Why wet feels wet? A neurophysiological model of human cutaneous wetness sensitivity

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Running head:
Neural pathways of cutaneous wetness sensitivity

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Abstract

Although the ability to sense skin wetness and humidity is critical for behavioral and autonomic adaptations, humans are not provided with specific skin receptors for sensing wetness. It has been proposed that we “learn” to perceive the wetness experienced when the skin is in contact with a wet surface or when sweat is produced through a multisensory integration of thermal and tactile inputs generated by the interaction between skin and moisture. However, the individual role of thermal and tactile cues and how these are integrated peripherally and centrally by our nervous system is still poorly understood. Here we tested the hypothesis that the central integration of coldness and mechanosensation, as subserved by peripheral A-nerve afferents, might be the primary neural process underpinning human wetness sensitivity. During a quantitative sensory test, we found that individuals perceived warm-wet and neutral-wet stimuli as significantly less wet than cold-wet ones, although these were characterized by the same moisture content. Also, when cutaneous cold and tactile sensitivity was diminished by a selective reduction in the activity of A-nerve afferents, wetness perception was significantly reduced. Based on a concept of perceptual learning and Bayesian perceptual inference, we developed the first neurophysiological model of cutaneous wetness sensitivity centered on the multisensory integration of cold and mechano sensitive skin afferents. Our results provide evidence for the existence of a specific information processing model which underpins the neural representation of a typical wet stimulus. These findings contribute to explain how humans sense warm, neutral and cold skin wetness.

Keywords

Skin, wetness, thermoreceptors, mechanoreceptors, A-nerve fibers
INTRODUCTION

The ability to sense humidity and wetness is an important attribute in the animal kingdom. For many insects, discriminating between dryness and wetness is vital for procreation and survival (Liu et al., 2007). Sensing wetness is also critical for humans, both for behavioral and autonomic adaptations. Perceiving changes in ambient humidity and skin wetness has been shown to impact thermal comfort (Fukazawa and Havenith, 2009) and thus the thermoregulatory behavior (Schlader et al., 2010), both in healthy and clinical populations (e.g. individuals suffering from rheumatic pain) (Strusberg et al., 2002). From an autonomic perspective, decreases in ocular wetness seem to initiate the lacrimation reflex in order to maintain a tear film to protect the ocular surface (Hirata and Oshinsky, 2012). Also, tactile roughness and wetness discrimination is critical for precision grip (Augurelle et al., 2003) and object manipulation (André, 2010). However, although the ability to sense wetness plays an important role in many physiological and behavioral functions, the neurophysiological mechanisms underlying this complex sensory experience are still poorly understood (Montell, 2008).

In contrast with insects, in which humidity receptors sub-serving hygrosensation have been identified and widely described (Tichy and Kallina, 2010), humans’ largest sensory organ i.e. the skin seems not to be provided with specific receptors for the sensation of wetness (Clark and Edholm, 1985). Thus, as human beings, we seem to “learn” to perceive the wetness experienced when the skin is in contact with a wet surface or when sweat is produced (Bergmann Tiest et al., 2012) through a complex multisensory integration (Driver and Spence, 2000) of thermal (i.e. heat transfer) and tactile (i.e. mechanical pressure and friction) inputs generated by the interaction between skin, moisture and (if donned) clothing (Fukazawa and Havenith, 2009). The hypothesis of wetness as a “perceptual illusion” shaped by sensory
experience has been supported by our previous findings. We have recently shown that exposing the skin to cold-dry stimuli (resulting in cooling rates similar to the ones occurring during the evaporation of water from the skin) can evoke an illusion of local skin wetness (Filingeri et al., 2013, 2014a, 2014b). This could be due to the fact that we seem to interpret the coldness experienced during the evaporation of moisture from the skin as a signal of the presence of moisture (and thus wetness) on the skin surface. In line with this hypothesis, we have also observed that during the static contact with a warm-wet surface (with a temperature warmer than the skin) no local skin wetness was perceived, as no skin cooling, and thus no cold sensations occurred (Filingeri et al., 2014c).

These preliminary findings appeared to be in line with the Bayesian concept of perceptual inference (Knill and Richards, 1996). According to this framework, sensory systems (such as the somatosensory one) incorporate implicit knowledge of the environment and use this knowledge (i.e. sensory experiences) to infer about the properties of specific stimuli (Geisler and Kersten, 2002). As the sensory feedback received from the surrounding environment is by nature multimodal (i.e. involving different sensory cues), as well as noisy and ambiguous, perceptual systems are thought to perform on-line tasks aiming to predict the underlying causes for a sensory observation in a fashion which is considered as near optimal (Lochman and Deneve, 2011). In this context, humans have been shown to integrate the different sensory cues associated with an external stimulus and to infer the most probable multimodal estimate (i.e. perception) by taking into account the reliability of each sensory modality involved in the perceptual process (Weiss et al., 2002; Ernst and Banks, 2002).

The potential ability of our neural systems to solve the inherent uncertainty associated with sensory interpretation in a probabilistic and predictive manner (Lochman and Deneve, 2011), explains why many apparently idiosyncratic perceptual illusions (see e.g. the effects of luminance contrast on the perception of motion velocity) (Weiss et al., 2002) are instead what
one would expect from a rational perceptual system (Geisler and Kersten, 2002). Thus, sensory illusions, such as the perception of wetness, can be used as a powerful method to gain conceptual and functional understanding of the sensory processing operated by specific sensory systems such as the somatosensory one (Lochmann et al., 2012).

In this respect, our previous work has shown that the cold sensations resulting from the afferent activity of the cutaneous cold-sensitive, myelinated Aδ-nerve fibers (with conduction velocities ranging from 5-30m/s) (Campero et al., 2001), play a critical role in the ability to perceive skin wetness (Filingeri et al., 2013, 2014a, 2014b, 2014c). Furthermore, we have recently demonstrated that tactile inputs, which are likely to be encoded by cutaneous mechanosensory Aß-nerve fibers (with conduction velocities ranging from 16-100m/s) (Tsunozaki and Bautista, 2009), could have a role in modulating the perception of skin wetness (Filingeri et al., 2014a). Thus, these observations have led us to hypothesize that the central integration of coldness and mechanosensation, as subserved by peripheral myelinated A-nerve fibers, might be the primary neural process underpinning humans’ ability to sense wetness. However, what remains unclear is the individual role of thermal and tactile cues and how these are integrated peripherally as well as centrally. If the multimodal integration of coldness and mechanosensation was the main neural process for sensing wetness, it would be reasonable to hypothesize that during the contact with a wet surface, the absence of any coldness and mechanosensation, either if naturally (i.e. contact with a warm-wet or neutral-wet surface) or artificially induced (i.e. during a selective reduction in the activity of A-nerve fibers), would result in a reduced cutaneous sensitivity to wetness. Hence, in the present study, we used psychophysical methods to investigate the role of thermal and tactile afferents and their central integration in the perception of skin wetness under normal fiber function and under a selective reduction in the activity of A-nerve afferents.
We tested the hypothesis that under normal nerve fiber function, wetness perception is primarily driven by the integration of cold and tactile inputs as subserved by A-nerve fibers. Furthermore, we hypothesized that during a selective reduction in the activity of A-nerve fibers, the artificially induced reduction in cutaneous cold and mechano sensitivity would translate in a significant reduction in the extent of perceived wetness. Finally, given the anatomical and functional differences in cutaneous thermal and mechano sensitivity between hairy and glabrous skin (Abraira and Ginty, 2013; Haggard et al., 2013; Pleger and Villringer, 2013), here we investigated whether the proposed neurophysiological model of wetness sensitivity applies similarly to the forearm (i.e. hairy) as well as to index finger pad (i.e. glabrous). As hairy and glabrous skin sites have been shown to differ in terms of innervation and particularly in terms of density of thermo- and mechano-sensory afferents as well as in their biophysical properties (e.g. thickness and thermal conductance) (Abraira and Ginty, 2013), it was hypothesized that, due to the primary role of thermal cues in sensing wetness (Filingeri et al., 2013, 2014a, 2014b, 2014c), the higher thermal sensitivity of the hairy skin (due to its larger density of thermoreceptors and to its lower thermal conductance) (Norrsell et al., 1999) would translate in wetness being perceived in larger magnitude on this skin site as opposed to the glabrous skin. This, despite the latter presents a larger density of slowly adapting type 1 mechano-sensory afferents, also known as Merkel cells (low threshold mechanoreceptors transmitting acute spatial images of tactile stimuli with remarkably high spatial resolution) (Abraira and Ginty, 2013), which could potentially contribute to an increase in the haptic perception of wetness on this type of skin.

METHODS
Participants

Thirteen healthy university male students (mean age 21 years, SD 2; mean height 185 cm, SD 9; mean body mass 86 Kg, SD 12) with no history of sensory-related disorders volunteered to participate in this study. All participants gave their informed consent for participation. The test procedure and the conditions were explained to each participant. The study design had been approved by the Loughborough University Ethics Committee and testing procedures were in accordance with the tenets of the Declaration of Helsinki.

A sample size calculation was performed in order to determine the minimum number of participants required to be able to detect a significant change in thermal and mechano sensitivity as a result of the selective block protocol. Pilot tests data indicated that the difference in the thermal sensations of matched pairs (block vs. no block trials) was normally distributed with standard deviation of ~10 arbitrary units (a.u.). As we set the true difference in the mean thermal sensation of matched pairs at a value of 15 a.u., it was calculated that a minimum number of 12 participants was needed to be able to reject the null hypothesis that this response difference is zero with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis ($\alpha$) was 0.05. Sample size calculations were performed using Power and Sample Size Calculation version 3.0, 2009 (Vanderbilt University).

Experimental design

Participants took part in 3 experimental trials, during which the same quantitative sensory test was administered. The hairy skin of the ventral side of the left forearm (i.e. mid-distance between elbow and wrist) and the glabrous skin of the left index finger pad were exposed to the contact with a warm-wet (35°C), neutral-wet (30°C) and a cold-wet (25°C) stimulus during 3 phases: static, dynamic and evaporation (i.e. post-contact). During the contact with
the stimuli, participants reported their local thermal and wetness perceptions on a hand-scored 100mm visual analog scale for thermal (anchor points: hot and cold) and wetness perception (anchor points: completely dry and completely wet), while skin temperature at the contact site was continuously monitored. The 3 experimental trials differed with regards to the presence or absence of a selective reduction in the activity of A-nerve fibers and to the skin site stimulated. All 13 participants performed: one trial during which no nerve block was performed (NO-BLOCK) and the skin of the forearm and finger pad were exposed to the wet stimuli; two separate trials during which a selective reduction in the activity of A-nerve fibers was performed through local compression-ischemia, and the skin of the forearm (FA-BLOCK) or finger pad (FI-BLOCK) was exposed to the contact with the wet stimuli. Trials were performed on a balanced order, on separate days, with at least 72h in between.

The thermal stimuli were delivered by a thermal probe (Physitemp Instruments Inc., USA) with a contact surface of 25cm² and a weight of 269g. To make the contact with the probe’ surface wet, test fabrics (100% cotton) with a surface of 100cm², were placed on the thermal probe and fixed by an elastic band. These were wetted with 2000µL water at ambient temperature (~23°C), using a variable volume pipettor (SciQuip LTD, Newtown, UK). To ensure that the wet fabric would reach the required temperature (i.e. 35, 30 or 25°C), the contact temperature between the probe and the test fabric was monitored with a thin thermocouple (0.08mm wire diameter, 40 Gauge; 5SRTC-TT-TI-40-2M, Omega, Manchester, UK) placed on the thermal probe’ surface. Also, local skin temperature (Tsk) at the contact site of stimulation was measured continuously through the application of a thermocouple on the ventral side of the forearm or index finger pad using transpore tape (3M, Loughborough, UK), with the sensor tip touching the skin, but not covered by tape. Probe-fabric temperature as well as Tsk was monitored using a Grant Squirrel SQ2010 data logger (Grant Instruments Ltd., Cambridge, UK).
During all the trials, participants rested in a seated position in a thermo-neutral environment (air temperature: ~23°C; relative humidity: ~50%). Participants were informed only about the skin site subjected to the stimulation and the trial to be performed (block vs. no block). No information was made available on the type and magnitude of the stimulation to limit any expectation effects. To make this possible, an s-shaped wooden panel (width: 81cm; length: 74cm; height: 60cm) was placed on a table. A hole (width: 12cm; height: 13cm) in the panel allowed participants to enter their left forearm through the panel. This experimental setup did not allow the participants to see the stimulated area.

Experimental protocols

NO-BLOCK trial

In the NO-BLOCK trial, no compression ischemia was performed and participants interacted actively with the warm-wet, neutral-wet and cold-wet stimuli. Forearm and index finger pad skin sites were tested separately within this trial, allowing a 5min interval between them. The thermal probe was secured with surgical tape on the side of the table which was not visible to the participants, with the thermally controlled surface facing upward. Prior to interacting with each wet stimulus, and in order to set a baseline $T_{sk}$ of 30°C, participants were asked to insert their left arm through the hole in the panel and place the forearm or index finger pad for 30s on the dry thermal probe, which was set at 30°C. Participants then removed the arm from the thermal probe, placed it on the side of the table visible to them, and waited 1min for the first stimulus to be prepared. During this time, the probe was set to the required temperature (i.e. 35°C, 30°C or 25°C), the test fabric was secured to the probe and then wetted with the pipettor. Pilot tests indicated 1min as the time required for the wet test fabric to reach the selected temperature. Once the stimulus preparation was completed,
the interaction with the wet stimulus was initiated. This consisted of 3 phases (each lasting 10s): static, dynamic and evaporation (i.e. post contact). First, participants were instructed to insert their left arm through the hole in the panel and to lower it until the forearm or index finger pad was in full contact with the thermal probe. As soon as in static contact, they were encouraged to rate their local thermal and wetness perceptions by marking a point on the thermal and wetness scales they were provided with on the side of the table which was visible to them (response time ~5s). Then participants were asked to move the forearm or index finger pad forward (~2.5cm) and backward (~2.5cm) twice while maintaining full contact with the thermal probe. At the end of this dynamic interaction they were asked again to rate their local thermal and wetness perceptions (response time ~5s). Finally, they were asked to lift the forearm or index finger pad up from the thermal probe, thus allowing evaporation of any residual moisture on the skin, and as soon as not in contact with the probe, to rate their local thermal and wetness perceptions for the last time (response time ~5s). This sequence (i.e. setting the baseline skin temperature, preparing and then interacting with the wet stimulus) was repeated for each of the 3 wet stimuli in a balanced order, with at least 1 min in between them.

As no visual feedback was available during the stimulation, to assure consistency in the interaction with the stimuli (i.e. pressure applied to the probe and horizontal displacement during the dynamic phase), the investigator gently guided the participants’ arm throughout the interaction with each stimulus and provided verbal instructions on when to change the interaction (e.g. from static to dynamic). All participants were familiarized with the experimental protocol prior to testing. Participants also familiarized with the rating scales prior to testing. When reporting thermal sensations, they were instructed to associate the anchor point “Hot” (on the left of the scale) to the idea of a burning hot pan, and the anchor point “Cold” (on the right of the scale) to the idea of an ice cube, and to mark a point on the
scale which corresponded to the level of warmness or coldness experienced. The midpoint of
the scale was suggested as a neutral point (to be marked if neither hot nor cold sensations
were experienced). When reporting wetness perceptions, they were instructed to associate the
anchor point “Completely dry” (on the left of the scale) to the absence of any wetness. Thus,
any marked point which was not on the left edge of the scale was to be considered as to
correspond to the perception of wetness, with the closer this would be to the anchor point
“Completely wet” (on the right of the scale), the greater the level of wetness experienced.
The visual analog scales used in this study were hand-scored on laminated paper. Washable
markers were used by the participants to mark their sensation so that the same scale could be
re-used within the same test after participants’ ratings were recording and cleaned off with a
wet cotton pad.

**FA-BLOCK and FI-BLOCK trials**

In the FA-BLOCK and FI-BLOCK trials, participants underwent an initial selective reduction
in the activity of A-nerve fibers and then were passively exposed to the warm-wet, neutral-
wet and cold-wet stimuli. The aim of this procedure was to reduce cutaneous cold and
mechano sensitivity and it was performed through a modified local compression-ischemia
protocol. This method has been previously shown to induce a dissociated reduction in A-
fibers afferent activity (Yarnitsky and Ochoa, 1990, Davis 1998) as the compression ischemia
impacts transmission in myelinated A-fibers before C-fibers (i.e. primarily sub-serving
conscious warmth and pain sensitivity) are affected (Torebjörk and Hallin, 1973).

Compression-ischemia was induced by inflating a sphygmomanometer cuff on the upper arm
to a suprasystolic pressure (i.e.140mmHg) for a maximum duration of 25min. During the
compression ischemia protocol, thermal sensitivity to warm (i.e. 35°C) and cold dry stimuli
(i.e. 25°C) as well as mechanical sensitivity to light brush were checked every 5 min. It
deserves mention that, despite of changes in mechano and cold sensitivity, the maximal
duration of the compression-ischemia was set to 25min in order to limit the discomfort and
pain the participants could experience underneath the cuff (note: this duration does not
include the subsequent stimulation with the wet stimuli, whose approximate duration was
~8min). Although the literature reports compression blocks lasting between 27 to 60 min and
performed with pressures up to 100mmHg above systolic pressure (see e.g. Yarnitsky and
Ochoa, 1990 and Davis 1998), our pilot studies indicated the duration chosen as well as the
pressure used as to be sufficient to induce a gradual reduction in cold and mechano sensitivity,
while maintaining to a minimum participants’ overall discomfort. Indeed, during our
preliminary testing, participants could not bear the 140mmHg cuff pressure for longer than 35
to 40 min due to the excessive discomfort experienced underneath the cuff.

Prior to the application of the compression ischemia protocol, instrumentation and baseline
measurements were performed. Participants were asked to sit on a chair for 15min, at the end
of which resting blood pressure was measured from the left wrist with a digital wrist blood
pressure monitor (Speidel and Keller, Jungingen, Germany), while the arm was supported at
heart level. Participants then entered their left arm through the hole in the panel, laid it down
with the palm facing upward, while a 13cm wide sphygmomanometer cuff (Hokanson Inc.,
Bellevue, USA) was placed around the arm (i.e. mid-distance between shoulder and elbow).
The sphygmomanometer cuff was connected to a custom made cuff inflator. According to the
experimental trial, a thermocouple was then taped to the ventral side of the forearm or to the
index finger pad to record $T_{sk}$ throughout the test. An 8mm optic probe was taped to the
ventral side of the forearm (proximal to the elbow joint) and connected to a Laser Doppler
monitor (Moor Instruments, Devon, UK) to record skin blood flow. Finally, to allow thermal
stimulation of the skin, the thermal probe, set at 30°C, was secured with tape on the forearm
or index finger pad (with the thermally controlled surface in full contact with the skin), where it rested during the first part of the test. After instrumentation, baseline $T_{sk}$ and skin blood flow were recorded for 5 min, while participants were asked to maintain a comfortable seated position, having their left arm lying on the left hand side of the table (which was not visible to them) and their right arm on the right hand side, where the rating scale and washable marker were positioned to allow ratings of sensation when required. This position was maintained throughout the whole test. At this point pre-compression ischemia cutaneous thermal and mechano sensitivity was tested as follow: the thermal probe’s temperature was first set to 35°C (i.e. warm-dry stimulus) and as soon this temperature was reached (response time <4 s) participants were immediately asked to rate their thermal sensation only, by marking a point on the thermal sensation scale. The thermal probe was then re-set to 30°C. As soon as the $T_{sk}$ returned to 30°C (this was monitored on-line on the data logger recording from the thermocouple placed on the skin site stimulated), the thermal probe’s temperature was changed to 25°C (i.e. cold-dry stimulus) and as soon this temperature was reached participants were asked again to rate their thermal sensation only. The thermal probe was then re-set to 30°C. Finally, the skin near the stimulated site was gently touched with a cotton pad and participants were asked to report verbally whether they could sense the touch. As soon as the baseline measurements were completed, the custom made cuff inflator was started, the sphygmomanometer cuff was inflated with the required pressure (time to reach the pressure: ~5 s), and the compression ischemia protocol initiated. The cutaneous sensitivity test was then repeated as above every 5 min. When the inability to perceive the light brush was observed, along with a reduction in thermal sensitivity to the cold stimulus, the thermal probe was removed from the skin site, and the warm-wet, neutral-wet and cold-wet stimuli were prepared and then applied following a protocol identical to the one performed during the NO-BLOCK trial (i.e. static,
dynamic and evaporation phases), with the only difference being in the investigator applying
the thermal probe instead of the participants placing their forearm or finger pad on it.

Statistical analysis

In the present study, the independent variables were the temperature of the stimuli (i.e. 35, 30
and 25°C), the different phases of stimulation (i.e. static, dynamic and evaporation), the skin
site stimulated (i.e. forearm and index finger pad) and the condition (i.e. the presence or not
of a selective reduction in A-fibers’ activity). The dependent variables were local Tsk, thermal
sensation and wetness perception. All data were first tested for normality of distribution and
homogeneity of variance using Shapiro-Wilk and Levene’s tests respectively. To investigate
the role of thermal and mechanical cues on cutaneous thermal and wetness sensitivity, and
whether differences exist between hairy and glabrous skin, data from the NO-BLOCK trial
were analysed by a 3-way repeated measure ANOVA, with temperature of the stimuli (3
levels), phases of stimulation (3 levels) and skin site (2 levels) as repeated measure variables.
To investigate whether the compression ischemia protocol resulted effective in selectively
reducing A-nerve fibers’ function in both forearm and index finger pad skin sites, thermal
ratings recorded prior and at the end of the protocol (i.e. just before the wet stimuli were
applied) were compared for both warm and cold stimulations by using paired t-tests. To
investigate whether a reduction in cutaneous cold and mechano sensitivity decreased the
ability to perceive skin wetness, data from the NO-BLOCK and BLOCK trials were analysed
separately for the forearm and index finger pad by a 3-way repeated measure ANOVA, with
condition (2 levels), temperature of the stimuli (3 levels) and phases of stimulation (3 levels)
as repeated measure variables. Data were tested for sphericity and if the assumption of
sphericity was violated, Huynh–Feldt or Greenhouse-Geisser corrections were undertaken to
adjust the degrees of freedom for the averaged tests of significance. Estimated marginal
means and 95% confidence intervals (CI) were used to investigate the main effects and interactions of the variables. When a significant main effect was found, Tukey’s post-hoc analyses were performed. In order to quantify the power associated with the statistically non-significant results, observed power was computed using $\alpha=0.05$ and reported. In all analyses, $p<0.05$ was used to establish significant differences. Furthermore, according to Curran-Everett and Benos (2004), precise $p$ values were interpreted as follow: $p>0.1$ data are consistent with a true zero effect; $0.05<p<0.1$ data suggest there may be a true effect that differs from zero; $0.01<p<0.05$ data provide good evidence that the true effect differs from zero; $p<0.01$ data provide strong evidence that the true effect differs from zero. Data were analysed using SPSS Statistics 19 (IBM, Armonk, USA) and are reported as means and standard deviation (SD) and 95% CI.

RESULTS

Cutaneous sensitivity to wetness under normal A-nerve fibers function (NO-BLOCK trial)

During the initial static contact with the warm-wet, neutral-wet and cold-wet stimuli, forearm skin and index finger pad $T_{sk}$ respectively increased, remained unchanged or decreased (Fig. 1A,C). These variations in $T_{sk}$ remained stable during the following dynamic phase. During the evaporation phase, $T_{sk}$ started to return to pre-stimulation values after the warm-wet and cold-wet stimulations, whereas it started to decrease after the neutral-wet stimulation. As a result, participants reported thermal sensations which varied significantly according to the temperature ($F= 28.8_{(1,2,12.9)}, p<0.0001$) and phases of interaction ($F= 6.3_{(2, 22)}, p= 0.007$) with the wet stimuli. A trend was observed with the forearm being more thermally sensitive than the finger pad ($F= 3.6_{(1,11)}, p= 0.085$, observed power= 0.4). Overall, thermal sensations matched the variations observed in local $T_{sk}$, with the warm-wet stimulus resulting in warmer
sensations, the neutral-wet stimulus in neutral sensations and the cold-wet stimulus in colder
sensations (Fig.1E,G).

With regards to wetness sensitivity, although all the stimuli presented the same level of
physical wetness (i.e. 20 µL/cm²), participants reported wetness perceptions which increased
significantly with decreasing contact temperatures ($F= 5.3_{(2, 24)}, p= 0.012$) (Fig. 2A). Also,
wetness perception increased significantly during the dynamic as opposed to the static contact
($F= 11.5_{(2, 24)}, p<0.0001$) (Fig. 2B). Overall a trend was observed in the interaction between
temperature and phases of stimulation ($F= 2.38_{(4, 48)}, p= 0.064$, observed power= 0.6). This
indicated that during the static phase, the cold-wet stimulus was perceived as “wetter” than
the warm-wet and neutral-wet stimuli and that during the dynamic and evaporation phases,
wetness perceptions increased for all the stimuli (Fig.1I,K). Finally, a trend of the effect of
skin site on wetness perception was observed ($F= 3.5_{(1, 12)}, p=0.086$, observed power= 0.4),
with the forearm showing a tendency in having a higher sensitivity to wetness [mean= 30.4
a.u.; CI= 21.8, 39 a.u.] than the index finger pad [mean= 18.2 a.u.; CI= 8.3, 28.1 a.u.].

Overall these results indicate that the perception of skin wetness was driven by the coldness
experienced, and that when no coldness was perceived (e.g. warm-wet and neutral-wet
stimulations), participants’ ability to sense wetness relied on the mechanical inputs generated
during the dynamic interaction with the wet surface.

Selective reduction in the activity of A-nerve fibers

To test the effectiveness of the selective reduction in the activity of A-nerve fibers, during the
compression ischemia protocol, thermal sensitivity to warm (i.e. 35°C) and cold dry stimuli
(i.e. 25°C) as well as mechanical sensitivity to light brush were checked every 5 min. As a
result of the protocol, a statistically significant reduction in thermal sensitivity to cold was
observed, both in the forearm (mean difference= -17.3 a.u.; CI= -2.9, -31.7 a.u.; t= -2.6; two-
tailed \( p= 0.022; \) Fig. 3A) and index finger pad (mean difference= -16.8 a.u.; CI= -7.7, -25.9 a.u.; \( t= -1.5; \) two-tailed \( p= 0.002; \) Fig. 3B). No significant differences in thermal sensitivity to warmth were observed at the end of the selective block protocol, either in the forearm (mean difference= +5.1 a.u.; CI= -5.6, 15.9 a.u.; \( t= 1.04; \) two-tailed \( p= 0.32; \) Fig. 3C) or in the index finger pad (mean difference= -5.9 a.u.; CI= -14.4, 2.6 a.u.; \( t= -1.5; \) two-tailed \( p= 0.15; \) Fig. 3D). As the warm and cold-dry stimuli produced the same relative variations in local \( T_{sk} \) throughout the compression ischemia protocol (Fig. 4), these results indicate that this procedure was effective in selectively reducing cutaneous cold sensitivity of both forearm and finger pad, while maintaining warmth sensitivity intact. With regards to mechano sensitivity, at the end of compression ischemia protocol, 2 out of 13 participants were not able to sense the light brush on the forearm (FA-BLOCK trial), whereas during the FI-BLOCK trial 12 out of 13 participants were not able to sense the light brush on the finger pad. Changes in cold and mechano sensitivity occurred earlier for the finger pad than for the forearm. For 11 out of 13 participants, the selective block lasted 20 min during the FI-BLOCK trial and 25 min during the FA-BLOCK trial. It deserves mention that the selective block resulted in paradoxical heat sensations during cold stimulation in 4 participants (i.e. FA-BLOCK trial) and 6 participants (i.e. FI-BLOCK trial). Before the application of the selective block, average values for resting systolic and diastolic pressure were 135mmHg (SD 8) and 66mmHg (SD 6) respectively.

**Cutaneous sensitivity to wetness under selective reduction of A-nerve fibers’ function**

As soon as the compression ischemia protocol resulted effective, the quantitative sensory test was initiated. The results of the sensory test are presented individually for the forearm and then for the finger pad. Similar outcomes were observed for both forearm and finger pad
during the contact with the wet stimuli, after cold and mechano sensitivity was reduced with
the selective block protocol.

With regards to the forearm, during the initial static contact with the warm-wet, neutral-wet and cold-wet stimuli, forearm $T_{sk}$ showed similar variations as the ones recorded during the NO-BLOCK trial (Fig. 1B). However, a significant effect of the compression protocol ($F=10.6_{(1,11)}, p=0.008$) was found on thermal sensation. During the contact with the warm-wet and neutral-wet stimuli, participants’ thermal sensations did not differ significantly between NO-BLOCK and FA-BLOCK trials. However, as a result of the same cold-wet stimulus applied to the forearm, significantly “less cold” thermal sensations were reported during the FA-BLOCK trial [CI= 39.7, 65.5 a.u.] than during the NO-BLOCK trial [CI= 61.3, 82.5 a.u.] (Fig. 1F). These results confirmed that at the time of application of the wet stimuli, the forearm presented a reduced thermal sensitivity to cold.

This artificially induced reduction in cold sensitivity translated into a reduced perception of wetness of the forearm (Fig 1J). Overall, the magnitude of perceived wetness was significantly reduced during the FA-BLOCK [CI= 4.9, 18.8 a.u.] when compared to the NO-BLOCK trial [CI= 21.8, 39 a.u.] ($F=13.7_{(1,12)}, p=0.003$) (Fig. 5A). A trend in the interaction between the effect of the block and the temperature of the stimuli was observed ($F=3.3_{(2,24)}, p=0.07$, observed power= 0.5), with the greatest reduction in perceived wetness occurring during the cold-wet stimulation (see comparison between figures II and 1J). Finally, a significant interaction between condition and phases of stimulation was found ($F=11.7_{(2,24)}, p<0.0001$). As opposed to the NO-BLOCK trial, during which wetness perception increased from static to dynamic and evaporation, during the FA-BLOCK trial, no changes in the forearm wetness perception from static to dynamic and a decrease from dynamic to evaporation occurred (Fig. 2D). Overall these results indicate that the significant reduction in
the magnitude of perceived wetness observed during the FA-BLOCK trial was mainly due to
the reduced cutaneous cold and mechano sensitivity of the forearm.

Similar results were observed during the index finger pad contact with the wet stimuli (i.e.
FI-BLOCK trial). During the initial static contact with the warm-wet, neutral-wet and cold-
wet stimuli, finger pad $T_{sk}$ respectively increased (i.e. warm and neutral-wet) or decreased (i.e.
cold-wet) (Fig. 1D). As a result of the contact with the warm-wet and cold-wet stimuli, “less
warm” and “less cold” thermal sensations were reported during the FI-BLOCK trial than
during the NO-BLOCK trial (Fig. 1H). This interaction between condition (i.e. block vs. no
block) and temperature of the stimuli was found to be statistically significant ($F= 13.1_{(1, 1.5, 17.6)},
p= 0.001$). These results indicated that at the time of application of the wet stimuli, the index
finger pad presented a reduced thermal sensitivity to warmth and cold. This translated into a
reduced sensitivity to wetness (Fig. 1L). A significant effect of condition ($F= 13.9_{(1, 1.2)}, p=
0.003$), a trend in temperature of the stimuli ($F= 2.9_{(2, 24)}, p= 0.072$, observed power= 0.5) and
a significant effect of phases of stimulation ($F= 5.9_{(2, 24)}, p= 0.008$) was found on wetness
perception (Fig. 2E).

Overall wetness sensitivity was significantly reduced during the FI-BLOCK [CI= 0, 2.5 a.u.]
as compared to the NO-BLOCK trial [CI= 8.3, 28.1 a.u.] (Fig. 5B). A significant interaction
between condition and phases of stimulation was found ($F= 5.7_{(2, 24)}, p= 0.001$). As opposed
to the NO-BLOCK trial, during which wetness perceptions increased from static to dynamic,
during the FI-BLOCK trial no changes were observed from static to dynamic to evaporation
(Fig. 2F). Overall these results reflect those observed with the forearm during the FA-
BLOCK trial, and indicate that the significant reduction in wetness sensitivity observed on
the finger pad during the FI-BLOCK trial was mainly due to the reduced cutaneous thermal
and mechano sensitivity of this skin site.
DISCUSSION

The present study focused on the role of cutaneous thermal and tactile afferents and their central integration in the ability to sense wetness. By exposing hairy and glabrous skin sites to the static and dynamic contact with warm-wet, neutral-wet and cold-wet stimuli characterized by the same moisture content (i.e. 20µL/cm²), we demonstrated that during a static contact, wetness perception increases with decreasing contact temperatures and that during a subsequent dynamic interaction, wetness perception increases regardless of the thermal inputs available. Also, we demonstrated that when cutaneous cold and mechano sensitivity was significantly diminished through a selective reduction in the activity of A-nerve afferents, the extent of perceived wetness was also significantly reduced, both on the forearm and index finger pad. Finally, a trend was observed with the extent of perceived wetness being higher on the hairy than on the glabrous skin.

In summary, our results indicate that the central integration of conscious coldness and mechanosensation, as sub-served by peripheral myelinated A-nerve fibers, could be the primary neural process underpinning humans’ ability to sense wetness. To our knowledge the present study is the first to provide evidence in support of the hypothesis that a specific information processing model for cutaneous wetness sensitivity exists and that this is based on A-type somatosensory afferents. Based on these outcomes, we developed the first neurophysiological model of human cutaneous wetness sensitivity (Fig. 6).

A neurophysiological model of cutaneous wetness sensitivity

The proposed neurophysiological model is based on the concept of Bayesian perceptual inference for which sensory processing is considered an inference problem (Knill and Richards, 1996). Given noisy and ambiguous sensory inputs (such can be thermal and
mechanical stimuli on the skin), the brain is thought to estimate which events caused these inputs (e.g. the presence or not of physical wetness on the skin), based on prior knowledge which is acquired and shaped by sensory experience (Lochmann et al., 2012). In our proposed information processing model, two main neural pathways are suggested to subserve cutaneous wetness sensitivity: one referring to the afferent activity of cold sensitive A\(\delta\)-nerve fibers (projecting through the spinothalamic tract), and one referring to the afferent activity of mechano sensitive A\(\beta\) fibers (projecting through the dorsal-column medial lemniscal pathway). The outcomes of this study have indeed indicated that in order to sense cutaneous wetness, a multimodal integration of thermal (i.e. cold) and mechanical sensory inputs had to take place (Fig. 6A). From a functional point of view, this was confirmed by the fact that when the activity of A-nerve fibers was selectively reduced, the extent of perceived wetness was also significantly reduced (Fig. 6B). From a central processing point of view, this was confirmed by the fact that, although all the stimuli had the same moisture levels, warm-wet and neutral-wet stimuli were sensed as significantly less wet than the cold-wet one.

Perceptual learning and somatosensory decision making could contribute to explain why the central nervous system processes sensory information about the perception of wetness in such fashion (Pleger and Villringer, 2013). As the skin seems not to be provided with hygroreceptors (Clark and Edholm, 1985), we hypothesized that the primary and secondary somatosensory cortices, the insular cortex (a cortical region involved in cold temperature sensation) (Craig et al., 2000) as well as the posterior parietal lobe (a cortical region concerned with integrating the different somatic sensory modalities necessary for perception) (McGlone and Reilly, 2010) could be involved in generating a neural representation of a “typical wet stimulus”. This could be based on the multimodal transformation (i.e. information from one sensory sub-modality can be transformed into a map or reference frame defined by another sub-modality) of the somatosensory inputs generated when the skin is
physically wet (Haggard et al., 2013). As the sensory inputs associated to the physical experience of wetness are often generated by heat transfer in the form of evaporative cooling (Ackerley et al., 2012), and mechanical pressure in the form of friction and stickiness (Adams, 2013), the typical neural representation of a wet stimulus might rely on perceiving coldness and stickiness. As for perceptual learning and somatosensory decision making (Pleger and Villringer, 2013), this neural representation could be transformed into a firing rate code, representing the wet stimulus, and then associated to the perception of wetness. Hence, only if the memorized combination of stimuli (i.e. coldness and stickiness), as coded by the specific afferents (i.e. A-nerve fibers) is presented, wetness will be sensed. In the occurrence of physical wetness on the skin, the bottom-up processes (i.e. combination of thermal and mechanical sensory afferents) as well as the top-down ones (i.e. inference of the potential perception based on the neural representation of a typical wet stimulus) might therefore interact in giving rise (or not) to the perception of wetness (Lochman and Deneve, 2011).

At this point however, although perceiving coldness and stickiness is likely to be determinant in the ability to process wetness at a central level, studies by Gerrett et al. (2013) and everyday experience suggest that we are able to sense wetness even in the absence of coldness (e.g. during exposure to warm-humid environments or when in contact with warm water). In these particular conditions, the mechanical and pressure related sensations resulting from the afferent information generated by cutaneous mechanosensitive fibers could therefore play a critical role in the ability to sense wetness. Based on the results of this study, as well as on the available literature, we hypothesized possible mechanisms through which wetness is sensed, according to the sensory inputs available when the skin is in contact with warm, neutral or cold moisture.

Cutaneous sensitivity to warm, neutral and cold wetness
Figure 6C,D shows the process through which warm moisture could be sensed. When the skin is in static contact with warm moisture (i.e. temperature above $T_{sk}$), no activation of cold sensitive Aδ-nerve fibers occurs, and only C-fibers, (subserving conscious warmth sensitivity), and Aβ-nerve fibers (subserving light touch) are involved in the somatosensation of moisture (Fig. 6C). In this scenario, as Aβ are the only nerve fibers available within the processing model we suggest to subserve wetness, cutaneous wetness will be sensed only if a higher level of mechanosensory afferents i.e. a dynamic interaction between skin and warm moisture will occur (Fig. 6D). A similar mechanism applies if the skin is in contact with neutral moisture (i.e. with a temperature equal to $T_{sk}$) (Fig. 6E,F). In support of this, Bergmann Tiest et al. (2012) have recently observed that, during the interaction with wet materials (i.e. cotton wool and viscose), Weber fractions for wetness discrimination thresholds decreased significantly when individuals were allowed dynamic as opposed to the static touching. This indicated that individuals’ cutaneous sensitivity to wetness was increased by a higher availability of mechanosensory afferents, as occurring during the dynamic exploration of the wet materials. The authors concluded that, when thermal cues (e.g. thermal conductance of a wet material) provide insufficient sensory inputs, individuals seem to use mechanical cues (e.g. stickiness resulting from the adhesion of a wet material to the skin) to aid them in the perception of wetness.

In line with Bergmann Tiest et al. (2012), in this study we observed that the lack of thermal inputs (i.e. in the case of neutral wetness) translated in a reduced sensitivity to wetness. This, until a dynamic interaction with the wet stimuli was allowed, and a higher level of mechanosensory afferents was then made available for central integration (Fig. 6E,F). However, and in addition to the findings of Bergmann Tiest et al. (2012), in our proposed neural model we suggest that the extent of perceived wetness is reduced, and mechanosensory afferents are therefore more important, not only when thermal cues are
insufficient, but also when these are the “incorrect” ones. This seems to happen when in contact with warm moisture (Fig. 6C,D). Although in this case thermal cues in the form of warm sensations are available, as these are generated by sensory afferents (i.e. C-nerve fibers) which are “outside” the proposed model for wetness (i.e. relying on A-nerve fibers) and which are not associated with the neural representation of a “typical wet stimulus”, wetness sensitivity to warm moisture is reduced unless more mecanosensory afferents are activated (i.e. stickiness due to the skin friction with the wet stimulus) (Gerhardt et al., 2008; Adams, 2013). In line with this, we have recently shown that during static contact with a wet surface, warm stimuli (i.e. temperature above Tsk) can suppress the perception of cutaneous wetness (Filingeri et al., 2014c).

Behavioral and learning components could contribute to the concept of “incorrect” thermal cues. Psychophysical studies have indeed shown that as humans we tend to associate the blend of warmth and light pressure more to the perception of oiliness (Cobbey and Sullivan, 1922) than to perception of wetness (Bentley, 1900). Everyday’s life further provides evidence in support of why, in the absence of stickiness, warm sensations only seem not to be associated to the perception of wetness. For example, a bleeding nose is an experience we usually become aware of only after this has been pointed out to us, and the “wet area” has been haptically explored by touch. This could be due to the fact that blood temperature (~37°C) is usually higher than Tsk (~30°C) (Mekjavic and Eiken, 2006).

A combination of anatomical, physiological and learning factors could also explain the trend observed with the forearm (i.e. hairy skin) being more sensitive to wetness than the finger pad (i.e. glabrous skin). Hairy and glabrous skin sites differ in terms of innervation and particularly in terms of density of thermo- and mechano-sensory afferents as well as in their biophysical properties. As observed in this study and as previously shown (Norrsell et al., 1999), the hairy skin seems indeed to be more sensitive to thermal stimuli than the glabrous
skin, which on the contrary presents higher spatial acuity. From the receptors point of view, this could be due to the fact that, although both glabrous and hairy skin sites are innervated with slowly adapting type 1 mechano-sensory afferents, also known as Merkel cells (low threshold mechanoreceptors transmitting acute spatial images of tactile stimuli with remarkably high spatial resolution), glabrous skin presents a higher density of these specialized organs for tactile discrimination, a fact which could explain the higher spatial acuity to mechanical stimuli of this type of skin (Abraira and Ginty, 2013). From a biophysical point of view, the presence of a thicker stratum corneum (i.e. the outermost layer of the skin) on glabrous skin, resulting in a greater thermal insulation of this type of skin, contributes to the reduced thermal conductance of the finger pad (Rushmer et al., 1966) and therefore to the lower thermosensitivity of glabrous as opposed to hairy skin during short contact cooling and/or heating. This, as a result of the longer time that is needed for a given change in temperature of glabrous skin’ superficial layers to penetrate to the underlying tissues (e.g. stratum granulosum) where the thermoreceptors lay (McGlone and Reilly, 2010). In this context, as thermal sensitivity seems to play the key role in sensing wetness, it is therefore reasonable to hypothesize that, despite a larger content in highly spatially sensitive mechanoreceptive afferents (Abraira and Ginty, 2013) which could potentially contribute to an increase in the haptic perception of wetness, the lower thermal sensitivity of the glabrous skin might translate in the palm of the hands being generally less sensitive to wetness than the rest of the body. From a thermoregulatory standpoint, this could be supported by the fact that, as opposed to regions covered by hairy skin, human hands are indeed more of a specialized organ for heat exchange than a thermo-sensory organ (Romanowsky, 2014). Finally, from a behavioral point of view, the fact that the hairy skin presents a higher sweat production than the glabrous skin (due to thermoregulatory reasons) (Smith and Havenith, 2012) could result
in individuals expecting to experience cutaneous wetness in larger magnitude on hairy than
on glabrous skin sites.

Further support for the hypothesis of a possible neural representation of a “typical wet
stimulus” being based primarily on cold and mechanosensory A-type afferent, could be found
when looking at the perceptions evoked by the skin’s contact with cold moisture (Fig. 6G,H).

In case of skin’s contact with cold moisture (i.e. temperature below T_{sk}), Aδ-nerve fibers
(subserving cold sensitivity) and Aβ-nerve fibers (subserving light touch) are involved in the
somato-sensation of moisture. In this scenario, as both Aδ and Aβ afferents are available
within the processing pathway we suggest to subserve wetness, the extent of perceived
wetness will be greater as compared to the wetness experienced when in contact with warm
and neutral moisture. In this study we observed that, although all the stimuli had the same
moisture levels, cold-wet stimuli were sensed as significantly wetter than the warm-wet and
neutral-wet one, particularly during the static interaction, when only thermal cues were
available (Fig. 6G). Also, the selective block trials indicated that the extent of perceived
wetness was overall significantly decreased, mainly due to the reduced cutaneous cold and
mechano sensitivity.

The critical role of experiencing coldness in the ability to sense wetness is in line with our
previous findings. We have recently demonstrated that an illusion of local skin wetness can
be evoked during the skin’s contact with a cold-dry surface producing skin cooling rates in a
range of 0.14 to 0.41°C/s (Filingeri et al., 2013, 2014a, 2014b), a temperature course which is
similar to the one suggested to occur when the skin is physically wet (Daanen, 2009).

Evidence in support of the role played by thermal cold afferents in sensing wetness comes
from studies investigating the role of cold-sensitive neurons in ocular dryness and wetness
(Belmonte and Galler, 2011; Hirata and Oshinsky, 2012). Hirata and Oshinsky (2012) have
recently suggested that the sensation of “ocular wetness” could be based on the afferent
activity of corneal cold-sensitive neurons, carrying a sensation of gentle cooling via a
transient receptor potential (TRP) channel activation. The authors proposed this as a potential
eplanation to why tears on the ocular surface could feel wet (Hirata and Oshinsky, 2012).
The possibility that cold-sensitive neurons and TRP channels could be critical determinants
of the human ability to sense wetness represents an intriguing possibility (Montell, 2008),
particularly as TRP channels have been previously shown to be required for hygrosensation
and detection of both dry and moist air in some insects, such as the fruitfly *Drosophila*
*melanogaster* (Liu et al., 2007). However, the speculative nature of this hypothesis highlights
the need for further experimental evidence in order to better understand the still little
investigated neurophysiological mechanisms involved in such complex cognitive function
such as wetness sensitivity. For example, it has to be highlighted that based on the present
results, it cannot be concluded that coldness alone (without tactile component) is sufficient in
generating a perception of wetness. Although we believe that a perception of wetness always
results from the combination of thermal and tactile cues (and in this respect, our proposed
processing model provides evidence in support of which cues the central nervous system
relies more in its prediction of wetness) (Ernst and Banks, 2002) further research should deal
with e.g. whether wetness could be evoked without any tactile component (e.g. through
radiative cooling) or whether tactile stimuli only can evoke wetness, in order to further our
understanding of somatosensation in the context of perceptual inference.
It deserves mention that C-nerve fibers (i.e. polymodal afferents responding to nociceptive,
warm, cool and light mechanical stimulation with conduction velocities ranging from 0.2-
2m/s) (McGlone et al. 2014) have been previously shown to respond to innocuous cold
temperatures (Campero et al. 2001) as well as to touch (Lumpkin and Caterina, 2007).
Therefore, it might be argued that these fibers could also contribute to the sensory processing
of skin wetness. However, as their contribution to conscious cold sensations has not been
proven conclusively (Schepers and Ringkamp, 2010) (therefore suggesting an alternative autonomic thermoregulatory function) and as their mechanical sensitivity seems to be specifically tuned to affective as opposed to discriminative touch (Loken et al., 2009; Olausson et al., 2010), the contribution of C-nerve fibers to the perception of wetness seemed not to be critical, at least not within the experimental conditions of the present study. Indeed, we observed that the reduction in A-nerve fibers’ afferent activity, either when naturally (i.e. static contact with warm and neutral moisture) or artificially (i.e. during the compression ischemia protocol) induced, was sufficient to significantly change the dynamic of the perception of wetness (i.e. significantly diminishing the extent of perceived skin wetness). Nevertheless, due to the polymodal nature of these nerve fibers (McGlone et al. 2014), and due to the absence of a direct measurement of peripheral neural activity in the present study (e.g. by microneurographic recording), the hypothesis of C-fibers significantly contributing to the sensory integration of skin wetness cannot be ruled out conclusively.

In summary, a neurophysiological model of cutaneous wetness sensitivity, based on the multimodal transformation of A-type somatosensory afferents, was developed, in order to explain how humans could sense warm, neutral and cold cutaneous wetness. This model supports the hypothesis that the brain infers about the perception of wetness in a rational fashion, taking into account the variance associated with thermal and mechano afferents evoked by the contact with wet stimuli, and comparing this with a potential neural representation of a “typical wet stimulus”, which is based on prior sensory experience. In this respect, our findings have both a fundamental, as well as a clinical significance. They provide insights on the integration and processing of somatosensory information occurring between peripheral and central nervous system. Also, they provide insights on the possible origin of symptoms such as spontaneous sensations of cold wetness experienced across the body by individual suffering from multiple sclerosis or polyneuropathies (Rae-Grant et al., 1999;
Susser et al., 1999; Nolano et al., 2008; Hulse et al., 2010). As these disorders have been shown to affect peripheral A-nerve fibers functions and to alter somatic perception, the neurophysiological model of cutaneous wetness sensitivity developed in this study could be used as a frame of reference for normal and altered somatosensory function.

GRANTS

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REFERENCES


Fig. 1. Forearm and finger pad skin temperature (°C) and corresponding ratings for thermal sensation and wetness perception (arbitrary units, a.u.) during the static (STAT), dynamic (DYN) and evaporation (EVAP) phases of contact with the warm-wet (35°C), neutral-wet (30°C) and cold-wet (25°C) stimuli. Panels A and C, panels E and G and panels I and K show skin temperature, thermal sensation and wetness perception data respectively as recorded during the NO-BLOCK trial for the forearm and finger pad. Panels B and D, panels F and H and panels J and L show skin temperature, thermal sensation and wetness perception data respectively as recorded during the BLOCK trial for the forearm and finger pad. Two tendencies are illustrated. In the NO-BLOCK trials, thermal sensations matched the variation in skin temperature and wetness perceptions increased with decreasing contact temperatures (static phase) and from static to dynamic to post contact (evaporation). In the BLOCK trials, cold sensitivity was reduced in the forearm, and both warmth and cold sensitivity were reduced on the finger pad. This resulted in a significant decrease in wetness perceptions during all temperature stimulations (and particularly during the cold one) and during all phases of interaction. Data are reported as mean (group average n=13) and SD (vertical lines).

Fig. 2. Ratings for wetness perception (arbitrary units, a.u.) grouped for forearm and finger pad and averaged over (A) temperature of the stimuli (35, 30 and 25°C) and (B) phases of stimulation [static (STAT), dynamic (DYN) and evaporation (EVAP)] as recorded during the NO-BLOCK trial. Panels C and D show data as recorded for the forearm during the FA-BLOCK trial, whereas panels E and F show data as recorded for the finger pad during the FI-
BLOCK trial. Two tendencies are illustrated. During the NO-BLOCK trial, wetness perception increased with decreasing contact temperatures, and from static to dynamic and evaporation phases. During the BLOCK trials, wetness perception was reduced at any temperature for both forearm and finger pad, and no changes occurred from static to the dynamic phase. Data are reported as mean (group average n= 13) and 95% CI (vertical lines).

Fig. 3. Ratings for thermal sensation (arbitrary units, a.u.) as a result of the cold (25°C) and warm (35°C) stimuli as recorded before (PRE-BLOCK) and at the end (i.e. just before application of wet stimuli, POST-BLOCK) of the compression ischemia protocol. Panels A and C show average and individual ratings for thermal sensation for the forearm. Panel B and D show average and individual ratings for thermal sensation for the finger pad. Mean difference (group average n= 13) and 95% CI between pre and post-block are also shown. One main tendency is illustrated. At the end of the BLOCK trials, thermal sensitivity on the cold side was significantly reduced while no significant changes in sensitivity on the warm side occurred, both for forearm and finger pad. Data are reported as mean (group average n= 13) and 95% CI (vertical lines).

Fig. 4. Representative skin blood flow (A) (arbitrary units, a.u.), forearm (B) and finger pad (C) skin temperature (°C) as recorded for participant 4 during the cutaneous thermal sensitivity test performed during the BLOCK trials. Cutaneous thermal sensitivity was tested as follow: the thermal probe’s temperature was first set to 35°C and as soon this temperature was reached (response time < 4s) participants were asked to rate their thermal sensation only. The thermal probe was then re-set to 30°C. As soon as the skin temperature returned to 30°C, the thermal probe’s temperature was changed to 25°C (i.e. cold stimulus) and participants were asked again to rate their thermal sensation only. The thermal probe was then re-set to
30°C. Throughout the compression ischemia protocol, the cold and warm dry stimuli always resulted in the same variation in skin temperature.

Fig. 5. Ratings for wetness perception (arbitrary units, a.u.) averaged over condition (NO-BLOCK vs. BLOCK) for the forearm (A) and finger pad (B). A significant reduction in wetness sensitivity was recorded during the BLOCK trials as compared to the NO-BLOCK, both for the forearm and finger pad. Data are reported as mean (group average n= 13) and 95% CI (vertical lines).

Fig. 6. Neurophysiological model of cutaneous wetness sensitivity. Mechano Aβ, cold Aδ and warm C sensitive nerve fibers and their projections from the skin, through peripheral nerve, spinal cord (via the dorsal-column medial lemniscal pathway and the spinothalamic tract), thalamus and somatosensory cerebral cortex (including the primary and secondary somatosensory cortex cortices SI and SII, the insular cortex and the posterior parietal lobe) are shown. Panel A and B shows the neural model of wetness sensitivity (consisting of Aδ and Aβ afferents) under normal and under selective reduction in the activity of A-nerve fibers respectively. Panel C, E and G show the pathways for wetness sensitivity during static contact with warm, neutral and cold moisture. Panel D, F and H shows the pathways for wetness sensitivity during dynamic contact with moisture.
A
Forearm (group average n = 13)

B
Finger pad (group average n = 13)