Clinical Autonomic Research (2024) 34:379–382
https://doi.org/10.1007/s10286-024-01047-y

LETTER TO THE EDITOR

Effect of T2-T4 sympathicotomy in skin temperature of pediatric patients with hyperhidrosis: a thermographic follow-up

Fátima Carvalho[1] · Carolina Magalhaes[2,3] · Fernando Fernandez-Llimos[4] · Joaquim Mendes[2,3] · Jorge Gonçalves[4]

Received: 29 August 2023 / Accepted: 12 June 2024 / Published online: 24 June 2024

Keywords Hyperhidrosis · Sympathetic tonus · Sympathicotomy · Thermography

Abbreviations

95%CI	95% Confidence interval
AVAs	Arteriovenous anastomoses
HH	Hyperhidrosis
OR	Odds ratio
LA	Left axilla
LF	Left foot
LH	Left hand
RA	Right axilla
RF	Right foot
RH	Right hand
ROI	Region of interest
SD	Standard deviation

✉ Fernando Fernandez-Llimos
fllimos@ff.up.pt

Fátima Carvalho
fcarvalho.dia@chporto.min-saude.pt

Carolina Magalhaes
up201607752@fe.up.pt

Joaquim Mendes
jgabriel@fe.up.pt

Jorge Gonçalves
jgoncalves@ff.up.pt

1 Department of Pediatric Surgery, Centro Hospitalar Universitário do Porto, Porto, Portugal

2 Faculdade de Engenharia, Universidade do Porto, Porto, Portugal

3 LABIOMEP, UISPA-LAETA-INEGI, Porto, Portugal

4 UCIBIO–Applied Molecular Biosciences Unit, i4HB–Institute for Health and Bioeconomy, Laboratory of Pharmacology, Faculty of Pharmacy, Universidade of Porto, Rua de Jorge Viterbo Ferreira, 228, 4050-313 Porto, Portugal

Introduction

Hyperhidrosis (HH) is associated with excessive sympathetic tone through the T2 and T3 ganglia, in both cholinergic and adrenergic components [1]. In HH patients, excessive sweating is caused by increased cholinergic activity on muscarinic receptors of eccrine sweat glands, and the lower skin temperature of the hands and feet is caused by increased adrenergic activity on alpha1 adrenoceptors in glabrous skin areas, reducing skin perfusion through arteriovenous anastomoses (AVAs) [2].

Various surgical approaches have been used for years to interrupt the sympathetic chain, with thoracoscopic sympathectomy becoming a reliable alternative [3]. The level at which the chain is blocked has been controversial, ranging from a single T3 block to a complete T2-T4 block [4]. However, postoperative complications have been described: compensatory sweating, dissatisfaction with the procedure and recurrence of symptoms. Several studies have evaluated changes in skin temperature, mainly in the palms, during surgery and immediately after sympathectomy, but a long-term evaluation of the effects of the surgical procedure on skin temperature has not yet been performed. Therefore, our aim was to evaluate the effects of T2-T4 sympathectomy on skin temperature in patients with hyperhidrosis during a 6-month follow-up period.

Methods

A longitudinal study (ethics approval ref: 2018.140 (121-DEFI/120-CES)) enrolled participants from the paediatric surgery department of Hospital Santo António (Porto, Portugal) between Jan-2017 and Jul-2019. Patients diagnosed with primary HH and scheduled for sympathicotomy were invited to participate as part of the HH group. To create a sex- and age-matched control group (CG), individuals admitted to the department for reasons unrelated to HH were invited to participate.

Participants in both groups underwent thermography according to the Glamorgan protocol [5]. One set of thermograms comprised 44 regions of interest (ROIs) distributed between the hands, feet and armpits (including the face). For the HH patients, the procedure was repeated four times: 24 h before the HH patients' surgery, 24 h after the HH patients' surgery, and 3 and 6 months after surgery, during the follow-up visits. At these visits, each patient's sweating was also assessed by interview as a patient-reported outcome measure.

All HH patients underwent a single stage bilateral T2-T4 sympathicotomy. During this procedure, the sympathetic nerve bundle was identified and dissected by electrocautery over the 2nd, 3rd and 4th costal arches within a 2 cm extension.

Differences between the two groups were assessed using independent samples null hypothesis tests (i.e. *t*-test) and effect size measures (i.e. Cohen's d). To assess the influence of temperature variations caused by the phase of the menstrual cycle in female participants, similar analyses were performed in a subset of male participants. A detailed description of the study methods can be found in Supplementary Material 1.

Results

A total of 37 HH patients who underwent T2-T4 sympathicotomy and 16 CG patients completed follow-up. CG patients were slightly younger than HH patients (HH 15.1 years, CG 13.1 years; Cohen's d = − 0.726; 95%CI = − 1.326: − 0.120), but there were no differences in sex at birth between the two groups (HH 56. 8% female, CG 50.0%; OR = 0.762; 95%CI = 0.235: 2.470), body mass (HH 57.6 kg, CG 48.8 kg; Cohe's d = − 0.576; 95%CI = − 1.170:-0.024) or stature (HH 1.62 m, CG 1.59; Cohen's d = − 0.238; 95%CI = − 0.825: + 0.351). The most common conditions in CG patients were acute appendicitis, biliary lithiasis (three patients each), pectus excavatum, phimosis, varicocele (two patients each).

Preoperative body and skin temperatures were analysed in detail in a previous publication [1]. The core body temperature of the HH patients was significantly higher at 20°C (35.3° C and 35.5° C) compared to the control group (34.8° C both sides) (*p*-value 0.014 right and < 0.001 left inner canthus), showing a moderate to high effect size (Cohen's d 1.3 95%CI 0.7:2.0; and 0.8 95%CI 0.2:1.4). No statistical differences were observed in skin temperature at the palms, soles and axillae of the hands between HH patients and the control group (Fig. 1A).

Sympathicotomy produced a significant increase in skin temperature in virtually all ROIs (Fig. 1B). The increase was more pronounced in all palm ROIs (paired Cohen's d between 2.5 and 2.8). The temperature in the palms increased from about 23°C in the fingertips (ROIs 1−5) to

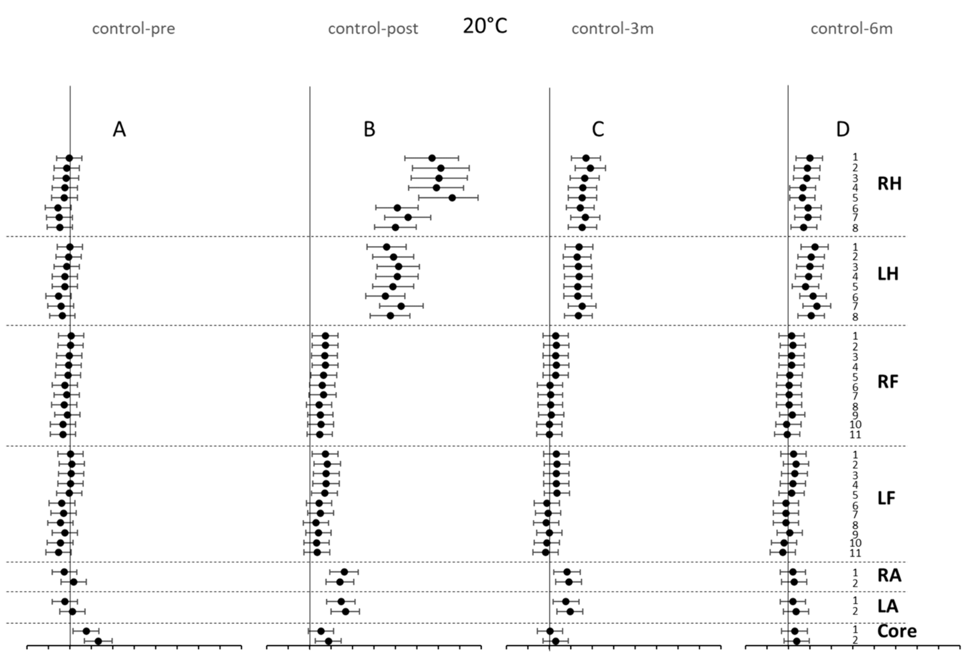

Fig. 1 Effect size (Cohen's d) comparing skin temperature of control group with hyperhidrosis patients at four stages: (**A** pre-surgery; **B** post-surgery, **C** 3 months after surgery; and **D** 6 months after surgery). *RH* right hand, *LH* left hand, *RF* right foot, *LF* left foot, *RA* right axilla, *LA* left axilla

34° C and from 28° C in the palms (ROIs 6–8) to 35° C. This increase in skin temperature produced a strong difference between the CG and sympathicotomised HH patients in all ROIs on the hands (Cohen's d between 3.5 and 6.6) and less marked in the axillae (Cohen's d between 1.4 and 1.6). The temperature difference in all hand ROIs between sympathicotomised HH and CG decreased at 3 months (Cohen's d between 1.3 and 1.9; Fig. 1C) and 6 months (Cohen's d between 0.3 and 1.3; Fig. 1D), with some fingertips (ROIs 4 and 5) reaching almost zero difference. A similar situation was found in the axillae, with a smaller difference at 3 months (Cohen's d between 0.8 and 0.9) and no difference at 6 months ($p > 0.05$).

Sympathicotomy produced a moderate increase in skin temperature of the feet from preoperative to 24 h postoperative in all ROIs (paired Cohen's d between 0.5 and 0.7), which disappeared at the 3 month and 6 month follow-up ($p > 0.05$). The initial increase in sole skin temperature was sufficient to produce a difference between sympathicotomised HH patients and CG toes (Cohen's d between 0.7 and 0.8), but not in the heel ROIs ($p > 0.05$) (Fig. 1B). This difference in toe temperature completely disappeared at the 3 month (Fig. 1C) and 6 month follow-up (Fig. 1D).

Core body temperature did not show any differences between the preoperative and the 24-h postoperative period (paired t-test $p = 0.437$ and 0.101). However, at the 3 month follow-up, the core body temperature of HH patients decreased significantly from the preoperative values (paired Cohen's d between 0.5 and 0.6). A similar but less pronounced effect was observed at the 6-month follow-up (paired Cohen's d between 0.3 and 0.5). Compared to the CG, the sympathicotomised HH patients showed a slightly higher core temperature (Fig. 1B), although less marked than before surgery, which completely disappeared at the 3-month (Fig. 1C) and 6-month follow-up (Fig. 1D).

Identical patterns of temperature differences and very similar effect sizes were obtained in the analysis of the subset of male participants (Supplementary Material 2).

Discusion

Sympathicotomy is expected to cause destruction of postganglionic sympathetic adrenergic and cholinergic neurons, eliminating both tone and consequently sweating and AVA vasoconstriction. As commonly reported [6], in the present study skin temperature in the palms increased after sympathicotomy with a marked effect size, reaching a significantly higher temperature in sympathicotomised HH patients than in CG, reflecting a loss of vasoconstrictive noradrenergic tone. Also in agreement with previous studies [7], plantar temperature increased to a lesser extent after sympathicotomy. At the 3-month and 6-month follow-up visits, the skin temperatures of the sympathicotomised HH patients tended to normalise, reaching values similar to those of the CG patients. At these follow-up visits, the patients reported no excessive sweating in the palms of their hands. This means that sympathicotomised HH patients should have recovered some of the noradrenergic tone that causes vasoconstriction, but not the cholinergic tone that causes sweating.

The mechanisms involved in the selective restoration of adrenergic vascular tone remain elusive. Recovery of adrenergic vasoconstrictor tone may be due to increased sensitivity to plasma catecholamines in the area of sympathicotomy, by a process similar to that observed in patients with spinal lesions [8]. Loss of adrenergic nerves can lead to hypersensitivity of postsynaptic adrenoceptors and loss of neuronal uptake, the main inactivation system of adrenaline and noradrenaline [9]. Both factors contribute to the potentiation of responses to plasma adrenaline and noradrenaline reaching the denervated area. Recovery of the cholinergic response is not expected because denervation does not cause hypersensitivity to acetylcholine [10] and because plasma levels of acetylcholine are insufficient to activate muscarinic receptors (approximately three orders of magnitude lower than its EC_{50}) [11].

In addition, regeneration of transected axons or the use of alternative neuronal pathways to bypass the nerve transection may also facilitate recovery of vasoconstrictor tone. Regeneration of transected axons has been demonstrated in rats [12]. In addition, the upper thoracic sympathetic chain has a complex anatomy where the presence of rami communicantes and interneurons, as well as the nerve of Kuntz [13] may create alternative pathways to allow recovery of tonus [14].

Limitations

The study did not take into account the phase of the menstrual cycle of the female patients, as recommended to take into account the effects of oestrogens on vascular function [15]. However, due to the observational nature of the study, it would not be feasible or ethical to change the time of surgery to coincide with menstruation. The results obtained in the subset of male patients showed that our overall results were reliable. Furthermore, sweating was assessed subjectively and the study was limited to 6 months.

Conclusion

Cholinergic and adrenergic tone are lost immediately after T2-T4 sympathicotomy, resulting in the elimination of palm sweating and vasoconstriction in HH patients. Vasoconstriction, but not sweating, was progressively recovered during a six-month thermographic follow-up, with a skin temperature pattern similar to that of non-HH subjects, suggesting a selective recovery of adrenergic tonus.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10286-024-01047-y.

Author contributions Conceptualization: Fátima Carvalho, Carolina Magalhaes, Joaquim Mendes, Jorge Gonçalves; Methodology: Carolina Magalhaes, Joaquim Mendes, Jorge Gonçalves; Formal analysis and investigation: Fátima Carvalho, Fernando Fernandez-Llimos, Jorge Gonçalves; Writing—original draft preparation: Fátima Carvalho, Fernando Fernandez-Llimos, Jorge Gonçalves; Writing—review and editing: Fátima Carvalho, Fernando Fernandez-Llimos, Jorge Gonçalves; Funding acquisition: Fátima Carvalho, Joaquim Mendes; Supervision: Joaquim Mendes, Jorge Gonçalves.

Funding This research was funded the governmental agency Fundação para a Ciência e Tecnologia (FCT), the official funding body of the Portuguese Ministry of Science, LAETA–UIDB/50022/2020, UIDP/50022/2020.

Data availability Data are available upon reasonable request.

Declarations

Conflict of interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. The study was funded by the Fundação para a Ciência e a Tecnologia (FCT), the official funding body of the Portuguese Ministry of Science.

Declaration of generative AI in scientific writing Artificial intelligence (AI) and AI-assisted technologies were not used in this article.

References

1. Carvalho F, Magalhaes C, Fernandez-Llimos F, Mendes J, Goncalves J (2022) Skin temperature response to thermal stimulus in patients with hyperhidrosis: a comparative study. J Therm Biol 109:103322. https://doi.org/10.1016/j.jtherbio.2022.103322
2. Walloe L (2016) Arterio-venous anastomoses in the human skin and their role in temperature control. Temperature (Austin) 3(1):92–103. https://doi.org/10.1080/23328940.2015.1088502
3. Kux M (1978) Thoracic endoscopic sympathectomy in palmar and axillary hyperhidrosis. Arch Surg 113(3):264–266. https://doi.org/10.1001/archsurg.1978.01370150036005
4. Li X, Tu YR, Lin M, Lai FC, Chen JF, Dai ZJ (2008) Endoscopic thoracic sympathectomy for palmar hyperhidrosis: a randomized control trial comparing T3 and T2–4 ablation. Ann Thorac Surg 85(5):1747–1751. https://doi.org/10.1016/j.athoracsur.2008.01.060
5. Ammer K (2008) The Glamorgan Protocol for recording and evaluation of thermal images of the human body. Thermol Int. 18:125–144
6. 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 A Cent Eur Neurosurg 80(2):67–71. https://doi.org/10.1055/s-0038-1666790
7. Chen HJ, Liang CL, Lu K (2001) Associated change in plantar temperature and sweating after transthoracic endoscopic T2–3 sympathectomy for palmar hyperhidrosis. J Neurosurg 95(1 Suppl):58–63. https://doi.org/10.3171/spi.2001.95.1.0058
8. Teasell RW, Arnold JM, Krassioukov A, Delaney GA (2000) Cardiovascular consequences of loss of supraspinal control of the sympathetic nervous system after spinal cord injury. Arch Phys Med Rehabil 81(4):506–516. https://doi.org/10.1053/mr.2000.3848
9. Trendelenburg U (1966) Mechanisms of supersensitivity and subsensitivity to sympathomimetic amines. Pharmacol Rev 18(1):629–640
10. Hata F, Takeyasu K, Morikawa Y, Lai RT, Ishida H, Yoshida H (1981) Role of alpha-adrenergic receptors in denervation supersensitivity of rat vas deferens. Jpn J Pharmacol 31(3):383–390. https://doi.org/10.1254/jjp.31.383
11. Kawashima K, Oohata H, Fujimoto K, Suzuki T (1987) Plasma concentration of acetylcholine in young women. Neurosci Lett 80(3):339–342. https://doi.org/10.1016/0304-3940(87)90478-2
12. Zheng ZF, Liu YS, Min X, Tang JB, Liu HW, Cheng B (2017) Recovery of sympathetic nerve function after lumbar sympathectomy is slower in the hind limbs than in the torso. Neural Regen Res 12(7):1177–1185. https://doi.org/10.4103/1673-5374.211200
13. Marhold F, Izay B, Zacherl J, Tschabitscher M, Neumayer C (2008) Thoracoscopic and anatomic landmarks of Kuntz's nerve: implications for sympathetic surgery. Ann Thorac Surg 86(5):1653–1658. https://doi.org/10.1016/j.athoracsur.2008.05.080
14. Ireland DR (1999) Preferential formation of strong synapses during re-innervation of guinea-pig sympathetic ganglia. J Physiol. https://doi.org/10.1111/j.1469-7793.1999.00827.x
15. Wenner MM, Stachenfeld NS (1985) Point: investigators should control for menstrual cycle phase when performing studies of vascular control that include women. J Appl Physiol. https://doi.org/10.1152/japplphysiol.00443.2020