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Skin temperature response to thermal stimulus in patients with hyperhidrosis: A comparative study

Fátima Carvalho [a], Carolina Magalhaes [b,c], Fernando Fernandez-Llimos [d,e,*], Joaquim Mendes [b,c], Jorge Gonçalves [d,f]

[a] Department of Pediatric Surgery, Centro Hospitalar Universitário do Porto, Porto, Portugal
[b] Faculdade de Engenharia, Universidade do Porto, Porto, Portugal
[c] LABIOMEP, UISPA-LAETA-INEGI, Porto, Portugal
[d] Laboratory of Pharmacology, Faculty of Pharmacy, Universidade do Porto, Porto, Portugal
[e] CINTESIS@RISE – Center for Health Technology and Services Research, Porto, Portugal
[f] I3S: Instituto de Investigação e Inovação em Saúde da Universidade do Porto, Porto, Portugal

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ABSTRACT

Primary hyperhidrosis (HH), the excessive sweating exceeding physiological demand, has been associated to a complex dysfunction of the autonomic nervous system which may explain the disfunction in sweating but may also cause unrevealed alterations in skin blood flow regulation. In fact, HH patients present a sympathetic over-function with less reflex bradycardia in response to the Valsalva maneuver and higher sympathetic skin responses. We aimed to identify response patterns to room thermal stimulus in HH patients compared to a control group in order to investigate putative differences in blood flow assuming that skin temperature in glabrous (non-hairy) areas reflect the sympathetic tone in arteriovenous anastomoses (AVAs). Infrared thermography images were obtained from a cohort of patients diagnosed with HH, followed at a hospital pediatric surgical department and to a sex- and age-matched control group of patients admitted for other surgical procedures. With the participants in Fowler's position, a set of 3 images were captured simultaneously and 44 regions of interest were analyzed, distributed on the palms of the hands, soles of the feet, axilla, and inner canthus. After an acclimatization period at 20 °C, the room temperature was increased to 24, 28 and 32 °C to obtain similar sets of thermograms. A total of 37 patients with HH and 16 participants in the control group were included in the study. At baseline (20 °C), body core temperature (measured in the inner canthus) was significantly higher in the HH patients compared to the controls ($p = 0.019$ and $p = 0.003$ in right and left inner canthi, respectively), without any significant differences in the other thermograms. When room temperature was increased, differences in core temperature disappeared, while differences appeared in axilla and palms of the hands with HH patients presenting significantly lower temperature at the three thermal stimulus stages. Patients with HH presented a lower thermoregulatory response when submitted to room temperature increase, which may reflect a vasomotor sympathetic over-function in AVAs.

1. Introduction

Primary hyperhidrosis (HH) is a chronic condition characterized by an excessive sweating exceeding physiological demand. Eccrine sweat glands are innervated by the sympathetic nervous system through sudomotor neurons, using acetylcholine as neurotransmitter to stimulate muscarinic M3 postganglionic receptors (Hu et al., 2018; Shibasaki et al., 2006), while apocrine glands are mainly innervated by adrenergic neurons, using noradrenaline as neurotransmitter, to stimulate α_1-, β_2-and β_3-adrenoreceptors (Hu et al., 2018).

The prevalence of HH is not well established with estimates ranging from 1.5 to 5.8%. Sex and racial differences in HH prevalence were found, with women and Asians being more affected (Fujimoto et al., 2013; Lear et al., 2007). The pathophysiology of HH is not entirely known. Excessive sweating in HH patients is constituted by a thin,

* Corresponding author. Laboratório de Farmacologia, Faculdade de Farmácia, Universidade do Porto, Rua de Jorge Viterbo Ferreira, 228, 4050-313, Porto, Portugal.
E-mail addresses: fcarvalho.dia@chporto.min-saude.pt (F. Carvalho), up201607752@fe.up.pt (C. Magalhaes), fllimos@ff.up.pt (F. Fernandez-Llimos), jgabriel@fe.up.pt (J. Mendes), jgoncalves@ff.up.pt (J. Gonçalves).

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Abbreviations

ASA	American Statistical Association
AVA	Arteriovenous anastomoses
BMI	Body mass index
CG	Control group
HH	Hyperhidrosis
ROI	Region of interest

odorless, hypotonic fluid, which corresponds with the sweat produced by eccrine sweating glands (Benson et al., 2013). The number, size, and microscopic or macroscopic characteristics of eccrine sweating glands are not different in patients with HH (Nawrocki and Cha, 2019). In the absence of an anatomical explanation, HH is becoming to be regarded as a consequence of a complex dysfunction of the autonomic nervous system (Nawrocki and Cha, 2019). The hypothesis of sympathetic over-function in HH patients was supported by their less reflex bradycardia in response to Valsalva maneuver and by a higher sympathetic skin responses in HH patients (Ghandali et al., 2020; Shih et al., 1983), eventually with parasympathetic dysfunction (Birner et al., 2000; De Marinis et al., 2012).

Body core temperature and skin temperature are involved in the feedback signal to initiate a thermoregulatory process, including sweating (Gagnon and Crandall, 2018; Romanovsky, 2014). Skin temperature has been used in HH patients to evaluate the effectiveness of the thoracic sympathectomy surgical procedure used to correct palmar and axillary HH (Liu et al., 2019; Lu et al., 2000; Saiz-Sapena et al., 2000). However, despite of the well-known association between skin temperature and sweating (Nadel et al., 1971), a comparison between HH patients and non-HH individuals of their skin temperature response after thermal stimulus has not yet been performed.

We hypothesized that differences in core and skin temperature exist between patients with HH and a control group when exposed to an external thermal stimulus, which would suggest the existence of alterations in the autonomic mechanisms in HH patients.

2. Methods

The study was approved by the Ethics Committee of the Centro Hospitalar Universitário do Porto (CHUP) [reference number 2018.140 (121-DEFI/120-CES)].

2.1. Participants

Patients followed in a pediatric surgery out-patient department at the Hospital Santo António (Porto – Portugal) from Jan 2017 to Jul 2019 with a diagnosis of primary HH were invited to participate in the study. Diagnosis of primary HH was based on symptoms described in the ambulatory clinic (i.e., persistent excessive, and disproportionate bilateral palmar, plantar, and axillary sweating that limits routine activities) together with the absence of other excessive sweating medical conditions (e.g., hypotension, hypoglycemia, pheochromocytoma, hyperthyroidism) (Nawrocki and Cha, 2019; Robertshaw, 1979). Simultaneously, patients admitted for reasons other than HH were also invited to participate with the aim of creating a sex and age paired control group (CG).

HH patients and CG patients were informed about the thermography procedure, and a written informed consent was obtained by those who agreed to participate. Participants were requested to attend a thermography procedure following the Glamorgan Protocol (Ammer, 2018). Participants were instructed not to use creams/moisturizers or make up, to avoid heavy meals, coffee, or tea for the 2 h before the exam; to stop during the previous 24 h any pharmacological treatment containing steroids, autonomic nervous system drugs, opioids, and vasoactive drugs; and to wear light clothes. Phase of menstrual cycle was not contemplated in the female participants.

2.2. Data gathering procedure

On the scheduled date of the thermography, participants of both groups were requested to take off their clothes and to remain in their underwear. Afterwards, participants were requested to move to an adjoining room adapted for thermography procedures. They remain seated for 10 min (acclimatization period) with their feet resting on a bench. Room temperature was previously adjusted to 20 °C. The entire procedure was performed with the patients seated (Fowler's position) to avoid the potential peripheral vasoconstriction produced during orthostasis (Kellogg et al., 1990), particularly relevant in HH patients (De Marinis et al., 2012). After a 10-min acclimatization period, the first set of infrared images, corresponding to the baseline (20 °C), was obtained. Room temperature was then increased to produce a thermal stimulus. Four convection heaters were used to raise the room temperature. An alarm-sound thermometer was set to beep at 24, 28 and 32 °C, when three sets of infrared images were taken.

Infrared images were obtained using a FLIR E60sc IR Camera, focal plane array of 320 × 240 pixels, NETD <0.05 °C at 30 °C, uncertainty of ±2 °C or ±2% of the reading (FLIR Systems Inc. Wilsonville, OR, USA), using an emissivity value of 0.98, as recommended for the skin temperature as previously described (Togawa, 1989). Images were taken from a 90-degree angle to minimize the errors associated with capture (Vardasca et al., 2017). Images were processed with the FLIR Tools 6.4 software (FLIR Systems Inc. Wilsonville, OR, USA). For each room temperature, a set of 3 thermograms per participant were analyzed, corresponding to the hands, feet, and axilla. The regions of interest (ROIs) were set as shown in Fig. 1 and 8 in each hand, 11 in each foot, 2 in each axilla, and one in each epicanthic fold of the upper eyelid (inner canthus) used as an indirect measure of body core temperature (Teunissen and Daanen, 2011). The palmar, plantar, and axillar regions were

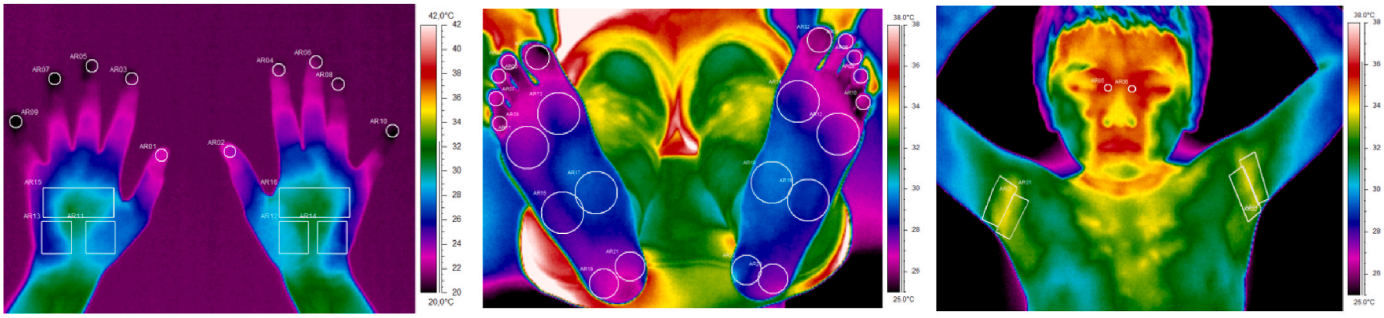

Fig. 1. Set of 44 regions of interest were analyzed per participant: 8 per hand, 11 per foot, 2 per axilla, and one in each epicanthic fold of the upper eyelid (inner canthus).

Table 1
Participants baseline characteristics.

	Hyperhidrosis (n = 37)	Control (n = 16)	p-value
Female; n (%)	21 (56.8)	8 (50.0)	
Age in years; mean (SD)	15.1 (2.7)	13.1 (3.1)	0.650*
Body mass in kg; mean (SD)	57.6 (16.5)	48.8 (12.7)	0.060**
Stature in cm; mean (SD)	163 (12)	159 (14)	0.430**
BMI; mean (SD)	21.4 (4.3)	18.7 (2.8)	0.026**
ZScore; mean (SD)	0.35 (0.9)	−0.18 (0.8)	0.045**

*chi-square; **t-test

selected because they are regions especially affected in HH patients. Although the use of inner canthi infrared thermography as indirect measure of body core temperature is controversial (Fernandes et al., 2016), studies demonstrated that, when properly calibrated, inner canthi temperature performs better than any other site for non-contact infrared measurements (Wang et al., 2021). The same is confirmed by the international standard ISO/TR13154 (International Organization for Standardization, 2017), which assumes there exists a small difference between the inner canthi temperature and the core body but recommend the first as the better location for infrared no contact temperature measurements.

2.3. Data analysis

Normality of skin temperature distribution was assessed by the Shapiro-Wilk test supplemented with visual inspection of the quantile-quantile (Q-Q) plots. Since close to normality distributions were found, temperatures were presented as mean and standard deviation (SD) and differences between groups were evaluated with *t*-test. Significance threshold was set at 0.05, and no adjustments were used to reduce the increased chance of making a type-1 error; however, following American Statistical Association recommendations (Wasserstein and Lazar, 2016) to measure the size of the differences and to avoid the influence of sample size, Hedges and Olkin's modified Cohen's d were calculated (Hedges and Olkin, 1985), and the intervals defined as: 0.1 to 0.4: small effect; 0.4 to 0.7: intermediate effect; over 0.7: strong effect (Cohen, 1988).

3. Results

Forty-one patients with HH agreed to participate in this study. However, four dropped out, resulting in 37 HH patients included for the analysis. The control group was composed by 16 patients (who accepted to participate in the study). Baseline characteristics of the participants in the two groups are presented in Table 1.

Body core temperature at 20 °C was significantly higher in the HH patients compared to the controls (Fig. 2; p = 0.019 right and p = 0.003 left inner canthus). The remaining 42 ROIs from the hands, foot and axillae showed no significant differences between the two groups at 20 °C, although values from control group temperatures tend to be higher. Detailed temperatures are presented in Supplementary material.

Thermal stimulus produced a different response in both groups. Body core temperature differences disappeared since beginning of the thermal stimulus, with no statistical differences between the groups at 24 °C, 28 °C or 32 °C (Fig. 2), which was confirmed by the strong effect size differences at 20 °C and the null o small effect sizes at all the thermal stimulus steps (Supplementary material).

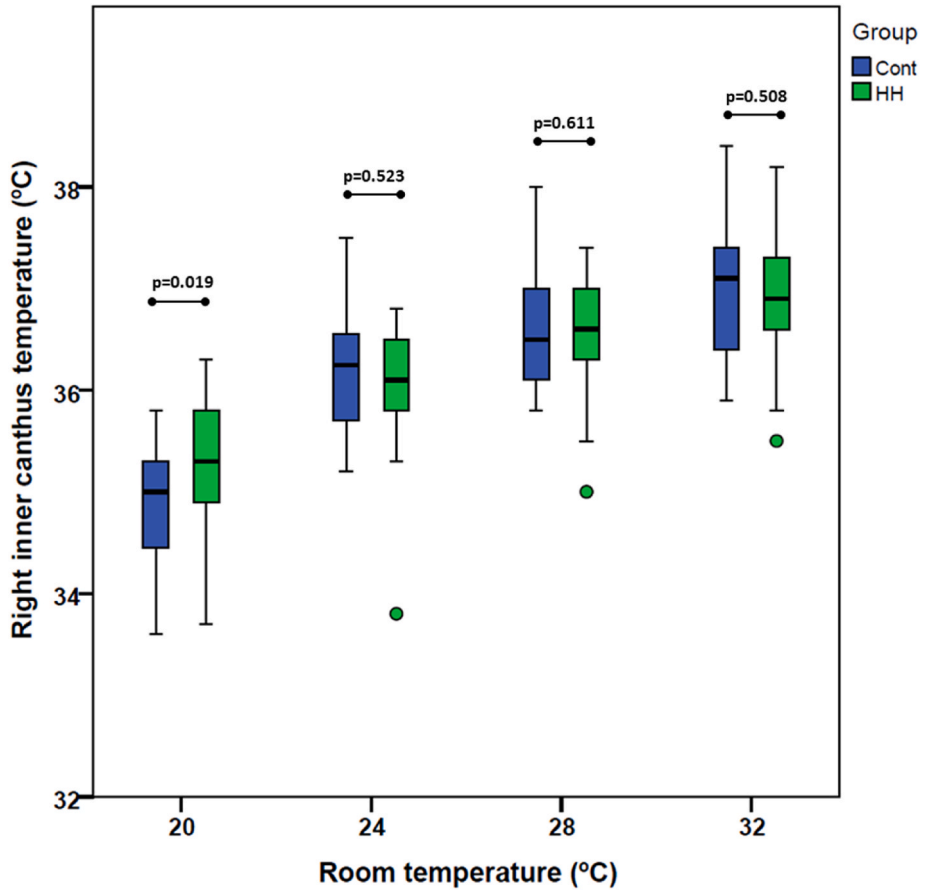

Fig. 2. Right inner canthus temperature, which represents core temperature, measured at the four room temperatures. Horizontal thick bars represent the median, boxes represent interquartile range, and circles represent outliers.

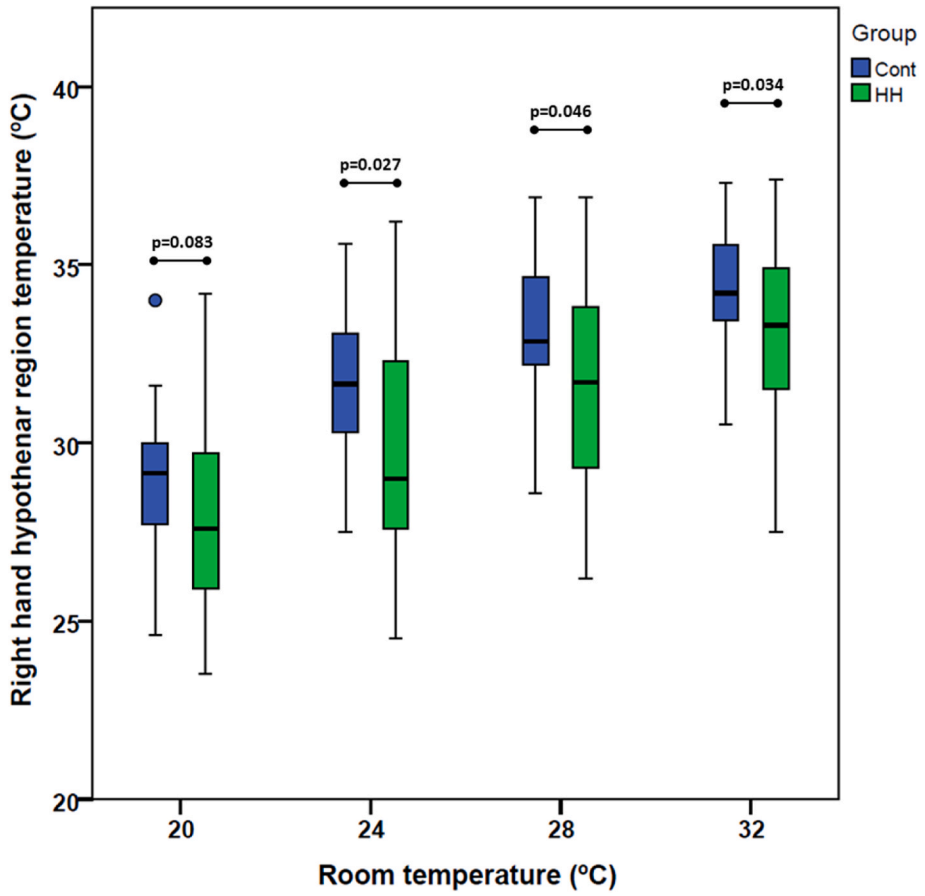

Fig. 3. Right hand hypothenar region temperature measured at the four room temperatures. Horizontal thick bars represent the median, boxes represent interquartile range, and circles represent outliers.

Palmar regions of the hands shifted from non-difference at 20 °C, to significant differences at the three stages of the thermal stimulus, with control group temperatures presenting higher values than HH patients, showing an increasingly strong effect size difference during the thermal stimulus (Supplementary material). These differences were more intense in the right hand (Fig. 3). At the fingertips, temperatures maintained without differences between the two groups, except at 32 °C where right hand thumb and 5th finger were statistically higher in control group than in HH patients.

Axillary temperature showed a similar pattern than hands. Starting from a non-difference between groups, control group responded to the thermal stimulus increasing temperature to reach a significantly higher value than HH patients. This difference maintained at all room temperatures (Fig. 4), showing increasingly strong effect size differences (Supplementary material).

Toes temperature maintained with no differences between groups at all the room temperatures, however plantar temperatures showed differences in some points close to the heel at 24 °C and 28 °C with control group presenting higher values than HH patients. These results were confirmed by the null or small effect sizes in the toes, but medium or strong differences in the heels.

4. Discussion

Skin temperature and the response to local heating are used as a noninvasive proxy to estimate skin blood flow and microvascular function, which contributes to identify microvascular dysfunctions in several medical conditions (e.g., end-stage renal disease, Raynaud's or Parkinson's diseases, and neuropathies) (Antonio-Rubio et al., 2015; Martini et al., 2019; Wu et al., 2017). The use of thermography associated to artificial intelligence methods for interpretation of thermal data demonstrated high sensitivity and specificity as a diagnostic tool (Magalhaes et al., 2021). However, skin temperature responses to thermal stimulus have not been thoroughly studied in HH patients. Using thermography, we found a different response to thermal stimulus in skin temperature of glabrous areas (e.g., palms of hands and soles of feet) of HH patients compared to a control group. Starting from a higher body core temperature but similar skin temperature, HH patients were less responsive to room temperature elevations.

Sweating is a natural response of thermoeffector regions to increase heat loss when exposed to an ambient thermal stimulus. The lower skin temperature seen in HH patients as response to the thermal stimulus could be associated to a higher sweating response to heat environment, but this is not supported by several considerations. HH patients present an excessive sweating at rest in thermoneutral zone, being less responsive to exercise or thermal stimulus (Shih et al., 1983). Therefore, at 20 °C, the sweating would favor heat loss whereas in the present study it was observed the opposite, with an increase in central temperature. Additionally, sweat evaporation is not immediate; it was shown that surgical thoracic sympathectomy increases 5 °C palmar skin temperature measured by thermography only 2 min after the procedure, which cannot be explained only by the sweating interruption (Gozdziuk et al., 2008). The involvement of a central vasomotor neural control in HH patients' skin temperature was demonstrated by Wu et al. where ipsilateral palmar temperature increased after unilateral T2 sympathetic ganglion coagulation, while contralateral palmar temperature decreased, both only 2 min after the procedure (Wu et al., 1996). These temperature changes are likely caused by changes in blood flow, as thoracic sympathectomy was shown to cause an increase in palmar blood flow, assessed by laser doppler (Li et al., 2009) or through pulse

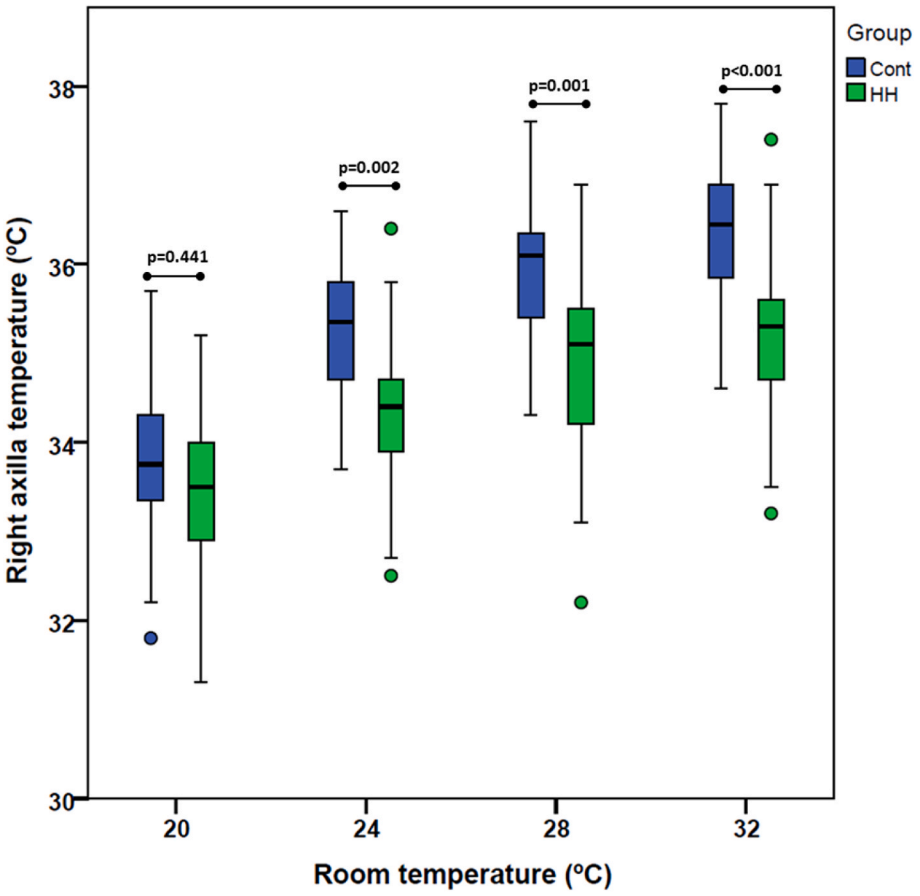

Fig. 4. Right axilla temperature measured at the four room temperatures. Horizontal thick bars represent the median, boxes represent interquartile range, and circles represent outliers.

oximetry-derived perfusion index (Jeng et al., 2017).

Anatomically, glabrous skin is characterized by a existence of massive arteriovenous anastomoses (AVAs), which have a crucial role in the transport of heat from the body core to the surface (Walloe, 2016). AVAs are heavily enervated by noradrenergic fibers, as demonstrated by immunofluorescence revealed by confocal microscopy (Donadio et al., 2006). Therefore, skin temperature in glabrous areas reflect the local vasomotor tone (high temperature reflects low vasoconstriction and higher heat dissipation capacity) and not the room temperature (Romanovsky, 2014). In our study, both HH patients and controls augmented their skin temperature during the thermal stimulus produced with the three room temperature elevations. This is the expected behavior occurring after a thermal stimulus and acting as a feedforward of the thermoregulatory system (Romanovsky, 2014), due to a decrease in the local vasomotor tone (lower need to preserve the inner temperature), likely due to a decrease of the adrenergic-induced vasoconstriction of the skin blood vessels. However, HH patients and controls present differences in the way local vasomotor tone responds to room temperature elevations. At the baseline (20 °C room temperature), HH patients presented identical skin temperature at peripheral ROIs as control individuals. Increasing room temperature produced a smaller response in HH patients (i.e., less marked reduction in the vasomotor tone), with more notorious differences in the most irrigated areas: axilla with the greatest differences, palms of the hands greater differences than fingers, and soles greater than toes. It seems that HH patients have the vasomotor control altered, with less marked vasodilation in response to elevation of the room temperature, compared to control individuals and, therefore, indicating HH may have less heating dissipation capacity (or higher heat retention capacity) through peripheral circulation.

The sympathetic control of blood flow in glabrous skin areas involves noradrenergic nerves, since it can be blocked by iontophoretically applied bretylium (Yamazaki and Sone, 2006), and comprises an α1-adrenoceptor vasoconstrictor effect (Johnson et al., 2014). Therefore, the lower capacity of HH patients to cause skin vasodilation in response to the increase in room temperature may be explained by a more marked α1-adrenoceptor induced vasoconstriction.

In neutral thermal zone, an individual presents fluctuations in blood velocity passing AVAs with a frequency of 2–3 cycles per minute (Walloe, 2016). These blood velocity fluctuations are not modified by thermal stimulus in the neutral thermal zone (Bergersen et al., 1995; Metzler-Wilson et al., 2012). In control individuals, skin temperature at the palm increases virtually with thermal stimulus onset: 1.2 min alter initiating the heating, with a peak at 6 min (Johnson et al., 1995). In our study, HH patients presented a much slower temperature increase rate than control individuals. It seems that HH patients have a delayed response to abandon the vasoconstrictor tone of thermoneutral environment, which may suggest a higher sympathetic tone in these patients. Whether this higher sympathetic tone has a common origin with the higher sympathetic cholinergic tone that produces HH patient excessive sweating should be further explored.

4.1. Limitations

In our study, only one thermogram per patient and area was captured at each room temperature. This procedure impeded us to identify if the limited AVA response to thermal stimulus was associated to a limited AVA-opening or to a more rapid AVA-closure during blood flow fluctuations. In addition, the increase in sweat generated as a response to an increase in the room temperature may block infrared radiation, preventing to reach the skin surface thus contributing to the certain

variability of the measurements. We preferred not using any method to adjust the increased chances of type-1 error after multiple comparisons (e.g., Bonferroni method) because a) they are considered too conservative (Barnett et al., 2022; Perneger, 1998), and b) p-values in isolation are not sufficient to measure an effect size (Ioannidis, 2018). Thus, ASA recommendations were followed, and effect size measures were calculated, which showed where actual differences were found. We have not controlled for menstrual cycle phase in female participants. However, despite the estradiol has an influence on vasculature (Wenner and Stachenfeld, 2020), in our study male and female skin temperatures showed no differences at any ROI at the ambient temperature (supplementary materials), which is coincident with other studies (Nagashima, 2015).

5. Conclusion

HH patients seem to present a higher sympathetic tone in AVAs compared to non-HH individual, demonstrated by a lower skin temperature response to an increase in room temperature, making them less responsive to be released from a heat retention status through vasodilation.

Author statement

Fátima Carvalho. **Investigation; Resources; Data Curation; Writing - Original Draft; Visualization;** Funding **acquisition,** Carolina Magalhaes. **Investigation; Data Curation; Writing - Original Draft,** Fernando Fernandez-Llimos. **Validation; Formal analysis; Data Curation; Writing - Original Draft; Visualization,** Joaquim Mendes. **Conceptualization; Methodology; Software; Validation; Resources; Writing - Review & Editing; Supervision;** Funding **acquisition,** Jorge Gonçalves. **Conceptualization; Methodology; Resources; Writing - Review & Editing; Project administration; Supervision;** Funding **acquisition**.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Fatima Carvalho reports financial support was provided by Fundação para a Ciência e Tecnologia.

Data availability

Data will be made available on request.

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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.2022.103322.

References

Ammer, K., 2018. The Glamorgan Protocol for recording and evaluation of thermal images of the human body. Thermol Int 18, 125–144.
Antonio-Rubio, I., Madrid-Navarro, C.J., Salazar-Lopez, E., Perez-Navarro, M.J., Saez-Zea, C., Gomez-Milan, E., Minguez-Castellanos, A., Escamilla-Sevilla, F., 2015. Abnormal thermography in Parkinson's disease. Park. Relat. Disord. 21, 852–857.
Barnett, M.J., Doroudgar, S., Khosraviani, V., Ip, E.J., 2022. Multiple comparisons: to compare or not to compare, that is the question. Res. Soc. Adm. Pharm. 18, 2331–2334.
Benson, R.A., Palin, R., Holt, P.J., Loftus, I.M., 2013. Diagnosis and management of hyperhidrosis. BMJ 347, f6800.
Bergersen, T.K., Eriksen, M., Walloe, L., 1995. Effect of local warming on hand and finger artery blood velocities. Am. J. Physiol. 269, R325–R330.
Birner, P., Heinzl, H., Schindl, M., Pumprla, J., Schnider, P., 2000. Cardiac autonomic function in patients suffering from primary focal hyperhidrosis. Eur. Neurol. 44, 112–116.
Cohen, J., 1988. Statistical Power Analysis for the Behavioral Sciences. Erlbaum, Hillsdale, NJ.
De Marinis, M., Colaizzo, E., Petrelli, R.A., Santilli, V., 2012. Alterations in cardiovascular autonomic function tests in idiopathic hyperhidrosis. Auton. Neurosci. 167, 34–38.
Donadio, V., Nolano, M., Provitera, V., Stancanelli, A., Lullo, F., Liguori, R., Santoro, L., 2006. Skin sympathetic adrenergic innervation: an immunofluorescence confocal study. Ann. Neurol. 59, 376–381.
Fernandes, A.A., Moreira, D.G., Brito, C.J., da Silva, C.D., Sillero-Quintana, M., Pimenta, E.M., Bach, A.J., Garcia, E.S., Bouzas Marins, J.C., 2016. Validity of inner canthus temperature recorded by infrared thermography as a non-invasive surrogate measure for core temperature at rest, during exercise and recovery. J. Therm. Biol. 62, 50–55.
Fujimoto, T., Kawahara, K., Yokozeki, H., 2013. Epidemiological study and considerations of primary focal hyperhidrosis in Japan: from questionnaire analysis. J. Dermatol. 40, 886–890.
Gagnon, D., Crandall, C.G., 2018. Sweating as a heat loss thermoeffector. In: Romanovsky, A.A. (Ed.), Thermoregulation: from Basic Neuroscience to Clinical Neurology. Elsevier, Amsterdam.
Ghandali, E., Hosseini, S.M., Moghimi, H.R., Khademi-Kalantari, K., Talebian Moghadam, S., Baghban, A.A., Mortazavi, S.M., 2020. Intra tester reliability of sympathetic skin responses in subjects with primary palmar hyperhidrosis. J. Bodyw. Mov. Ther. 24, 57–62.
Gozdziuk, K., Baranowski, P., Mazurek, W., Kalisz, O., Wolski, T., Sawicki, M., Rojowski, A., 2008. Application of Thermography in Surgical Curing of Hand Oversweating. 9th International Conference on Quantitative InfraRed Thermography, Krakow - Poland.
Hedges, L.V., Olkin, I., 1985. Statistical Methods for Meta-Analysis. Academic Press, New York.
Hu, Y., Converse, C., Lyons, M.C., Hsu, W.H., 2018. Neural control of sweat secretion: a review. Br. J. Dermatol. 178, 1246–1256.
International Organization for Standardization, 2017. Medical electrical equipment: Deployment, implementation and operational guidelines for identifying febril e humans using a screening thermograph, vol. 2017. ISO/TR, p. 13154.
Ioannidis, J.P.A., 2018. The proposal to lower P value thresholds to .005. JAMA 319, 1429–1430.
Jeng, E.I., Gravenstein, N., Klodell, C.T., 2017. Perfusion index: an indicator of success during endoscopic thoracic sympathectomy for hyperhidrosis. Ann. Thorac. Surg. 104, 426–430.
Johnson, J.M., Minson, C.T., Kellogg Jr., D.L., 2014. Cutaneous vasodilator and vasoconstrictor mechanisms in temperature regulation. Compr. Physiol. 4, 33–89.
Johnson, J.M., Pergola, P.E., Liao, F.K., Kellogg Jr., D.L., Crandall, C.G., 1995. Skin of the dorsal aspect of human hands and fingers possesses an active vasodilator system. J. Appl. Physiol. 78 (1985), 948–954.
Kellogg Jr., D.L., Johnson, J.M., Kosiba, W.A., 1990. Baroreflex control of the cutaneous active vasodilator system in humans. Circ. Res. 66, 1420–1426.
Lear, W., Kessler, E., Solish, N., Glaser, D.A., 2007. An epidemiological study of hyperhidrosis. Dermatol. Surg. 33, S69–S75.
Li, X., Tu, Y.R., Lin, M., Lai, F.C., Chen, J.F., Miao, H.W., 2009. Minimizing endoscopic thoracic sympathectomy for primary palmar hyperhidrosis: guided by palmar skin temperature and laser Doppler blood flow. Ann. Thorac. Surg. 87, 427–431.
Liu, G., Kang, G., Huang, J., Xie, S., Hu, H., 2019. Changes in palm temperature as predictor of long-term cure of sympathicotomy for palmar hyperhidrosis? J. Neurol. Surg. Cent. Eur. Neurosurg. 80, 67–71.
Lu, K., Liang, C.L., Cho, C.L., Cheng, C.H., Yen, H.L., Rau, C.S., Tsai, Y.D., Chen, H.J., Lee, T.C., 2000. Patterns of palmar skin temperature alterations during transthoracic endoscopic T2 sympathectomy for palmar hyperhidrosis. Auton. Neurosci. 86, 99–106.
Magalhaes, C., Mendes, J., Vardasca, R., 2021. Meta-analysis and systematic review of the application of machine learning classifiers in biomedical applications of infrared thermography. Appl. Sci. 11, 842.
Martini, G., Cappella, M., Culpo, R., Vittadello, F., Sprocati, M., Zulian, F., 2019. Infrared thermography in children: a reliable tool for differential diagnosis of peripheral microvascular dysfunction and Raynaud's phenomenon? Pediatr Rheumatol Online J 17, 68.
Metzler-Wilson, K., Kellie, L.A., Tomc, C., Simpson, C., Sammons, D., Wilson, T.E., 2012. Differential vasodilatory responses to local heating in facial, glabrous and hairy skin. Clin. Physiol. Funct. Imag. 32, 361–366.
Nadel, E.R., Bullard, R.W., Stolwijk, J.A., 1971. Importance of skin temperature in the regulation of sweating. J. Appl. Physiol. 31, 80–87.
Nagashima, K., 2015. Thermoregulation and menstrual cycle. Temperature (Austin) 2, 320–321.
Nawrocki, S., Cha, J., 2019. The etiology, diagnosis, and management of hyperhidrosis: a comprehensive review: therapeutic options. J. Am. Acad. Dermatol. 81, 669–680.
Perneger, T.V., 1998. What's wrong with Bonferroni adjustments. BMJ 316, 1236–1238.

Robertshaw, D., 1979. Hyperhidrosis and the sympatho-adrenal system. Med. Hypotheses 5, 317–322.
Romanovsky, A.A., 2014. Skin temperature: its role in thermoregulation. Acta Physiol. 210, 498–507.
Saiz-Sapena, N., Vanaclocha, V., Panta, F., Kadri, C., Torres, W., 2000. Operative monitoring of hand and axillary temperature during endoscopic superior thoracic sympathectomy for the treatment of palmar hyperhidrosis. Eur. J. Surg. 166, 65–69.
Shibasaki, M., Wilson, T.E., Crandall, C.G., 2006. Neural control and mechanisms of eccrine sweating during heat stress and exercise. J. Appl. Physiol. 100 (1985), 1692–1701.
Shih, C.J., Wu, J.J., Lin, M.T., 1983. Autonomic dysfunction in palmar hyperhidrosis. J. Auton. Nerv. Syst. 8, 33–43.
Teunissen, L.P., Daanen, H.A., 2011. Infrared thermal imaging of the inner canthus of the eye as an estimator of body core temperature. J. Med. Eng. Technol. 35, 134–138.
Togawa, T., 1989. Non-contact skin emissivity: measurement from reflectance using step change in ambient radiation temperature. Clin. Phys. Physiol. Meas. 10, 39–48.
Vardasca, R., Marques, A.R., Diz, J., Seixas, A., Mendes, J., Ring, E.F.J., 2017. The influence of angles and distance on assessing inner-canthi of the eye skin temperature. Thermol Int 27, 130–135.
Walloe, L., 2016. Arterio-venous anastomoses in the human skin and their role in temperature control. Temperature (Austin) 3, 92–103.
Wasserstein, R.L., Lazar, N.A., 2016. The ASA statement on p-values: context, process, and purpose. Am. Statistician 70, 129–133.
Wenner, M.M., Stachenfeld, N.S., 2020. Point: investigators should control for menstrual cycle phase when performing studies of vascular control that include women. J. Appl. Physiol. 129 (1985), 1114–1116.
Wu, J.J., Hsu, C.C., Liao, S.Y., Liu, J.C., Shih, C.J., 1996. Contralateral temperature changes of the finger surface during video endoscopic sympathectomy for palmar hyperhidrosis. J. Auton. Nerv. Syst. 59, 98–102.
Wu, Y., Nieuwenhoff, M.D., Huygen, F.J., van der Helm, F.C., Niehof, S., Schouten, A.C., 2017. Characterizing human skin blood flow regulation in response to different local skin temperature perturbations. Microvasc. Res. 111, 96–102.
Yamazaki, F., Sone, R., 2006. Different vascular responses in glabrous and nonglabrous skin with increasing core temperature during exercise. Eur. J. Appl. Physiol. 97, 582–590.