargas *et al.* 2018). Yet it remains unclear whether physical as opposed to perceived skin wetness is a more important trigger of discomfort and related behaviours (Vargas *et al.* 2018). The results of the present study indicate that skin wetness sensitivity is probably reduced following exercise, and so it could be argued that, if a behavioural response was maintained to the same level of physical wetness following exercise, then this probably arises from physical skin wetness being a greater trigger of thermal behaviours, rather than from its conscious experience. In support of the latter, we recently showed that modifying skin wetness perception independently of physical skin wetness in exercising humans (Filingeri *et al.* 2015*a*) resulted in no meaningful change in thermal discomfort (i.e. a key trigger of thermal behaviours) and the latter was better described by changes in physical than perceptual skin wetness (Gagge *et al.* 1967). Nevertheless, future studies should combine perceptual and behavioural assessments to untangle the independent role of physical and perceptual skin wetness on human thermoregulatory responses.

Limitations and experimental considerations

There are two experimental considerations to be made when interpreting our findings. First, we did not control for the phase of menstrual cycle of our female participants. There is direct evidence that thermal sensations in females are not independently modified by menstruation (Matsuda-Nakamura *et al.* 2015). Yet tactile sensitivity (which plays a role in dynamic skin wetness sensitivity) is influenced by the phase of the menstrual cycle (Robinson & Short, 1977). Accordingly, future studies should consider the independent role of menstruation on local skin wetness sensitivity, particularly under dynamic skin interactions with wet stimuli. Second, we recognize that infrared thermometry for measuring tympanic T_{core} and local T_{sk} carries an estimation error of up to 0.5°C and 1°C, respectively. This estimation error could have biased some perceptual responses based on local measurements of T_{sk}. Accordingly, we quantified the potential impact of this error in our findings, by determining the relationship between thermal sensations and absolute temperature of the stimuli in both males and females. The resulting regression model (i.e. stimuli temperature *vs.* thermal sensation; $y = 11.152x - 259.69$, $r^2 = 0.89$) allowed calculation of the perceptual change arising from a 1°C change in local stimulus temperature, which corresponded to the maximal error of our local T_{sk} measurement. When converted into a percentage of the 200 mm VAS scale, this gave a maximum perceptual change of 5.6%. This value is well below the range of effect sizes observed for the sex-, regional- and exercise-induced differences in wetness perception reported in the present study. Yet, the implications of those measurement errors should be carefully considered when interpreting perceptual results obtained using similar methodologies to ours.

Conclusions

For the first time to our knowledge, we show that young healthy females are more sensitive to cold, but not neutral or warm, skin wetness than healthy young males. We also show that regional differences to skin wetness exists, although, under static contact with moisture, these are greater for cold than warm wet stimuli. Finally, we demonstrate that maximal incremental running induces hygro-hypoesthesia, which is strongly driven by the quality and extent of exercise-induced thermo-hypoesthesia. Our findings confirm the importance that afferent thermosensory inputs from cold-sensitive skin thermoreceptors play in human wetness sensing and demonstrate that the central integration mechanisms for wetness sensing are shared by males and females. The outcomes of the present study have fundamental physiological significance because they provide mechanistic evidence for sex differences in thermoregulatory behaviours. They also have applied significance because the body maps created, along with the wetness models developed, will inform the design of more effective sport and protective clothing, and they will feed into the optimization of individualized thermoregulatory models.

References

Ackerley R, Carlsson I, Wester H, Olausson H & Backlund Wasling H (2014). Touch perceptions across skin sites: differences between sensitivity, direction discrimination and pleasantness. *Front Behav Neurosci* **8**, 54.

Ackerley R, Olausson H, Wessberg J & McGlone F (2012). Wetness perception across body sites. *Neurosci Lett* **522**, 73–77.

Bergmann Tiest WM, Kosters ND, Kappers AML & Daanen HAM (2012). Haptic perception of wetness. *Acta Psychol (Amst)* **141**, 159–163.

Cabanac M, Massonnet B & Belaiche R (1972). Preferred skin temperature as a function of internal and mean skin temperature. *J Appl Physiol* **33**, 699–703.

Clark R & Edholm O (1985). *Man and his thermal environment.* London: E. Arnold, 1985. Available at: http://www.getcited.org/pub/102393103 [Accessed March 12, 2013].

Crawshaw L, Nadel E, Stolwijk J & Stamford B (1975). Effect of local cooling on sweating rate and cold sensation. *Pflugers Arch* **354**, 19–27.

Darian-Smith I (1984). Thermal sensibility. In *Supplement 3: Handbook of Physiology, The Nervous System, Sensory Processes*, pp. 879–913. Available at: http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:Thermal+sensibility#2 [Accessed September 11, 2014].

Filingeri D (2014). *Why wet feels wet? An investigation into the neurophysiology of human skin wetness perception.* Loughborough University.

Filingeri D (2015). Humidity sensation, cockroaches, worms, and humans: are common sensory mechanisms for hygrosensation shared across species? *J Neurophysiol* **114**, 763–767.

Filingeri D (2016). Neurophysiology of skin thermal sensations. *Compr Physiol* **6**, 1429–1491.

Filingeri D, Fournet D, Hodder S & Havenith G (2014*a*). Why wet feels wet? A neurophysiological model of human cutaneous wetness sensitivity. *J Neurophysiol* **112**, 1457–1469.

Filingeri D, Fournet D, Hodder S & Havenith G (2014*b*). Body mapping of cutaneous wetness perception across the human torso during thermo-neutral and warm environmental exposures. *J Appl Physiol* **117**, 887–897.

Filingeri D, Fournet D, Hodder S & Havenith G (2015*a*). Tactile cues significantly modulate the perception of sweat-induced skin wetness independently of the level of physical skin wetness. *J Neurophysiol* **113**, 3462–3473.

Filingeri D & Havenith G (2015). Human skin wetness perception: psychophysical and neurophysiological bases. *Temperature* **2**, 86–104.

Filingeri D & Havenith G (2018). Peripheral and central determinants of skin wetness sensing in humans. *Handb Clin Neurol* **156**, 83–102.

Filingeri D, Morris NB & Jay O (2017*a*). 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.

Filingeri D, Redortier B, Hodder S & Havenith G (2013). The role of decreasing contact temperatures and skin cooling in the perception of skin wetness. *Neurosci Lett* **551**, 65–69.

Filingeri D, Redortier B, Hodder S & Havenith G (2014*e*). Thermal and tactile interactions in the perception of local skin wetness at rest and during exercise in thermo-neutral and warm environments. *Neuroscience* **258**, 121–130.

Filingeri D, Redortier B, Hodder S & Havenith G (2015*c*). Warm temperature stimulus suppresses the perception of skin wetness during initial contact with a wet surface. *Ski Res Technol* **21**, 9–14.

Filingeri D, Zhang H & Arens EA (2017*b*). Characteristics of the local cutaneous sensory thermoneutral zone. *J Neurophysiol* **117**, 1797–1806.

Filingeri D, Zhang H & Arens EA (2018). Thermosensory micromapping of warm and cold sensitivity across glabrous and hairy skin of male and female hands and feet. *J Appl Physiol* **125**, 723–736.

Fukazawa T & Havenith G (2009). Differences in comfort perception in relation to local and whole body skin wettedness. *Eur J Appl Physiol* **106**, 15–24.

Gagge A, Stolwijk J & Hardy J (1967). Comfort and thermal sensations and associated physiological responses at various ambient temperatures. *Environ Res* **1**, 1–20.

Gagnon D, Jay O, Lemire B & Kenny G (2008). Sex-related differences in evaporative heat loss: the importance of metabolic heat production. *Eur J Appl Physiol* **104**, 821–829.

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**, 1451–14629.

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.

Havenith G (2001). Individualized model of human thermoregulation for the simulation of heat stress response. *J Appl Physiol* **90**, 1943–1954.

Hensel H & Iggo A (1971). Analysis of cutaneous warm and cold fibres in primates. *Pflügers Arch* **329**, 1–8.

Janal MN, Colt EWD, Clark WC & Glusman M (1984). Pain sensitivity, mood and plasma endocrine levels in man following long-distance running: effects of naloxone. *Pain* **19**, 13–25.

Johansson RS & Vallbo AB (1979). Tactile sensibility in the human hand: relative and absolute densities of four types of mechanoreceptive units in glabrous skin. *J Physiol* **286**, 283–300.

Koltyn K (2000). Analgesia following exercise: a review. *Sport Med* **29**, 85–98.

Koltyn KF (2002). Exercise-induced hypoalgesia and intensity of exercise. *Sports Med* **32**, 477–487.

Lee J, Nakao K & Tochihara Y (2011). Validity of perceived skin wettedness mapping to evaluate heat strain. *Eur J Appl Physiol* **111**, 2581–2591.

Lund DD & Gisolfi CV (1974). Estimation of mean skin temperature during exercise. *J Appl Physiol* **36**, 625–628.

Matsuda-Nakamura M, Yasuhara S & Nagashima K (2015). Effect of menstrual cycle on thermal perception and autonomic thermoregulatory responses during mild cold exposure. *J Physiol Sci* **65**, 339–347.

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.

Ouzzahra Y, Havenith G & Redortier B (2014). Regional distribution of thermal sensitivity to cold at rest and during mild exercise in males. *J Therm Biol* **54**(Suppl 1), NP.

Robinson JE & Short RV (1977). Changes in breast sensitivity at puberty, during the menstrual cycle, and at parturition. *Br Med J* **1**, 1188–1191.

Russell J, Vidal-Gadea AG, Makay A, Lanam C & Pierce-Shimomura JT (2014). Humidity sensation requires both mechanosensory and thermosensory pathways in Caenorhabditis elegans. *Proc Natl Acad Sci U S A* **111**, 8269–8274.

Schlader ZJ, Simmons SE, Stannard SR & Mündel T (2011). The independent roles of temperature and thermal perception in the control of human thermoregulatory behavior. *Physiol Behav* **103**, 217–224.

Smith C & Havenith G (2011). Body mapping of sweating patterns in male athletes in mild exercise-induced hyperthermia. *Eur J Appl Physiol* **111**, 1391–1404.

Smith CJ & Havenith G (2012). Body mapping of sweating patterns in athletes: a sex comparison. *Med Sci Sports Exerc* **44**, 2350–261.

Stevens J, Marks L & Simonson D (1974). Regional sensitivity and spatial summation in the warmth sense. *Physiol Behav* **13**,825–836.

Stevens JC & Choo KK (1996). Spatial acuity of the body surface over the life span. *Somatosens Mot Res* **13**, 153–166.

Vargas NT, Chapman CL, Johnson BD, Gathercole R & Schlader ZJ (2018). Skin wettedness is an important contributor to thermal behavior during exercise and recovery. *Am J Physiol Regul Integr Comp Physiol* **315**, R925–R933.

Vargas NT, Chapman CL, Johnson BD, Gathercole R & Schlader ZJ (2019*a*). Exercise intensity independently modulates thermal behavior during exercise recovery, but not during exercise. *J Appl Physiol* **128**, 1150–1159.

Vargas NT, Chapman CL, Sackett JR, Johnson BD, Gathercole R & Schlader ZJ (2019*b*). Thermal behavior differs between males and females during exercise and recovery. *Med Sci Sports Exerc* **51**, 141–152.

Additional information

Competing interests

The authors declare that they have no competing interests.

Author contributions

AV, AB and DF conceived and designed the work. AV acquired the data. AV, AB and DF analysed and interpreted the data, drafted the work and revised it critically for intellectual content. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Author summary video