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High-density thermal sensitivity maps of the body of people with multiple sclerosis: Implications for inclusive personal comfort systems

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ABSTRACT

Inclusive thermal comfort solutions should accommodate the need of clinical groups such as people with Multiple Sclerosis (pwMS), who experience abnormal thermal sensitivity. The aim of this study was to develop high-density body maps of temperature sensitivity in pwMS to inform the design of patient-centred personal comfort systems.

Fourteen pwMS (6 M/8 F; 48.6 ± 10.0 y) and 13 healthy individuals (CTR; 5 M/8 F; 47.8 ± 10.4) underwent a quantitative sensory test in a thermoneutral environment, during which they rated their local thermal sensations arising from the application of warm (39°C) and cold (27°C) stimuli to 115 bilateral body sites across the face, torso, upper and lower limbs. We used a z-transformation to create maps of hypo- and hyper-sensitivity for each individual MS participant using normative CTR data.

We found that 50% of pwMS (N = 7/14) presented a loss of cold sensitivity over the upper limb, and a loss of warm sensitivity over the feet. Furthermore, 36% of pwMS (N = 5) presented warm hyper-sensitivity over the upper limb. Finally, cold sensitivity loss and warm sensitivity gain were more evenly distributed and affected a greater proportion of skin sites in MS (i.e. cold hypo-sensitivity = 44% of tested sites; warm hyper-sensitivity = 14%) than warm sensitivity loss (i.e. 10%), which was more focused on sites such as the feet.

Our findings highlight the need to consider "thermosensory corrective power" when designing personal comfort systems, to accommodate either thermosensory loss or gain in pwMS. Our approach to clinical body mapping may support this process and help meeting the unique thermal needs of vulnerable individuals.

1. Introduction

In 2021, the built environment sector alone was responsible for ~40% of global energy-related CO_2 emissions, which are a key contributor to climate change and global warming (UN, 2022). Temperature extremes and extreme weather events induced by climate change (such as heat waves and cold spells) severely limit people's work and exercise capacity, with consequent detrimental effects on individuals' health, comfort, and productivity (Ebi et al., 2021). This is translating in a growing social and economic burden on healthy and vulnerable groups, as well as on businesses and health services worldwide (Jay et al., 2021).

A large part of CO_2 emissions related to the built environment arise from the need to heat or cool buildings to maintain occupants' thermal comfort (Yang et al., 2014). While thermal comfort models and solutions for building occupants are available (Mamulova et al., 2023), these do not fully capture how individual differences in thermal sensitivity, such as those resulting from sex, age, and importantly, clinical status, contribute to people's responses, preferences, and vulnerability to different thermal environments (Schweiker et al., 2018). As a result, we are still far from reaching thermal comfort, thermal health, and thermal safety for all in buildings.

The development of personal comfort systems such as heating and cooling wearables, devices, and smart clothing, that condition local body parts via radiant beams, jets of air, or by contact with warmed or cooled conductive surfaces (Zhang et al., 2015), has recently received significant attention within the built environment sector (Rawal et al., 2020; Song et al., 2022). These energy-efficient systems serve to both

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mitigate thermal discomfort and to induce positive sensations of thermal pleasure through heating or cooling specific body parts (Pasut et al., 2015; Zhang et al., 2015). As a result, personal comfort systems can offer significant energy-savings by de-centralising and offsetting the reliance of building occupants on central heating and cooling (Rawal et al., 2020).

Designers of personal comfort systems have recently benefitted from the development of high-density body maps of thermal sensitivity in healthy young males and females (Filingeri et al., 2018; Valenza et al., 2019, 2023a,b Luo et al., 2020). These maps can guide the provision and optimization of person-centred thermal comfort via wearables [e.g. see (Arens et al., 2023)] that target highly thermally-sensitive skin sites within specific body parts such as the hands, feet, or torso (Filingeri et al., 2014; Filingeri et al., 2018). This approach is maximising the potential for these devices to offer significant energy- and cost-benefits to the built environment sector. However, to develop more inclusive solutions that can help mitigate the impact of global warming, designers of personal comfort systems should also consider how the performance of such devices may change when end-users experience impairments in their ability to detect temperature across their body due to underlying pathology (Stein and Stein, 2022; Zallio and Clarkson, 2022, 2023).

For example, we know that individuals affected by chronic illness e.g. common neurodegenerative diseases such as Multiple Sclerosis (MS), experience a heightened sensitivity to thermal discomfort resulting from exposures to warm or cold environments (Christogianni et al., 2018a, Christogianni et al., 2023); and they may also present an impaired ability to detect changes in temperature (and wetness) across their body when warm or cold stimuli contact their skin (Filingeri et al., 2017, 2021; Christogianni et al., 2021, 2022a). From a physiological standpoint, we have previously reported that cold sensitivity appear to be more widely affected than warm sensitivity across the body of people with MS (Filingeri et al., 2017a, 2021), and that this is likely due to the characteristic neural demyelination associated with MS, which may have a greater impact on the central, myelinated afferent pathways for cold sensing, as compared to central, non-myelinated, warm-sensitive neural pathways (Filingeri et al., 2017a, 2021).

The underlying neural mechanisms of impaired thermal sensitivity in pwMS remain to be elucidated (e.g. central vs. peripheral mechanisms involved in thermo-sensation and MS-induced demyelination) (Misawa et al., 2008). Nevertheless, the pathophysiological evidence of thermosensory abnormalities in this group indicates that the design and provision of personal comfort systems that leverage thermal body maps acquired from healthy individuals, is unlikely to meet the unique thermosensory needs of clinical groups such as people with MS. The lack of personalised solutions that consider the specific thermal and comfort needs of people with disabilities within the built environment can create further barriers to conducting normal working activities (Zallio and Clarkson, 2022, 2023), with significant socio-economic implications for employment loss, early retirement, and healthcare cost burdens (Coyne et al., 2015; Persechino et al., 2019; Stein and Stein, 2022).

Our group has recently acquired preliminary evidence that people with MS present an impaired ability to detect cold stimuli on their skin as well as a heightened sensitivity to heat discomfort (Filingeri et al., 2017a, Christogianni et al., 2023). However, we still lack high-density maps of temperature sensitivity and impairments across the body of people with MS, which could inform the optimization of design parameters for personal comfort systems (e.g. corrective power and/or alternative body location), which can better meet the thermal needs of individuals with physical and mental disabilities. Developing such (patho-)physiological evidence on thermal sensitivity across the body of groups such as people with MS could inform the design of more effective, user-centred personal comfort systems that support clinical thermal needs and facilitate equality, diversity and inclusion within the built environment (Zallio and Clarkson, 2022). Furthermore, this methodological approach to clinical body mapping could offer a research platform to better understand individual comfort needs amongst other neurological conditions (e.g. Alzheimer's and Parkinson's disease) (Coon and Low, 2018) and beyond (e.g. vascular syndromes such as Raynoud's disease) (Bergersen and Walløe, 2018).

The aim of this study was to develop high-density body maps of temperature sensitivity in people with MS, and to identify body parts that are more likely to experience thermosensory abnormalities. MS is the most common neurodegenerative disease in young adults, with ~3 million people affected worldwide (Walton et al., 2020); hence, it offers a unique model to understand clinical thermosensory needs in individuals that spend a significant proportion of their (working) life with a disease that has a significant impact on their heat and cold tolerance (Christogianni et al., 2018a). To achieve our aim, we utilised a standardized quantitative sensory test (Filingeri et al., 2018) to evaluate warm and cold sensitivity across 115 body sites in a cohort of people with MS, as well as in a group of age- and sex-matched healthy individuals, in order to develop individual and group body maps of thermosensory abnormalities. We believe that these novel clinical body maps will facilitate the development of energy-efficient and inclusive thermal comfort solutions within the built environment which meet the needs of individuals with (thermal) disabilities.

2. Methods

Ethical approval

The testing procedures 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 (#R17-P094), and testing procedures were in accordance with the tenets of the Declaration of Helsinki (note: the study was not registered in a database).

2.1. Participants

We performed a power calculation (G*Power 3 software (Heinrich-Heine-Universität Düsseldorf, Germany) with α of 0.05, β of 0.20 using an effect size of 16.8, calculated from the mean difference in thermal sensation on the skin between an MS and a control group (Filingeri et al., 2014*b*, 2017*b*), to determine a minimum sample size of 8 individuals per group. Considering potential inter-individual variability in the heterogeneity of MS symptoms, we set a minimum target sample of 12 participants per group (i.e. minimum sample size +50%).

Based on the above, we were able to recruit 14 people with MS (6 M/8 F; mean age = 48.6 years, SD = 10.0; mean height = 173.0 cm, SD = 0.1; mean body mass = 79.1 Kg, SD = 17.9, mean Expanded Disability Status Scale (EDSS): 5, range = 1–7) who presented with various disease courses [i.e. relapsing-remitting (N = 7), primary (N = 5) and secondary progressive (N = 2) MS]. We appreciate that those disease courses present distinct pathophysiological pathways, and the inclusion of various MS types in this experiment was also driven by constraints associated with convenience sampling. Upon completion of the MS group recruitment, we went on recruiting a sex- and age-matched healthy control (CTR) individual for each MS participant. CTR individuals (N = 13) reported no sensory, cardiovascular, neurological, or metabolic diseases (5 M/8 F; mean age = 47.8 years, SD = 10.4; mean height = 171.0 cm, SD = 0.1; mean body mass = 76.2 kg, SD = 18.2). All participants had lived in the UK for at least 2 years before the test and they had not travelled out of the UK for at least 3 months before the beginning of the study.

Participants' individual characteristics are reported in Table 1.

In the MS group, MS participant M reported taking the immunomodulator Copaxone, and the MS participant D reported taking the spasticity medication Baclofen. In addition, MS participant D self-reported commonly experiencing moderate anxiety and pain catastrophizing; MS participant N self-reported commonly experiencing moderate stress, depression and anxiety, and pain catastrophizing; MS

Table 1
Participants' individual characteristics.

Group	ID	Age (y)	Height (m)	Weight (kg)	Sex	Ethnicity	EDSS	MS type	Body side affected	HS	CS
MS	A	61	1.78	89.5	M	WE	6	PP	Left	Y	Y
	B	53	1.74	61.0	M	WE	4	SP	Unknown	Y	N
	C	44	1.78	76.3	M	WE	1	RR	Unknown	Y	Y
	D	51	1.57	99.4	F	WE	6.5	PP	Left	Y	N
	E	33	1.68	104.6	F	WE	3.5	RR	Left	Y	N
	F	33	1.63	63.6	F	WE	3.5	RR	Unknown	Y	Y
	G	40	1.61	63.5	F	Asian	3	RR	Right	Y	Y
	H	47	1.74	105.0	F	WE	7	PP	Unknown	Y	N
	I	53	1.74	61.1	F	WE	6	PP	Left	Y	Y
	J	59	1.60	47.8	F	WE	6.5	PP	Left	Y	N
	K	58	1.73	68.9	F	WE	6.5	RR	Left	Y	N
	L	38	1.66	68.9	M	Asian	1	RR	Unknown	Y	Y
	M	47	1.92	77.6	M	WE	7	RR	Unknown	Y	Y
	N	63	1.97	95.9	M	WE	6.5	SP	Right	Y	N
CTR	A	55	1.60	66.2	F	WE	–	–	–	–	–
	B	50	1.54	83.8	F	Asian	–	–	–	–	–
	C	31	1.72	116.7	F	WE	–	–	–	–	–
	D	37	1.77	70.5	M	WE	–	–	–	–	–
	E	60	1.63	76.5	F	WE	–	–	–	–	–
	F	52	1.73	64.0	M	WE	–	–	–	–	–
	G	32	1.71	58.4	F	WE	–	–	–	–	–
	H	48	1.82	73.9	F	WE	–	–	–	–	–
	I	61	1.68	63.1	F	WE	–	–	–	–	–
	J	49	1.83	108.2	M	WE	–	–	–	–	–
	K	62	1.70	83.3	M	WE	–	–	–	–	–
	L	44	1.78	56.4	M	WE	–	–	–	–	–
	M	42	1.67	68.8	F	WE	–	–	–	–	–

MS: Multiple Sclerosis; CTR: control; Sex: M = Male; F= Female; Ethnicity: WE= White European; EDSS = Expanded Disability Status Scale; MS type: RR= Relapsing Remitting; PP= Primary Progressive; SP= Secondary Progressive. HS = experience heat sensitivity; CS = experience cold sensitivity. Note: average heights and weights were not statistically different between MS and CTR groups (independent *t*-test height, $p = 0.634$; independent *t*-test weight, $p = 0.863$).

participant I self-reported commonly experiencing moderate stress, depression, and anxiety; and MS participant G self-reported commonly experiencing moderate anxiety.

Matching MS and CTR groups by age, sex, and (to the extent possible) body dimensions, aimed to minimize confounding factors. Exclusion criteria for relapsing-remitting MS participants were having had a (self-reported) relapse in the three months prior to the experiment (i.e. defined as being at least 3 months out from receiving a steroid injection and/or being hospitalized), and (applicable to all MS participants) to be currently taking medications that directly affect cognition. Three MS participants (Participant D, G, M) reported previous experience of abnormal sensitivity to wetness on their skin. The phase of the menstrual cycle was not controlled in the female participants.

Participants were instructed to refrain from: 1) performing strenuous exercise in the 48 h preceding testing; 2) consuming caffeine or alcohol in the 24 h preceding testing; 3) consuming food in the 3 h preceding testing. All testing took place at Loughborough (UK) between June 2017 and July 2019, spanning different seasons. There were no differences between the MS and CTR groups in the frequency of testing across seasons (i.e. MS group: 12 tests carried out during winter months/8 tests carried out during spring months/16 tests carried out during summer months; CTR group: 10 tests carried out during winter months/6 tests during spring months/17 tests during summer months) as well as in average outdoor temperatures (i.e. MS group: 15.8 ± 6.2 °C vs. CTR group: 12.8 ± 8.2 °C; T-test $p = 0.09$). It should be noted that the participants of the current study are the same as the ones who took part in related investigations recently reported in (Christogianni et al., 2022*a*, 2023).

2.2. Experimental design and protocol

We used a single-blind psychophysical approach based on a well-established quantitative sensory test of skin temperature sensitivity that we have developed (Filingeri et al., 2018), to map individual differences between MS and CTR groups in regional warm and cold sensitivity over 115 bi-lateral sites across the front and back of the body (Fig. 1). Supplementary Material Table 1S presents exact anatomical locations for all tested sites.

Due to the large number of body sites to be tested (N = 115), and the resulting risk of participants' fatigue, we deemed it appropriate to test the 115 sites across 3 separate visits to the laboratory, during which a different portion of the body was evaluated [i.e. 1st session: 35 body sites over the front and back of the face and torso); 2nd session: 40 body sites over the front and back of arms and hands; 3rd session: 40 body sites over the front and back of legs and feet). As a result, all participants took part in 3 experimental sessions on different days (note: time of day between sessions was maintained for each participant) and separated by a minimum of 48 h, during which they underwent seated resting in a climatic chamber regulated to thermoneutral environmental conditions (24°C air temperature and 50% relative humidity).

During the quantitative sensory test, participants had to report the perceived magnitude of local thermal sensations arising from the short-duration static (i.e. 10s) application (i.e. counter-balanced) of either a cold (i.e. 27 °C) or warm (i.e. 39 °C) hand-held temperature-controllable probe (surface area: 1.32 cm^2; NTE-2A, Physitemp, USA). The probe was initially applied onto the skin (i.e. 5s) at a thermo-neutral temperature of 33 °C. At this point, the probe's temperature would be either increased or decreased to the target warm or cold temperatures (note: stimuli' order was counter-balanced between body sites and participants). Upon reaching the target temperature (i.e. 10s), the participants would be verbally required to report the perceived magnitude of local thermal sensation using a 0–10 numerical rating scale whose anchor points 0 and 10 were labelled as "Not hot/Not cold at all" and "Very Hot/Very Cold", respectively (Filingeri et al., 2018). Application pressure was not measured but was controlled to be sufficient to ensure full contact, while not resulting in pronounced skin indentation. Upon

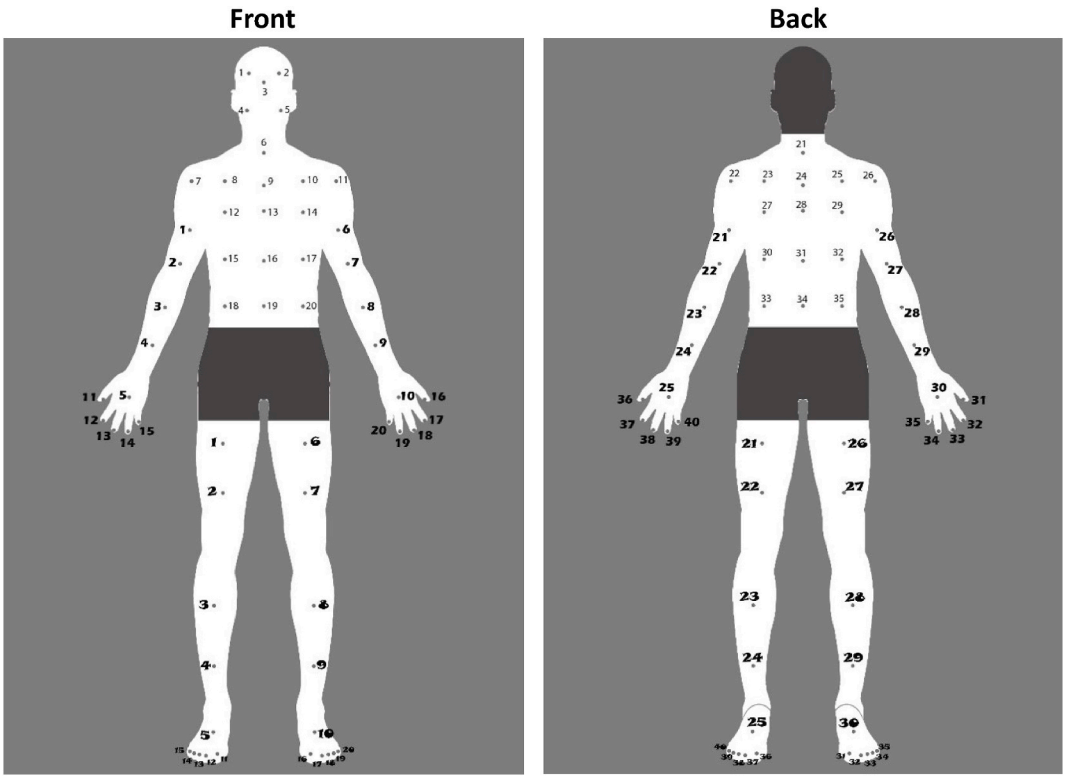

Fig. 1. The location of the 115 bi-lateral sites across the front and back of the body.

acquisition of the local perceptual score to e.g. the warm stimulus, the investigator tested the e.g. cold stimulus at the same body site, before moving onto the next body site and repeat the same procedure (note: a 30-s pause was allowed in between testing sites). Assessment of all sites for the specified testing session required between 35 and 40 min.

During all quantitative sensory testing, we continuously monitored whole-body mean skin temperature and core (rectal) temperature in all participants. This was accomplished by using skin thermistors (Grant Instruments, Cambridge, UK) attached to 6 skin sites (i.e. cheek, chest, arm, hand, thigh, back) with medical tape, to record local skin temperatures (2 Hz). Local measurements were then used to calculate a weighted whole-body mean skin temperature according to the following equation by Palmes and Park (1947) (Park and Palmes, 1947):

Whole-body mean skin temperature = (Cheek x 0.14) + (Chest x 0.19) + (Arm x 0.11) + (Hand x 0.05) + (Thigh x 0.32) + (Back 0.19).

Core temperature was recorded continuously during all testing using rectal thermistors (Viamed Ltd, West Yorkshire, UK), which the participants self-inserted at the start of each session 12 cm beyond the anal sphincter.

3. Data analysis

3.1. Thermophysiological variables

To determine the independent and interactive roles of group (i.e. MS vs. CTR), testing sessions (i.e. 3 levels) and time (i.e. 5-min epochs during 35 or 40-min sessions) on changes in whole-body mean skin temperature and core (rectal) temperature, data were tested for normality (Shapiro-Wilk test) and then analysed by means of a 3-way mixed ANOVA [statistical software package SPSS (v18, IBM, USA)].

3.2. Determination of thermosensory profiles

Thermal sensation data were analysed individually for each MS participants according to a z-transformation using a method we have previously reported (Filingeri et al., 2021). This transformation allowed for the creation of thermosensory profiles for each individual MS participant, and for their subsequent assessment against normative data arising from the CTR group. This standardized approach is widely used in the context of assessing sensory loss in individual patients. For a detailed overview of the method, see Rolke et al. (Rolke, 2006a; Rolke et al., 2006b). Analytical procedures used in this study are detailed below.

First, thermal sensation data for each MS and CTR participants were log-transformed (Log 10). Second, log-transformed individual MS datasets (i.e. for each body site and for each thermal stimulus) were z-transformed according to the following equation:

$$\text{Thermal sensation Z score} = \frac{\text{Thermal sensation}_{\text{MS participant}} - \text{Mean thermal sensation}_{\text{CTR group}}}{\text{Standard Deviation of mean thermal sensation}_{\text{CTRgroup}}}$$

This transformation results in a sensory profile where thermal sensations are presented as standard normal distributions [zero mean, unit variance]. Once the z transformation is performed, it is easy to compare individual MS participants' sensory profiles with the group mean of the CTR group. Indeed, the 95% Confidence Interval (CI) of a standard normal distribution is given by the following equation:

95% CI = Mean thermal sensation$_{CTR\ group}$

± 1.96 Standard Deviation of mean thermal sensation$_{CTRgroup}$

Accordingly, if a thermal sensation z score for an individual MS participant is >+1.96, then the participant exhibits gain of thermosensory function (i.e. their sensation is more intense than the 95% CI of the CTR group); on the contrary, if a z score for an individual MS participant is > -1.96, then the participant exhibits loss of thermosensory function (i.e. their sensation is less intense than the 95% CI of the CTR group).

Z scores were calculated and analysed as above for both cold and warm stimuli, across all tested 115 body sites, for all 14 MS participants.

3.3. Creation of individual thermal sensitivity maps in MS

To aid in visualization of individual thermosensory patterns across the body, the z-transformed data for each MS participant were used to generate individual, high-density warm and cold sensitivity maps. High-density maps were generated using a custom-written MatLab script (The MathWorks, Inc., Natick, MA), as we have previously reported (Filingeri et al., 2018). MatLab interpolation and extrapolation functions were used to create HeatMap objects, which were then superimposed over images of a standard body silhouette and morphed accordingly with an imaging software (Photoshop, Adobe Systems Inc., San Jose, CA). The individual maps were colour-coded to highlight excursions of individual z-values beyond the 95% CI for normative thermal sensitivity.

3.4. Creation of group-level maps of hyper- and hypo-sensitivity in MS

To identify whether specific body sites across the bodies of people with MS may be more likely to undergo thermosensory loss or gain, we calculated the frequency of MS participants presenting a Z score beyond (i.e. ±) the 95% CI for normative thermal sensitivity for each of the 115 body sites tested. In this way we were able to create group-level maps of hyper- and hypo-sensitivity to warm and cold stimuli as identified in the MS cohort.

4. Results

4.1. Thermophysiological responses

Whole-body mean skin temperature did not differ between groups ($F_{1,19} = 0.001$; $p = 0.97$; MS mean value = 31.4°C; SD = 0.1; CTR mean value = 31.3°C; SD = 0.5), nor it changed over time or amongst the 3 sessions ($F_{57.292,2.748} = 0.73$; $p = 0.53$). Similarly, core (rectal) temperature did not differ between groups ($F_{1,19} = 0.08$; $p = 0.77$; MS mean value = 36.9°C; SD = 0.1; CTR mean value = 36.8°C; SD = 0.8) nor it changed over time or amongst the 3 sessions ($F_{10,190} = 1.03$; $p = 0.42$). These data indicated that all groups maintained a thermo-neutral state during all testing (i.e. whole-body mean skin temperature = ~31.3 °C; core temperature = ~36.8°C).

4.2. Individual thermal sensitivity maps in MS

We found a high heterogeneity in individual thermosensory patterns across the body of our 14 MS participants. Specifically, participants experienced various degrees of 1) hyposensitivity (e.g. the same warm/cold stimulus is perceived as less warm/cold than the CTR group reported); 2) hyper-sensitivity (e.g. the same warm/cold stimulus is perceived as warmer/colder than what healthy CTR would report); or 3) paradoxical sensations (e.g. a warm stimulus is perceived as cold and vice-versa). These thermo-sensory abnormalities were experienced either alone or in combination (i.e. over different body sites). All individual body maps are reported in Figs. 2 and 3. Furthermore, individual thermal sensation and z-score data are reported in Supplementary Material Table 2S. Below we report 4 examples participants per thermal stimulus to illustrate such patterns.

When considering warm sensitivity (Fig. 2), participant A presented warm sensitivity loss above the umbilicus (z-score = −4.92), left abdomen (z-score = −4.59) and middle back (z-score = −4.23), as well as some paradoxical (cold) sensations on the forehead (z-score = −5.42). Participant M presented warm sensitivity loss mostly in the (bi-) lateral lower back (z-score range = −2.42 to −2.56), and upper legs (z-score range = −2.63 to −3.85). On the other hand, Participant I presented increases in warm sensitivity mostly over the back of the torso (z-score range = −1.96 to −2.37) and the back of right leg (z-score range = −2.01 to −2.68). Similarly, participant N presented increases in warm sensitivity on the forehead (z-score range = −2.06 to −2.15), right shoulder (z-score = −2.00), and lateral torso (z-score range = −2.07 to −2.47).

When considering cold sensitivity (Fig. 3), participant J presented cold sensitivity loss across most of the front torso (z-score range = −2.35 to −3.74), as well as the front and back upper legs (z-score range = −1.99 to −7.71). Similarly, participant K presented cold sensitivity loss on the front neck (z-score = −3.43), hands (z-score range = −2.35 to −3.74) and left leg (z-score range = −2.36 to −2.96). On the contrary,

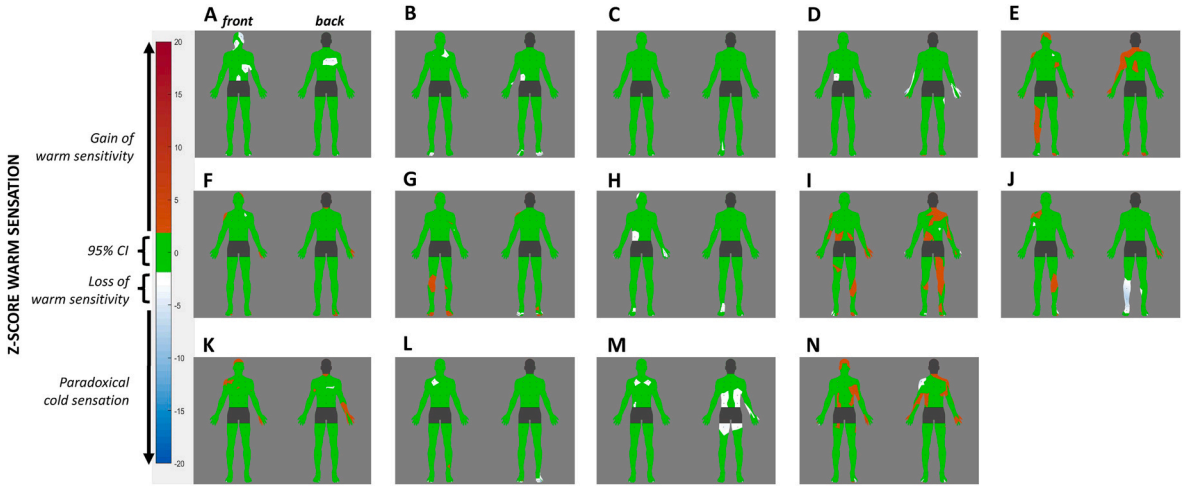

Fig. 2. Individual body maps highlighting abnormalities in warm sensitivity across the front and back of each MS participant (N = 14). The individual maps are colour-coded to highlight excursions (i.e. gain or loss of warm sensitivity) of individual z-values beyond the 95% CI for normative thermal sensitivity (coded in green). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

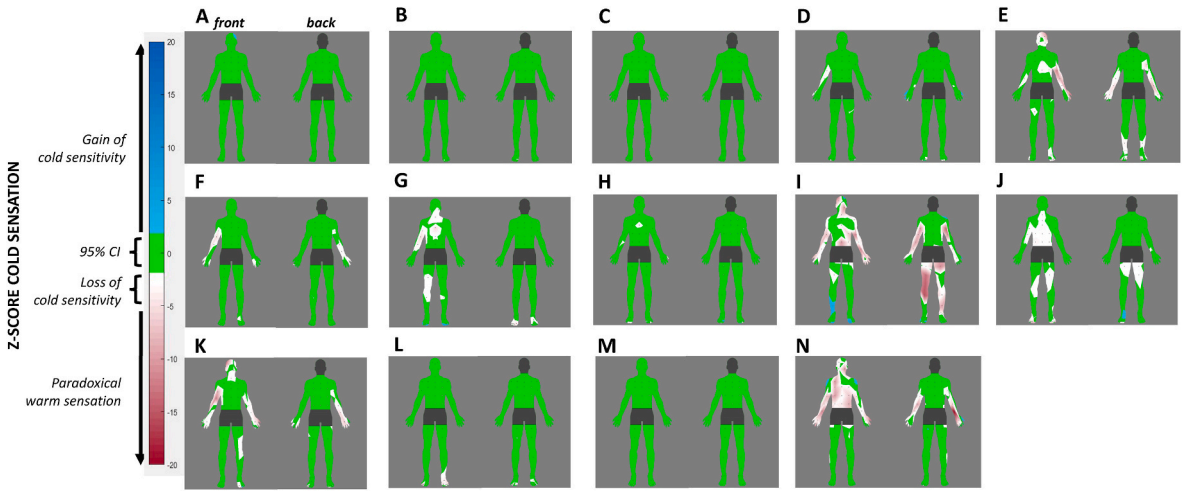

Fig. 3. Individual body maps highlighting abnormalities in cold sensitivity across the front and back of each MS participant (N = 14). The individual maps are colour-coded to highlight excursions (i.e. gain or loss of cold sensitivity) of individual z-values beyond the 95% CI for normative thermal sensitivity (coded in green). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

participant N presented paradoxical (warm) sensations over most of the front torso z-score range = −2.35 to −10.63). Similarly, participant I presented paradoxical (warm) sensations over most of the arms (z-score range = −2.00 to −11.83) and back of the legs (z-score range = −2.36 to −15.29).

4.3. Group-level maps of hyper- and hypo-sensitivity in MS

Despite a high heterogeneity of individual thermosensory patterns across the body of our 14 MS participants, when considering group-level maps of hyper- and hypo-sensitivity, we identified some general observations. Frequency data for all tested regions data are reported in Supplementary Material Table 2S.

First, we found that cold hyposensitivity was highly prevalent across almost half of the body sites tested [i.e. it occurred in at least 20% of the MS cohort (N = 3/14) over 51 sites (i.e. 44% of the total)], and it was particularly frequent at the upper limb [i.e. 50% of the MS cohort, N = 7 experienced cold hypo-sensitivity at the right arm (site 2 of the arms/hands area) and at the right dorsal forearm (site 29 of the arms/hands area)] (Fig. 4A). On the contrary, cold hyper-sensitivity was fairly rare in our MS cohort (e.g. only ~14% of participants presented this on sites 16, 17, and 31 of the legs/feet area, i.e. ~3% of the total) (Fig. 4B).

Second, we found that 50% of our MS cohort (N = 7) reported warm hypo-sensitivity in the left foot toe (site 17 of legs/feet areas).

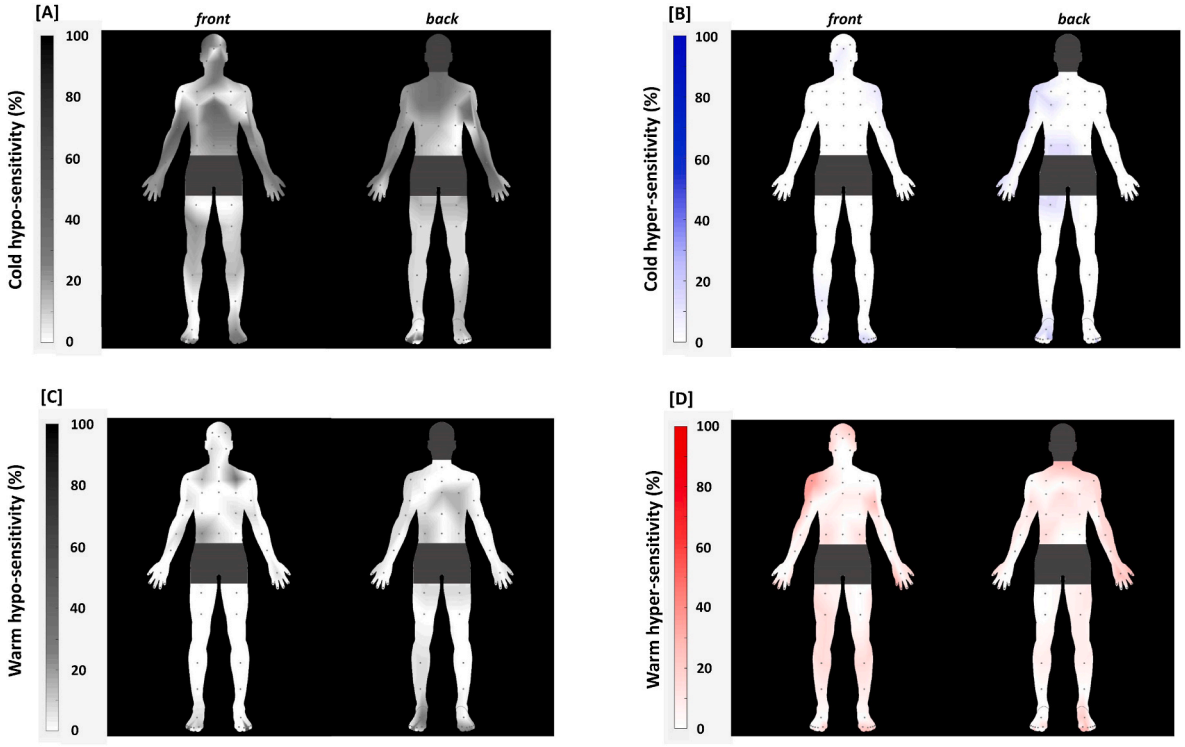

Fig. 4. Group-level body maps representing the frequency of MS participants presenting a Z score beyond (i.e. ±) the 95% CI for normative thermal sensitivity for each of the 115 body sites tested. Group-level maps refer to the body regional frequency of hypo- [A] and hyper-sensitivity to cold [B], and of hypo- [C] and hyper-sensitivity to warm [D].

Furthermore, ~30% of the sample (N = 4) also presented warm hypo-sensitivity over the upper left (front) torso (site 10 of front of body torso areas), the left foot's sole (site 25 of legs/feet areas), and the right foot toe (site 34 of legs/feet areas) (Fig. 4C). Altogether, warm hypo-sensitivity appeared more prominent over the feet in our MS cohort.

Third, we found that 36% of the MS cohort (N = 5) reported warm hyper-sensitivity on the right shoulder (site 7 of the front of body torso area) and finger of the left hand (site 20 of the arm/hands area). Furthermore, ~30% of the sample (N = 4) reported warm hypersensitivity in the upper left forearm (site 6 of the arm/hands area), in the left finger (site 19 of the arm/hands area), in the right hand dorsum (site 30 of the arm/hands area) and in the left foot toe (site 37 of the legs/feet area) (Fig. 4D). Altogether, warm hyper-sensitivity appeared more prominent over the upper limb in our MS cohort.

5. Discussion

The aim of this study was to develop high-density body maps of temperature sensitivity in people with MS, and to identify body parts that are more likely to experience thermosensory abnormalities.

The first key finding of this study is that thermosensory abnormalities were very frequent in people with MS, as evidenced by i) 50% of our sample (N = 7/14) presenting a loss of cold sensitivity over the upper limb; ii) 50% of our sample presenting a loss of warm sensitivity at the feet; iii) 36% of our sample (N = 5) presenting a gain of warm sensitivity over the upper limb. The second key finding of this study is that cold sensitivity loss and warm sensitivity gain were more evenly distributed and affected a greater proportion of body sites (i.e. cold hypo-sensitivity = 44%; warm hyper-sensitivity = 14%) than warm sensitivity loss (i.e. 10%), which was more focused on specific body sites such as the feet.

To our knowledge, the high-density body maps reported here are the most detailed maps of thermosensory abnormalities in a thermally-vulnerable clinical group (such as people with MS) ever reported.

From a fundamental standpoint, our findings are in line with our previous evidence that cold sensitivity appear to be more widely affected than warm sensitivity across the body of people with MS (Filingeri et al., 2017a, 2021). This observation is in keeping with our previous suggestion that the characteristic neural demyelination associated with MS may have a greater impact on the central, myelinated afferent pathways for cold sensing, as compared to central, non-myelinated, warm-sensitive neural pathways (Filingeri et al., 2017a, 2021). Importantly, our current data expands on our previous evidence by providing detailed thermosensory responses across 115 body sites in people with MS.

Fundamentally, it is also worth noting that warm hyper-sensitivity was more evenly distributed and affected a greater proportion of body sites than loss of warm sensitivity. We have long known that people with MS are particularly heat sensitive and that increases in body temperature are accompanied by a worsening of symptoms (Christogianni et al., 2018a). In addition, we have recently demonstrated that this clinical group experience greater thermal discomfort for the same increases in ambient and skin temperature, regardless of changes in internal (core) temperature (Christogianni et al., 2023). Our data on warm hyper-sensitivity may therefore indicate that some people with MS may present a lower tolerance to warm discomfort due to a heightened skin sensitivity to warm stimuli.

Finally, when considering the participants with MS who experienced some of the most pronounced thermo-sensory abnormalities, e.g. ID(s) A, I, M, and N for warm sensitivity (see Fig. 2), we found that they differed quite broadly in terms of their individual characteristics, i.e., sex (both males and females), age (range: 47–63 y), and MS type (i.e. primary and secondary progressive as well as relapsing remitting). Yet, we noticed that all 4 participants presented high EDSS scores (i.e. 6 to 7) indicating significant motor disability. This finding in line with our previous survey data in a large cohort of ~800 people with MS, for whom we identified the level of motor disability as a strong predictor of individual vulnerability to heat-related symptom worsening (Christogianni et al., 2022b). However, it is important to note that the current sample is too limited to allow for meaningful inference on the role of the accumulation of disability on individual susceptibility to thermosensory abnormalities. Accordingly, future studies should consider evaluating individual variability in thermosensory abnormalities in relation to risk factors such as EDSS score, in larger cohorts of pwMS. It should also be noted that a major limitation of the present study is that we did not have access to participants' clinical history with regards to their ongoing MS lesion distribution. Future studies should therefore consider assessing whether a correlation between nervous system damage (either new or established) and extent and location of thermosensory abnormalities exist, as this approach may provide mechanistic evidence on the nature of those sensing abnormalities, as well as a non-invasive marker of neural damage in MS.

The fundamental observations above have important applied implications for the design of indoor thermal comfort within the built environment. Specifically, our findings and body maps provide important insights for the optimization of design parameters for personal comfort systems that better meet the thermal needs of individuals with (thermal) disabilities.

For example, our physiological evidence indicates that a wearable personal comfort systems for the upper body that aims to provide localised cooling to the skin to reduce heat discomfort, would need to deliver greater cooling if used by people with MS. This corrective increase in power would be needed to accommodate this group's loss of cold sensitivity at the upper body. The same corrective adjustment may be required if one is designing a personal comfort system for the feet that aims to provide localised heating to the skin to reduce cold discomfort, to accommodate this group's loss of warm sensitivity at the lower body. Interestingly, our data may also indicate that a wearable personal comfort system that aims to offset cold discomfort may require reduced heating (and likely reduced power) if applied to the upper body of people with MS, due to the observed warm hyper-sensitivity of this body area.

The concept of corrective power has been previously used in the context of personal comfort systems to identify the difference between two ambient temperatures at which equal thermal sensation is achieved with the use of such devices (Zhang et al., 2015). This concept is important to quantify likely energy savings due to the use of personal comfort systems (Zhang et al., 2015).

In light of our results, here we propose an adaptation of this concept, and we introduce the term "thermosensory corrective power", i.e. the adjustment required in the localised heating or cooling provided by a standard personal comfort system to achieve equal thermal sensation between individuals with and without thermosensory abnormalities. On the basis of the examples provided earlier (e.g. the likely adjustments required to achieve warm or cold comfort in people with MS), we believe that determining the "thermosensory corrective power" of specific devices could be highly beneficial to better meet the unique thermosensory needs of clinical groups, thereby facilitating more inclusive approaches to the design of the bult environment (Zallio and Clarkson, 2022, 2023).

Initial evidence in support of the likely requirement of "thermosensory corrective power" for comfort gains in groups like people with MS is available from the work of Vargas et al. (2020), who has recently reported that people with MS sought more cooling during exercise heat stress to offset discomfort than healthy counterparts. We propose that such an adaptive behaviour may have resulted from this group's reduced cold sensitivity, as observed in the present study. In the context of the study of Vargas et al. (2020), the implementation of corrective power based on thermosensory loss may have resulted in people with MS in seeking less cooling where provided with greater cooling power.

Finally, it is important to note that a limitation of this study is that we did not directly assess thermal comfort associated with our regional thermal sensitivity assessments. While our recent empirical evidence in people this MS exposed to progressive heat stress indicates that their

heightened sensitivity to heat is associated with a heightened sensitivity to discomfort Christogianni et al. (2023), future studies should consider any potential non-linear association between thermal sensitivity loss and/or and thermal discomfort in people with MS. Such an approach it is essential to consider the application of "thermosensory corrective power" to existing personal comfort system for clinical groups and to ultimately support the development of more inclusive approaches to thermal comfort for all.

6. Conclusion

We conclude that thermosensory abnormalities can be very frequent in people with MS. Specifically, cold sensitivity loss and warm sensitivity gain appear more evenly distributed and affect greater proportion of body sites than warm sensitivity loss, which appears more focused on specific body sites such as the feet. Our findings are reported in the form of highly detailed maps of thermosensory abnormalities in our thermally-vulnerable clinical group. We believe that our clinical mapping approach highlights the need to consider "thermosensory corrective power" when designing personal comfort systems that aim to meet the unique thermal needs of clinical groups such as people with MS. We envisage that our proposed approach will support efforts in reaching thermal comfort, thermal health, and thermal safety for all in buildings.

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CRediT authorship contribution statement

Aikaterini Christogianni: Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Richard Bibb:** Writing – review & editing, Supervision, Software, Funding acquisition. **Davide Filingeri:** Writing – review & editing, Supervision, Software, Resources, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors report no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jtherbio.2024.103887.

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