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The contribution of cutaneous thermal signals to bodily self-awareness

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Gerardo Salvato[1,2,3] ✉, Paul Mark Jenkinson[4,5], Manuela Sellitto[1,2,3], Damiano Crivelli[3], Francesco Crottini[3,6], Teresa Fazia[1], Silvia Amaryllis Claudia Squarza[7], Mariangela Piano[7], Maria Sessa[8], Martina Gandola[1,2,3], Aikaterini Fotopoulou[5] & Gabriella Bottini[1,2,3]

Thermosensory signals may contribute to the sense of body ownership, but their role remains highly debated. We test this assumption within the framework of pathological body ownership, hypothesising that skin temperature and thermoception differ between right-hemisphere stroke patients with and without Disturbed Sensation of Ownership (DSO) for the contralesional plegic upper limb. Patients with DSO exhibit lower basal hand temperatures bilaterally and impaired perception of cold and warm stimuli. Lesion mapping reveals associations in the right Rolandic Operculum and Insula, with these regions linked to lower skin temperature located posterior to those associated with thermoception deficits. Disconnections in bilateral parietal regions are associated with lower hand temperature, while disconnections in a right-lateralized thalamus-parietal hub correlate with thermoception deficits. We discuss the theoretical implications of these findings in the context of the ongoing debate on the role of homeostatic signals in shaping a coherent sense of body ownership.

Signals from the skin informing on the current state of the body play a crucial role in supporting homoeostatic processes for human survival[1–4]. Among these, skin thermosensory signals provide crucial inputs to the central thermoregulatory system to safeguard the activity of metabolic processes and prevent physical harm[5,6]. The afferent pathway for cutaneous thermal signals is highly articulated and broadcasts thermal information broadly to various cerebral areas. Starting from skin thermoreceptors, the information is conveyed to the brain via myelinated and unmyelinated fibres that reach the spinal lamina I and then the ventromedial posterior nucleus of the thalamus[1,5–8]. Through this spinothalamic pathway, skin thermosensory information reaches the insula. This information is also forwarded to multiple cortical areas such as the parietal cortex, primary and secondary somatosensory cortices, and anterior cingulate and orbitofrontal cortices[9]. Such higher-level and diffuse processing delivers information to the central thermoregulatory system but also provides fine-graded internal signals representation[10,11] at the basis of the 'material me'[12]. Hence, the function of thermosensory signals originating from the skin may extend beyond mere homoeostatic regulation, contributing to the awareness of the material self as a feeling (sentient) entity[13–16], namely bodily self-awareness.

Bodily self-awareness is a multidimensional construct involving the feeling of one's own body as belonging to oneself and the feeling that a given body part belongs to one's body (i.e. the sense of ownership)[17,18]. A coherent sense of ownership originates from integrating different signals from inside and outside the body, and growing evidence suggests that thermosensory information may also play a role. Skin temperature changes and cutaneous thermal stimuli

[1]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy. [2]Cognitive Neuropsychology Centre, ASST "Grande Ospedale Metropolitano Niguarda", Milano, Italy. [3]NeuroMi, Milan Center for Neuroscience, Milano, Italy. [4]Faculty of Psychology, Counselling and Psychotherapy, The Cairnmillar Institute, Melbourne, VIC, Australia. [5]Clinical, Educational and Health Psychology Research Department, Division of Psychology and Language Sciences, University College London, London, UK. [6]School of Advanced Studies, IUSS, Pavia, Italy. [7]Neuroradiology Unit, ASST "Grande Ospedale Metropolitano Niguarda", Milano, Italy. [8]Neurology and Stroke Unit, ASST "Grande Ospedale Metropolitano Niguarda", Milano, Italy. ✉e-mail: gerardo.salvato@unipv.it

perception (i.e. thermoception) have been related to the experimental alteration of the sense of body ownership in healthy subjects[19–26]. However, the precise extent of their influence remains a subject of ongoing debate[19,23,24,27].

To explore the contribution of thermosensory information to body ownership, behavioural studies in healthy subjects have used multisensory integration paradigms based on psychophysiological mechanisms of illusion. These paradigms prompt an illusion of ownership for specific external body parts, such as the hand or the entire body[28–30]. One example of such a paradigm is the 'rubber hand illusion' (RHI)[28], where participants experience a sense of ownership over an anatomically congruent rubber hand through repeated simultaneous stimulation of the viewed rubber hand and the subject's covered own hand. Outcome measures include participants' ratings of the vividness of the illusion and quantification of the illusory perception of spatial displacement of the real arm, also known as proprioceptive drift. Studies using the RHI or similar paradigms (e.g., Mirror Box Illusion[30]) initially showed that a decrease in skin temperature may accompany temporary changes in limb ownership (e.g., refs. 19,23,25,31), but later studies found no consistent temperature changes in the real hand following the illusion of ownership[27,32–36]. Even a study that included five replication attempts, totalling 167 participants, did not show reliable cooling of the real hand during the RHI[27]. In addition, among smaller studies that found some temperature effect, there is substantial variability between subjects, measures, thermosensory signals domain, and the laterality of the body part affected. For example, while some studies reported cooling effects in relation to the vividness of illusion[23], others found it only in relation to the proprioceptive drift[19]. Furthermore, some studies showed both a unilateral reduction in skin temperature on the limb exposed to the illusion[23,26] and concomitant and equivalent temperature changes on the contralateral homologue[19,24,37,38]. Also, the modulation of limb ownership has been linked to a reduced perception of non-painful thermal stimulus (i.e., thermoception)[19,21]. However, there is no agreement on the type of thermal stimuli (warm or cold) involved. Indeed, following the alteration of the sense of ownership for the hand, the participant may misperceive warm compared to cold stimuli[19] or both warm and cold stimuli[21]. This variability suggests that studies with healthy volunteers that utilise experimental illusions to study body ownership have not been able to draw reliable conclusions about the role of thermosensory signals.

When delving into the neural correlates of thermosensory signals that may contribute to body ownership, the framework becomes even more complex. Insights into the neural mechanisms stem from research on the convergence of brain regions involved in the processing of internal and external signals relevant to bodily self-awareness[39,40]. The insula, also recognised as the thermoceptive cortex[3], and the adjacent Rolandic operculum may subserve the convergence between internal and external signals, building bodily self-awareness[39,40]. These regions are also part of the brain network subserving the multisensory integration relevant to body ownership, which also includes the inferior parietal, temporal, and somatosensory regions of the right hemisphere[40,41]. Only one neuromodulatory repetitive transcranial magnetic stimulation (rTMS) study investigated the idea that cortical areas supporting thermoregulatory functions may also be involved in multisensory representations of the body, finding that temporary interference with the posterior parietal cortex resulted in a decrease in limb temperature (but not changes to body ownership)[42]. However, this evidence cannot account for the potential contribution of deeper, critical brain areas, such as the insula, as rTMS is limited by its low reliability in stimulating these regions.

In sum, the causal relationship between thermosensory information and the sense of ownership remains poorly understood. Behavioural studies using multisensory illusion paradigms in healthy populations have produced conflicting and only correlational evidence, while the absence of tailored neuroimaging studies and the limitations of the application of the virtual lesion techniques contribute to the limited understanding of the topic. In this framework, the study of patients with focal brain damage, a golden standard in neuroscientific research[43], can provide important insights on the topic. Indeed, through the neuropsychological lesion-behaviour approach applied to the model of body ownership disorders, we would be able to provide behavioural and neural causal evidence on the contribution of skin thermosensory information to bodily self-awareness. Specifically, it would shed light on the debated issues as to whether thermosensory alterations: (1) are associated with the presence of pathological alterations of the sense of ownership, (2) involve only the limb affected by disownership or the contralateral homologue as well, (3) are associated not only with feelings of disownership but also with alterations in other components of body ownership (i.e., proprioception). Lastly, this method could offer insights on the neural correlates of the thermosensory contribution to body ownership by exploring the lesional correlates of those thermosensory alterations potentially characterising disturbed ownership.

The sense of ownership can deteriorate in many neurological conditions, and, in the case of right-hemisphere stroke, patients may present with the so-called 'Disturbed Sensation of Ownership' (DSO)[44]. DSO is a label mainly used in research settings that clusters symptoms, including the feeling of non-belonging or non-recognition of the contralesional paralysed limb (asomatognosia[45]) and/or delusional ideas of disownership (somatoparaphrenia)[46,47]. Interestingly, a recent scoping review, including 81 studies, revealed that somatosensations, especially concerning thermosensory signals, have been rarely explored in patients with DSO[48]. For instance, only anecdotal evidence in a single case report[49] and a group study[48] showed that right-brain damaged patients with DSO sometimes complain about peculiar sensations concerning the temperature of the affected arm. To date, however, no systematic group study on the objective (rather than the subjective) alterations of thermosensory signals in DSO has been conducted. Moreover, it has been suggested that lesions to and disconnections of high-order cortical regions (such as temporoparietal areas) would not allow thermal or other internal sensations from the body to be integrated appropriately into bodily self-awareness, thus contributing to DSO[50]. Nevertheless, this hypothesis too has yet to be empirically tested.

To fill this gap, we recruited 45 patients presenting right-hemisphere focal brain damage, including patients with DSO, to explore whether and how deficits in limb ownership relate to limb temperature alterations and thermoception deficits. As DSO is associated with the presence of contralesional hemiplegia, and since peripheral thermoregulation may vary according to movement disorders[51], we subsampled participants based on the presence of DSO and hemiplegia, resulting in three groups: a group with hemiplegia and DSO (HP+ DSO+), a group with hemiplegia without DSO (HP+ DSO−), and a group of patients without hemiplegia or DSO (HP− DSO−) (see below for details about the clinical assessment). We measured the basal skin temperature of the upper and lower limbs via an infrared thermometer in 40 patients (HP+ DSO+ $n = 9$; HP+ DSO− $n = 10$; HP− DSO− $n = 21$) and assessed the perception of cold and warm stimuli within an innocuous (non-painful) range applied to the skin of the upper limbs in 34 patients (HP+ DSO+ $n = 8$; HP+ DSO− $n = 7$; HP− DSO− $n = 19$). To our knowledge[48], our study represents the largest sample sizes recorded in the DSO syndrome research, employing objective, quantitative methods to assess skin temperature and thermoception ability. If the function of thermosensory signals extends beyond mere survival mechanisms to support bodily self-awareness, then, from a neuropsychological perspective, brain damage leading to symptomatic alterations in bodily self-awareness should likely result in changes in thermosensory functioning. Specifically, we predicted that patients with DSO would show thermosensory alterations, presenting

with lower skin temperature and reduced thermosensation as compared to the other two groups with and without left hemiplegia but without DSO. If present, the thermosensory signal alterations may involve the affected or both the affected and unaffected arms in DSO, and it could be related to the patients' disturbed sensation of ownership as well as to their proprioceptive ability. To further study the contribution of thermosensory signals to body ownership at the neural level, we took advantage of two advanced lesion-symptom mapping techniques. Lesion-symptom mapping techniques identify potential brain-behaviour relationships by correlating brain lesions or disconnections with an observed continuous variable (e.g., a test score or other measure such as temperature). In two regression models encompassing all patients' lesion maps along with their skin temperature and thermoception data, we conducted anatomo-clinical analyses to investigate the neural correlates of the thermosensory alterations (potentially characterising the HP+ DSO+ group) using voxel-based lesion-symptom mapping (VLSM). Additionally, we explored whether the potential disrupted communication between brain regions due to patients' lesions is relevant to altered thermosensory signals (potentially characterising the HP+ DSO+ group) through connectome-based lesion-symptom mapping (CLSM). If thermosensory information contributes to bodily self-awareness, we would expect altered thermosensory signals to be associated with lesions in regions implicated in body ownership disruptions, such as the insular and Rolandic operculum areas. Furthermore, structural disconnections in other areas, such as the temporoparietal regions, resulting from lesions to adjacent white matter tracts, are likely to be associated with altered thermosensory information processing, which may contribute to the characterisation of DSO.

Results

Skin temperature

Sample. The sample that completed the skin temperature measurement comprised 40 out of 45 patients (HP+ DSO+ $n = 9$; HP+ DSO− $n = 10$; HP− DSO− $n = 21$; see Supplementary Table 1). Five patients were not included as they did not complete the skin temperature measurement due to time constraints. In the HP+ DSO+ group, patients experienced a disturbed sensation of ownership exclusively for the left paralysed arm/hand. None of the patients exhibited DSO exclusively for the legs/feet, nor for the legs/feet in combination with the arms/hands. The three groups did not differ in age ($p = 0.622$), sex ($p = 0.20$), education ($p = 0.862$), Mini-Mental State Examination (MMSE) score ($p = 0.566$), and time from stroke onset ($p = 0.859$). HP+ DSO+ and HP+ DSO− differed in the presence of extrapersonal Unilateral Spatial Neglect (USN) ($p = 0.01$), with patients with DSO all presenting with the symptom. There were no significant differences between HP+ DSO+ and HP+ DSO− groups for the presence of personal USN ($p = 0.41$) and anosognosia for hemiplegia ($p = 0.88$). Importantly, the three groups did not differ in the tympanic (core) temperature on the day of testing ($p = 0.155$). Due to some clinical difficulties (i.e., compression medical stockings), feet skin temperature was collected only in a subsample (HP+ DSO+ $n = 7$; HP+ DSO− $n = 6$; HP− DSO− $n = 20$). To maintain the larger available sample for the hands temperature, we performed separate statistical models for the upper and lower limbs.

Baseline skin temperature results. To investigate whether the baseline skin temperature of the limb differed between the groups based on the subjective experience of disownership, we performed a General Linear Model with Group (HP+ DSO+, HP+ DSO−, HP− DSO−) and limb side (left, right) as fixed factors. The Celsius degree temperature was modelled as the dependent variable. We also included the left-hand proprioception score to test whether the potential subjective arm spatial displacement (i.e., proprioceptive deficit) influenced the baseline temperature[19,52]. Lastly, we checked whether demographics (e.g., age, sex) and neuropsychological deficits (e.g., extrapersonal USN) had an impact on the results by entering these variables as covariates in the models. Sex ($p = 0.005$) and proprioception ($p = 0.006$) were the only significant and, thus, included as covariates in the final model. For the hands' temperature, results showed a main effect of Group ($F_{(2,79)} = 6.126$, $p = 0.003$; $\eta^2_p = 0.145$) (Fig. 1). Post hoc Bonferroni-corrected comparisons indicated a difference between HP+ DSO+ ($M = 30.265$, SE = 0.487) and HP+ DSO− ($M = 31.995$, SE = 0.347; $p = 0.007$) and between HP+ DSO+ and HP− DSO− ($M = 32.427$, SE = 0.290; $p = 0.005$), and no difference between HP+ DSO− and HP− DSO − ($p > 0.05$). There was no effect of Side ($F_{(1,79)} = 0.583$, $p = 0.45$; $\eta^2_p = 0.008$) nor a Group by Side interaction ($F_{(2,79)} = 0.093$, $p = 0.911$; $\eta^2_p = 0.003$). To address the unbalanced group sample size and verify the robustness of the results, non-parametric bootstrap resampling based on distribution's quintiles with 5,000 replicates stratified by group was employed to estimate 95% bootstrap Confidence Intervals for post hoc pairwise comparisons. Results from bootstrap resampling confirmed statistically significant differences between HP+ DSO+ and HP+ DSO− (estimate = 1.73, 95% CI [0.71;2.76], $p_{adj} = 0.001$) and between HP+ DSO+ and HP− DSO− (estimate = 2.162, 95% CI [0.99;3.40], $p_{adj} = 0.004$), and no difference between HP+ DSO− and HP− DSO− (estimate = 0.43, 95% CI [−0.56;1.38], $p_{adj} > 0.05$).

For the feet temperature analyses, we did not find any significant result (main effect of Group: ($F_{(2,65)} = 0.169$, $p = 0.845$; $\eta^2_p = 0.006$); main effect of Side: ($F_{(1,65)} = 0.366$, $p = 0.548$; $\eta^2_p = 0.006$); interaction Group by Side ($F_{(2,65)} = 0.072$, $p = 0.930$; $\eta^2_p = 0.002$); see Supplementary Fig. 1). In this case, neither the demographics nor neuropsychological deficits were significant.

Voxel-based lesion-symptom mapping (VLSM) results. The above findings showed that patients with DSO present with lower hands temperature compared to the two control groups. To identify brain lesions associated with lower left and right hand temperature values, we employed a VLSM approach. We ran a *t*-test at each voxel to relate the voxel status (lesioned or spared) and a continuous temperature score, which was computed by averaging the left-right hand raw temperature, adjusted by sex and proprioception (to reflect the effects observed in the above findings). The VLSM analysis assumes that a brain lesion leads to impairment in the dependent variable (and thus lower skin temperature in the present case). We explored lesion-symptom associations including the whole sample of 40 patients to maximise the statistical power. The lesion overlay showed that the highest overlap ($n = 23$) corresponded to the MCA territory within subcortical regions (e.g., putamen) (see Supplementary Fig. 5). VLSM analysis identified 34 significant voxels, with 29 exhibiting a peak *Z*-score ($z = -3.6$) centred in the right Rolandic Operculum (MNI: $x = 46$, $y = -11$, $z = 16$; Fig. 2). A visual inspection of the resulting map, utilising the Jülich Brain Atlas parcellation[53], revealed an overlap with the parietal Operculum (OP) 1 and 3 areas. Some voxels also fell into the posterior insula, and specifically area Ig3. This suggests that damage to Rolandic Operculum/posterior Insula is associated with lower basal hand temperature. Some voxels also fell into the right Arcuate Anterior Segment and the right corticospinal tract (voxel $n = 5$). Interestingly, upon qualitative exploration of lesional overlaps, it is noted that most HP+ DSO+ patients (78%) had a lesion at the MNI peak $x = 46$, $y = -11$, $z = 16$ (HP+ DSO− = 20%, HP− DSO− = 5%; see Supplementary Fig. 3).

Connectome-based lesion-symptom mapping (CLSM) results. We employed CLSM to identify structural disconnections between brain regions associated with lower hands temperature values. CLSM data analyses were performed on the whole patient sample ($n = 40$) using the same temperature index computed for the VLSM analyses. Mapping hands temperature to ROI-to-ROI analysis identified 19 disconnections (see Fig. 3). The analysis revealed that lower hands temperature was associated with the disconnection of three hub-like structures, the right primary somatosensory cortex (SI), secondary

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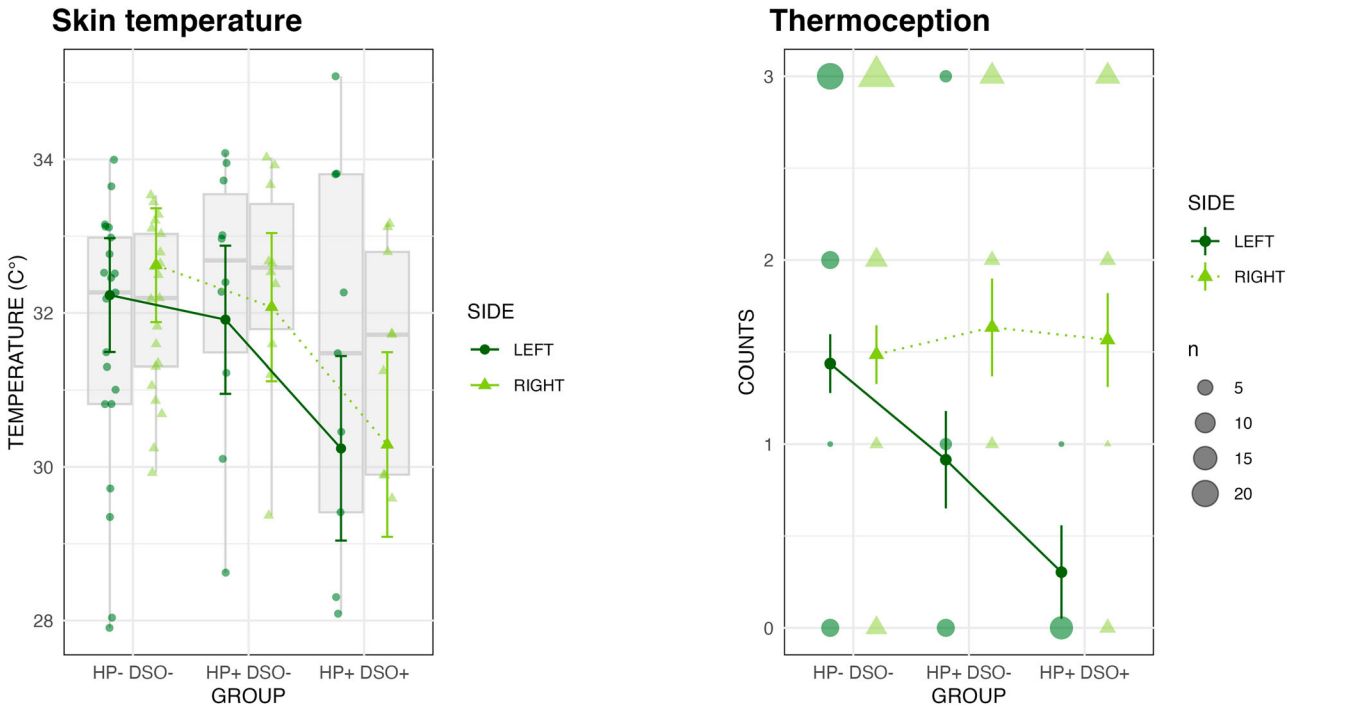

Fig. 1 | Skin temperature and thermoception results. In the left panel, the grey-shaded boxplots display the basal skin temperature (measured in Celsius) distribution across the three different groups of patients, separately by sides (left in light green vs. right in dark green). The central line indicates the median value (50th percentile), while the bounds of the box represent the 25th (lower bound) and 75th percentiles (upper bound), i.e., interquartile range (IQR). The whiskers extend to the minimum and maximum values within 1.5 times the IQR. Jittered points represent the individual data points, while the estimated marginal means for each group and side are shown as larger bold dots (circles for the left side, triangles for the right side), with error bars representing 95% confidence intervals. Solid lines indicate the left side, and dotted lines indicate the right side. To investigate whether the baseline skin temperature of the limb differed between the groups based on the subjective experience of disownership, we performed a General Linear Model with Group (HP+ DSO+ ($n = 9$), HP+ DSO− ($n = 10$), HP− DSO− ($n = 21$)) and Side (left, right) as fixed factors. The temperature was modelled as the dependent variable. Sex and proprioception were included as covariates in the final model. For the hands' temperature, results showed a main effect of Group ($F_{(2,79)} = 6.126$, $p = 0.003$; $\eta^2_p = 0.145$). Post hoc Bonferroni-corrected comparisons indicated a difference between HP+ DSO+ and HP+ DSO− ($p = 0.007$) and between HP+ DSO+ and HP− DSO− ($p = 0.005$), and no difference between HP+ DSO− and HP− DSO− ($p > 0.05$). There was no effect of Side ($F_{(1,79)} = 0.583$, $p = 0.45$; $\eta^2_p = 0.008$) nor a Group by Side interaction ($F_{(2,79)} = 0.093$, $p = 0.911$; $\eta^2_p = 0.003$). To address the unbalanced group sample size and verify the robustness of the results, non-parametric bootstrap resampling based on distribution's quintiles with 5000 replicates stratified by group was employed to estimate 95% bootstrap confidence intervals for post hoc pairwise comparisons. Results showed statistically significant differences between HP+ DSO+ and HP+ DSO− (estimate = 1.73, 95% CI [0.71;2.76], $p_{adj} = 0.001$) and between HP+ DSO+ and HP− DSO− (estimate = 2.162, 95% CI [0.99;3.40], $p_{adj} = 0.004$), and no difference between HP+ DSO− and HP− DSO− (estimate = 0.43, 95% CI [−0.56;1.38], $p_{adj} > 0.05$). The right panel shows the average number of stimuli detected in the thermoception task by the three groups of patients, separately by left (light green) and right (dark green) hand. The bold dots represent the estimated marginal means for each group and side, with error bars denoting 95% confidence intervals. Solid lines indicate the left side, and dotted lines indicate the right side. To investigate whether DSO was associated with reduced hand thermoceptive ability, we ran a Generalized Linear Model with Group (HP+ DSO+ ($n = 8$), HP+ DSO− ($n = 7$), HP− DSO− ($n = 19$)), Side (left, right), and Stimulus type (warm, cold) as fixed factors. The thermoception score (ranging from 0 to 3) was modelled as the dependent variable. We adopted a Poisson distribution with a square root link function to optimise the model stability. The results showed a main effect of Group ($x^2_{(2)} = 15.993$, $p < 0.001$), indicating that HP+ DSO+ performed worse than the other two groups. There was a main effect of Side ($x^2_{(1)} = 21.789$, $p < 0.001$), with an overall lower temperature detection on the left hand. We also found a Group by Side interaction ($x^2_{(2)} = 30.880$, $p < 0.001$). Bonferroni-corrected post hoc comparisons showed that HP+ DSO+ were less accurate in perceiving thermal stimuli on the left hand compared to HP+ DSO− ($p = 0.008$) and HP− DSO− ($p < 0.001$). Similarly, HP+ DSO− showed less accuracy on the left hand than HP− DSO− ($p = 0.009$). Furthermore, both HP+ DSO+ ($p < 0.001$) and HP+ DSO− ($p = 0.001$) showed a left-right side difference in thermoception, performing worse with the left hand as compared with the right hand, while HP− DSO− did not ($p > 0.05$). The main effect of Stimulus (cold vs. warm stimuli) was not significant ($x^2_{(1)} = 2.728$, $p = 0.099$), as well as the Group by Stimulus ($x^2_{(2)} = 0.388$, $p = 0.824$), Side by Stimulus ($x^2_{(1)} = 0.121$, $p = 0.727$), and Group by Side by Stimulus ($x^2_{(2)} = 0.111$, $p = 0.946$) interactions. Extrapersonal USN was the only covariate that was significant ($p = 0.005$). To address the unbalanced group sample size and verify the robustness of the results, non-parametric bootstrap resampling based on distribution's quintiles with 5000 replicates stratified by group was employed to estimate 95% bootstrap confidence intervals for planned post hoc pairwise comparisons. Results from bootstrap resampling showed statistically significant differences for thermoception on the left hand between HP+ DSO+ and HP+ DSO− (estimate = 0.612, 95% CI [0.178;0.921], $p_{adj} = 0.04$), HP+ DSO − and HP− DSO− (estimate = 0.522, 95% CI [0.222;0.919], $p_{adj} = 0.008$), and between HP+ DSO+ and HP− DSO− (estimate = 1.133, 95% CI [0.835;1.368], $p_{adj} < 0.001$). All analyses were two-sided. HP hemiplegia, present (+) or absent (−), DSO Disturbed Sensation of Ownership, present (+) or absent (−), HP+ DSO+ patients with hemiplegia and disturbances in the sense of body ownership, HP+ DSO− patients with hemiplegia and without disturbances in the sense of body ownership, HP− DSO− patients without hemiplegia or disturbances in the sense of body ownership, USN unilateral spatial neglect. Source data are provided as a Source Data file.

somatosensory cortex (SII), and the inferior parietal gyrus disconnected mainly from their contralateral homologue areas. Nine disconnections between the right postcentral gyrus and left temporoparietal regions were identified. We also found 6 disconnections between the right supramarginal gyrus and the left temporoparietal regions. Moreover, we identified 4 disconnections involving the right inferior parietal gyrus and left temporooccipital areas (see Table 1).

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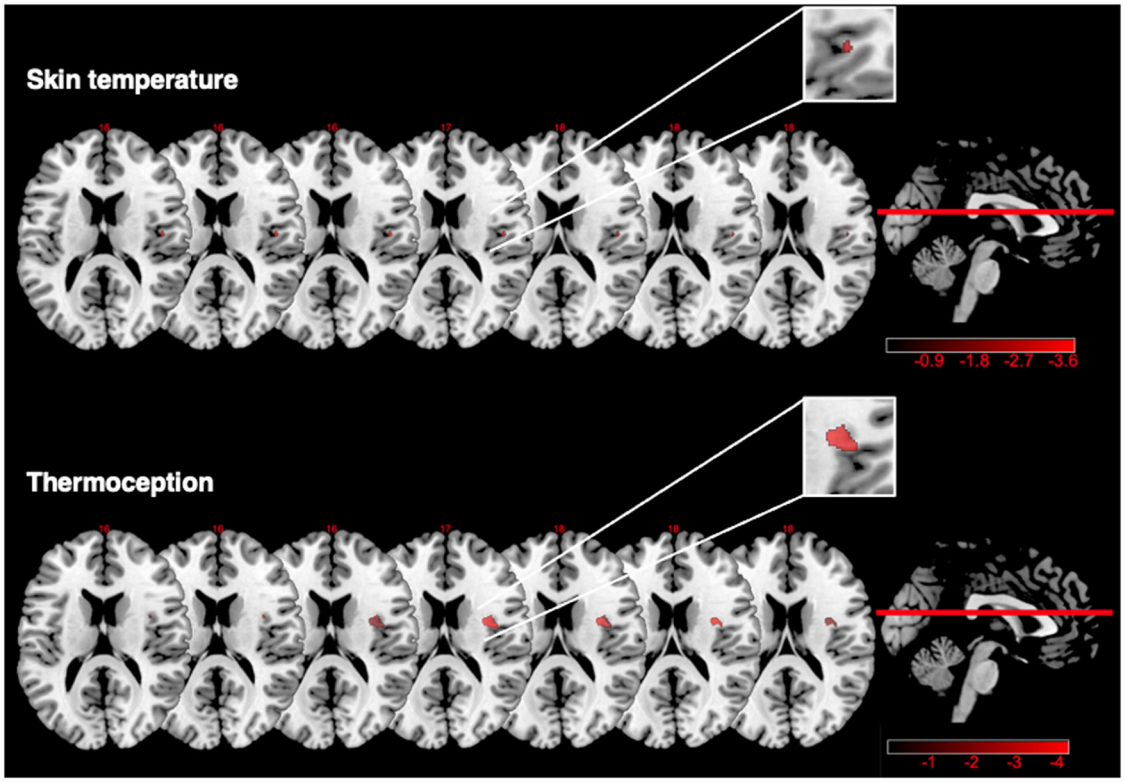

Fig. 2 | Voxel-based lesion-symptom mapping (VLSM) results. The upper panel shows the brain regions whose lesions were associated with lower basal left and right hand skin temperature in all patients. We ran a *t*-test at each voxel to relate the voxel status (lesioned or spared) and a continuous temperature score, which was computed by averaging the left-right hand raw temperature, adjusted by sex and proprioception. We explored lesion-symptom associations including the whole sample of 40 patients to maximise the statistical power. The lower panel shows the brain region whose lesion was associated with a reduced ability to discriminate both cold and warm stimuli. Using a voxelwise approach, we ran a *t*-test at each voxel to relate the voxel status (lesioned or spared) and a continuous thermoception score. This score was obtained by averaging the number of detected stimuli in the warm and cold conditions for the left hand, mirroring the effect found in the behavioural analyses. We explored lesion-symptom associations including the whole sample of 34 patients to maximise the statistical power. In both cases, we adopted a one-tailed 0.05 alpha threshold with 10,000 permutations. The permutation-based correction was applied to maximise power while maintaining control of the FWER. The statistical tests performed are one-tailed; that is, brain injury leads to impaired behavioural performance. Z-coordinates of each axial slice are given. In each axial slice, the right hemisphere is on the right side. The level of the axial slices has been marked by a red line on the sagittal view of the brain. The colour scale illustrates the corresponding *Z* values.

Thermoception

Sample. The sample that completed the thermoception task comprised 34 out of 45 patients (HP+ DSO+ $n = 8$; HP+ DSO− $n = 7$; HP− DSO − $n = 19$; see Supplementary Table 2). Eleven patients did not complete the thermoception task due to fatigue, typical in the acute phase of stroke. As in the case of the sample for the skin temperature analysis, in the HP+ DSO+ group, patients experienced a disturbed sensation of ownership exclusively for the left paralysed arm/hand. None of the patients exhibited DSO exclusively for the legs/feet, nor for the legs/feet in combination with the arms/hands. The three groups did not differ in age ($p = 0.772$), sex ($p = 0.91$), education ($p = 0.925$), time from stroke onset ($p = 0.511$), and MMSE score ($p = 0.659$). Notably, there were no significant differences between the HP+ DSO+ and HP+ DSO− groups for extrapersonal USN ($p = 0.44$), personal USN ($p = 0.14$), hemianaesthesia ($p = 0.10$), and anosognosia for hemiplegia ($p = 0.88$).

Thermoception task results. To investigate whether DSO was associated with reduced hand thermoceptive ability, we ran a Generalized Linear Model with Group (HP+ DSO+, HP+ DSO−, HP− DSO−), Side (left, right), and Stimulus type (warm, cold) as fixed factors. The thermoception score (ranging from 0 to 3) was modelled as the dependent variable. We adopted a Poisson distribution with a square root link function to optimise the model stability. Lastly, we controlled whether demographics (e.g., age, sex) and neuropsychological deficits (e.g., extrapersonal USN) could impact the results by inserting these variables as covariates in the model. The results showed a main effect of Group ($x^2_{(2)} = 15.993$, $p < 0.001$), indicating that HP+ DSO+ performed worse than the other two groups (Fig. 1). There was a main effect of Side ($x^2_{(1)} = 21.789$, $p < 0.001$), with an overall lower temperature detection on the left hand. We also found a Group by Side interaction ($x^2_{(2)} = 30.880$, $p < 0.001$). Bonferroni-corrected post hoc comparisons showed that HP+ DSO+ were less accurate in perceiving thermal stimuli on the left hand (hits percentage = 2%) compared to HP+ DSO− (hits percentage = 29%, $p = 0.008$) and HP− DSO− (hits percentage = 70%, $p < 0.001$). Similarly, HP+ DSO− showed less accuracy on the left hand than HP− DSO− ($p = 0.009$). Furthermore, both HP+ DSO+ ($p < 0.001$) and HP+ DSO− ($p = 0.001$) showed a left-right side difference in thermoception, performing worse with the left hand as compared with the right hand, while HP− DSO− did not ($p > 0.05$). The main effect of Stimulus (cold vs. warm stimuli) was not significant ($x^2_{(1)} = 2.728$, $p = 0.099$), as well as the Group by Stimulus ($x^2_{(2)} = 0.388$, $p = 0.824$), Side by Stimulus ($x^2_{(1)} = 0.121$, $p = 0.727$), and Group by Side by Stimulus ($x^2_{(2)} = 0.111$, $p = 0.946$) interactions. Extrapersonal USN was the only covariate that was significant ($p = 0.005$), although it did not affect the results. To address the unbalanced group sample size and verify the robustness of the results, non-parametric bootstrap resampling based on distribution's quintiles with 5000 replicates stratified by group was employed to

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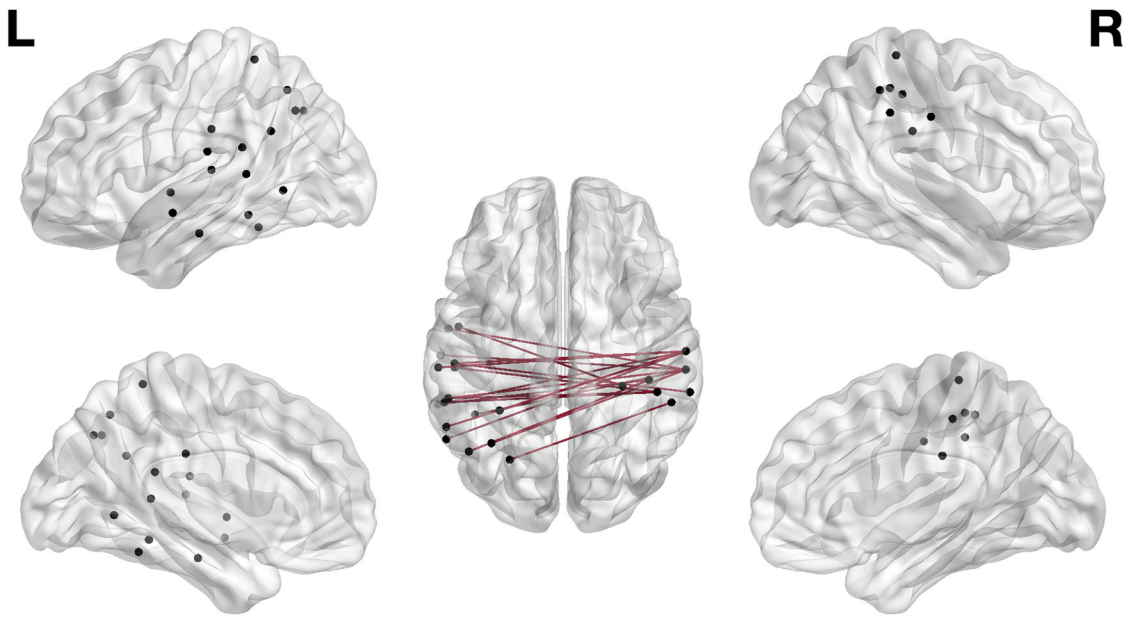

Fig. 3 | Skin temperature–connectome-based lesion-symptom mapping (CLSM) results. We analysed the patients' dysconnectivity matrices through a mass-univariate analysis to identify associations between parcel-to-parcel disconnections and skin temperature. Maximum statistic permutation ($n = 10{,}000$) was employed on permuted behavioural data and the original disconnection data to assess the distribution of maximum statistics under the null hypothesis. To adopt a more conservative approach, we applied a one-sided corrected threshold for statistical significance at $p < 0.01$ by identifying the 99th percentile of permutation-derived maximum statistics. Results are visualised with the BrainNet Viewer (http://www.nitrc.org/projects/bnv/). The image presents the disconnections significantly associated with lower left and right hand skin temperature. Dots indicate regions at the endpoints of significant disconnections.

Table 1 | Skin temperature–connectome-based lesion-symptom mapping (CLSM) results

Brain region	x	y	z		Brain region	x	y	z
Left sup. Temporal gyrus	−51	−4	−1	↔	Right Postcentral gyrus	29	−33	66
Left sup. Parietal gyrus	−31	−45	64			60	−16	36
Left Supramarginal gyrus	−53	−22	19					
Left Supramarginal gyrus	−57	−53	29					
Left Supramarginal gyrus	−60	−38	37					
Left mid. Temporal gyrus	−61	−42	−12					
Left mid. Temporal gyrus	−57	−59	0					
Left mid. Temporal gyrus	−61	−42	−12			42	−30	47
Left Angular gyrus	−46	−65	39					
Left inf. Temporal gyrus	−43	−47	−18	↔	Right Supramarginal gyrus	60	−25	29
Left sup. Temporal gyrus	−56	−39	21					
Left mid. Temporal gyrus	−60	−18	−21					
Left mid. Temporal gyrus	−56	−5	−11					
Left inf. Parietal gyrus	−35	−61	49					
Left Supramarginal gyrus	−53	−22	19			62	−36	38
Left sup. Temporal gyrus	−53	−24	10	↔	Right inf. Parietal gyrus	46	−36	50
Left sup. Temporal gyrus	−56	−39	21					
Left mid. Temporal gyrus	−58	−41	8					
Left mid. Occipital gyrus	−26	−69	39			53	−41	49

Parcel-to-parcel disconnections significantly associated with low hands temperature following the region-to-region disconnectivity analysis at $p < 0.01$ (corresponding to Fig. 3). Each row denotes exact label according to the Schaefer et al.[100] parcellations of each grey matter-to-grey matter disconnection. The anatomical label of the statistical results was assessed using the Automated Anatomical Labelling map (template AAL).

estimate 95% bootstrap Confidence Intervals for planned post-hoc pairwise comparisons. Results from bootstrap resampling confirmed statistically significant differences for thermoception on the left hand between HP+ DSO+ and HP+ DSO− (estimate = 0.612, 95% CI [0.178;0.921], $p_{adj} = 0.04$), HP+ DSO− and HP− DSO− (estimate = 0.522, 95% CI [0.222;0.919], $p_{adj} = 0.008$), and between HP+ DSO+ and HP− DSO− (estimate = 1.133, 95% CI [0.835;1.368], $p_{adj} < 0.001$). Statistically significant left vs. right hand differences in thermoception were observed in HP+ DSO+ (estimate = −1.26, 95% CI [−1.513;−0.927], $p_{adj} < 0.001$) and in HP+ DSO− ($\beta = -0.719$, 95% CI

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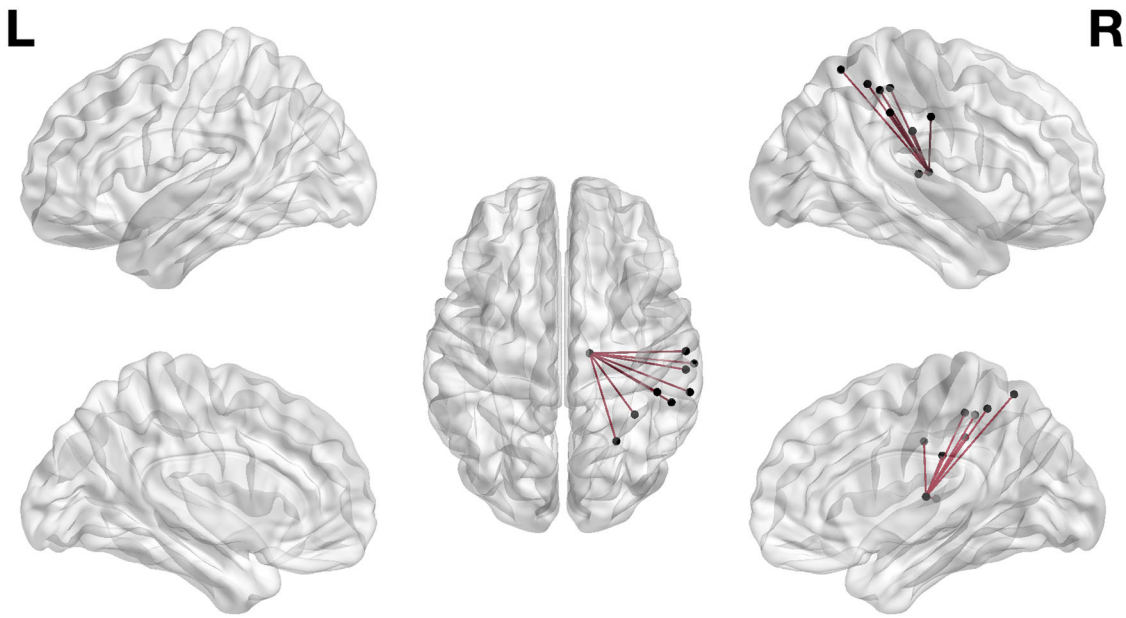

Fig. 4 | Thermoception–connectome-based lesion-symptom mapping (CLSM) results. We analysed the patients' dysconnectivity matrices through a mass-univariate analysis to identify associations between parcel-to-parcel disconnections and thermoception. Maximum statistic permutation ($n = 10{,}000$) was employed on permuted behavioural data and the original disconnection data to assess the distribution of maximum statistics under the null hypothesis. To adopt a more conservative approach, we applied a one-sided corrected threshold for statistical significance at $p < 0.01$ by identifying the 99th percentile of permutation-derived maximum statistics. Results are visualised with the BrainNet Viewer (http://www.nitrc.org/projects/bnv/). The image presents the disconnections significantly associated with reduced thermoception. Dots indicate regions at the endpoints of significant disconnections.

[−1.114;−0.4327], $p_{adj} < 0.001$), while no left vs. right hand difference in thermoception was observed in HP− DSO− ($\beta = -0.049$, 95% CI [−0.24;0.14], $p_{adj} > 0.05$).

Voxel-based lesion-symptom mapping (VLSM) results. The above behavioural findings demonstrated that patients with DSO presented thermoceptive deficits on the left hand compared to the two control groups. Thus, we explored the brain lesions associated with such deficits through a VLSM analysis. We include the whole sample of 34 patients to maximise the statistical power. Using a voxelwise approach, we ran a *t*-test at each voxel to relate the voxel status (lesioned or spared) and a continuous thermoception score. This score was obtained by averaging the number of detected stimuli in the warm and cold conditions for the left hand, mirroring the effect found in the behavioural analyses. The VLSM analysis assumes that a brain lesion leads to impairment in the dependent variable (and thus thermoception deficit in the present case). The lesion overlay showed that the highest overlap ($n = 22$) corresponded to the MCA territory within subcortical regions (e.g., putamen) (see Supplementary Fig. 5). VLSM results yielded 117 significant voxels, 116 of which with the peak *Z*-score ($z = -4.2$) centred within a region encompassing the right Rolandic Operculum and Insula, as well as the underlying white matter (MNI: $x = 35$, $y = -1$, $z = 17$; Fig. 2). Additionally, we visually inspected the resulting VLSM map for thermoception using the Jülich Brain atlas parcellation[53], and found that it primarily overlapped with the Insula Id4 area, and frontal Operculum (OP) 5 and 6 areas. This suggests that damage to the Operculum/Insula is associated with lower thermal stimuli perception. A qualitative examination of lesion overlaps revealed that most HP+ DSO+ patients (75%) had a lesion at the MNI peak $x = 35$, $y = -1$, $z = 17$ (HP+ DSO− = 43%, HP− DSO− = 16%; see Supplementary Fig. 3).

Connectome-based lesion-symptom mapping (CLSM) results. We used CSLM to identify structural disconnections between brain regions associated with thermoception deficits. CLSM data analyses were performed on the whole patients' sample ($n = 34$) using the same thermoception index computed for the VLSM analyses. The ROI-to-ROI analysis revealed that reduced perception of warm and cold stimuli for the left hand was mainly associated with the disconnection of a right-lateralised hub-like structure (i.e., thalamus). Specifically, we found eight significant disconnections (see Fig. 4) in the right hemisphere involving the right thalamus to parcels in the right inferior and superior parietal, postcentral and supramarginal gyri (see Table 2).

Discussion

Signals about the current physiological state of our body contribute to an optimal homoeostatic balance[2]. Notably, their role may extend beyond survival processes, participating in the sense of ownership. In healthy individuals, the contribution of skin temperature and thermoception to body ownership is still poorly understood. To provide causal insights on the issues sparked by correlational and conflicting

Table 2 | Thermoception–connectome-based lesion-symptom mapping (CLSM) results

Brain region	x	y	z		Brain region	x	y	z
Sup. Temporal gyrus	64	−22	8	↔	Thalamus	13	−17	9
Supramarginal gyrus	62	−36	38					
Supramarginal gyrus	60	−25	29					
Postcentral gyrus	60	−16	36					
Inf. Parietal gyrus	53	−41	49					
Inf. Parietal gyrus	46	−36	50					
Inf. Parietal gyrus	35	−47	52					
Sup. Parietal gyrus	26	−60	59					

Parcel-to-parcel disconnections significantly associated with reduced thermoception following the region-to-region disconnectivity analysis at $p < 0.01$ (corresponding to Fig. 4). Each row denotes exact label according to the Schaefer et al.[100] parcellation of each grey matter-to-grey matter disconnection. The anatomical label of the statistical results was assessed using the Automated Anatomical Labelling map (template AAL).

findings[19,23,27,31], we studied the pathological model of body ownership in right-hemisphere brain-damaged patients with Disturbed Sensation of Ownership (DSO)[44,50,54]. Specifically, the use of the classical neuropsychological approach, through the exploration of basal skin temperature alterations and thermoception deficits in brain-damaged patients with and without DSO, showed significant differences between the target, symptomatic group and the two control groups. This suggests that skin temperature and thermoception may contribute to bodily self-awareness. Furthermore, analysing how lesions and structural disconnections between specific brain regions led to reduced skin temperature and thermoception deficits has provided valuable insights into the brain areas involved in processing thermosensory signals, potentially linked to the sense of body ownership. Finally, since this processing was more impaired in patients with DSO compared to those without, we have drawn additional speculative inferences about the role of thermosensory signals in contributing to the sense of body ownership.

In the case of basal skin temperature, consistent with our hypothesis, data showed that patients with DSO for their plegic contralesional (left) limb presented with lower basal hands temperature compared to both plegic and non-plegic individuals without DSO. Although studies on limb temperature variations in patients with DSO are lacking, it is likely that these temperature changes may represent one of the somatosensory elements whose disruption contributes to the development of the disorder. It is possible that in DSO, the peripheral thermoregulatory system is distorted due to perturbation of the homoeostatic regulation mechanisms, implicating that also the areas indirectly connected to the autonomic nervous system, the insula in particular, are damaged. From a neuropsychological perspective, this finding in individuals with brain damage suggests that, in neurotypical people, skin temperature is likely to play a crucial role as one of the sensory sources participating in the maintenance of a coherent sense of body ownership. One aspect that remains to be investigated is the involvement of the central thermoregulatory system, as skin temperature represents peripheral body temperature. Future studies may address this issue through pharmacological experiments by inhibiting central thermoregulatory receptors and simultaneously assessing the sense of body ownership.

We additionally found that the temperature decrease in patients with DSO, compared to the other two groups, extended to the unimpaired limb, offering causal evidence for prior conflicting findings in healthy subjects[19,24,31,38,55]. One possibility to explain why patients with a unilateral DSO presented with a lower temperature than controls on both hands could be that their brain damage extends to areas that have a bilateral somatosensory representation of the arms. This phenomenon already occurs in other domains, such as tactile awareness, with the right SII subserving a bilateral representation of tactile stimuli[56]. Given the physiological association between touch and temperature, whose information is carried by similar mechanisms[57], and given our lesion-symptom mapping results, indicating that alterations involving the right SII (see also below) are associated with reduced skin temperature, the above reasoning could be applied to skin temperature as well. The fact that lower temperature was detected on both hands while our patients experienced disownership only toward the left limb might also be explained by the concomitant derangement of other components relevant to body ownership, such as the tactile, motor, and proprioceptive signals. In the case of the right unaffected limb, the cognitive system might still be capable of maintaining a coherent representation of that body part by prioritising other preserved information, such as motor and tactile signals, despite temperature alteration. Another possibility is that the temperature change is non-specific and involves the entire body regardless of the affected body part. However, this is unlikely as patients with DSO in the present study did not show any difference when considering the temperature of the feet, although caution should be paid due to the relatively small sample size when analysing basal feet temperature. Future research could examine the neural mechanisms underlying the laterality of skin temperature changes in response to unilateral ownership modulation through functional neuroimaging, additionally exploring potential correlations with skin temperature alterations across various body regions.

Our exploration of the pathological model of body ownership also revealed that skin temperature was influenced by proprioception, suggesting that the mechanisms of body ownership may require the integration of thermal and spatial information of the limb. The link between temperature and the location of the body in space is also supported by results from a study of patients with hand unilateral Complex Regional Pain Syndrome (CRPS)[52]. Moseley and collaborators found that the affected arm became warmer when these patients moved it into the contralateral hemispace. This spatial manoeuvre also triggered the reinstatement of the sense of ownership degraded by the CRPS. It is, therefore, plausible to hypothesise that limb temperature and limb position in space both contribute to the construction of a coherent representation of the self.

The use of VLSM has also revealed that lesions to the Rolandic Operculum/insula predicted lower hands temperature. HP+ DSO+ patients presented with lower left-right hand temperature compared to the two control groups. Thus, it is reasonable to hypothesise that damage to this area may contribute to both the observed lower skin temperature and disturbed ownership, although the current study has not provided direct evidence for this claim. Further indications of this hypothetical link can be provided by the visual inspection of the lesion distribution of the three patients' groups. Indeed, the majority of HP+ DSO+ patients (7 out of 9) presented lesions at the resulting MNI peak (see Supplementary Fig. 3), while far fewer patients show such lesions in the other two groups (HP+ DSO−: 2 out of 10, HP− DSO−: 1 out of 21). Congruently, the right posterior insula, consistently identified as the interoceptive cortex[2,12,40], has also been associated with the occurrence of DSO[44] and its damage with the failure in restoring a coherent sense of ownership in patients with DSO following an interoceptive tactile stimulation (i.e., affective touch), otherwise effective in patients with this region spared[54]. Nevertheless, it is important to note that both the neural basis of body ownership in healthy individuals and the lesional correlates of its alterations extend beyond the insula. Several studies showed that body ownership is also supported by an extensive frontoparietal network as well as by subcortical areas, mainly of the right hemisphere[40,46,58–61]. For instance, the SII, a region close to the one that emerged in our VLSM results, is known to be relevant in the processing of multiple somatosensory information pertinent to bodily self-awareness. A visual inspection of the resulting VLSM map for skin temperature, using the Jülich Brain Atlas parcellation[53], further revealed that the voxels in our statistical map were situated within OP1[62], a region previously identified as SII (see Supplementary Fig. 2). OP1 has also been implicated in processing temperature and proprioception, as evidenced in prior studies[62,63]. This connection may help explain our findings, which reveal complex interactions between limb temperature, spatial position, and the sense of ownership—possibly arising from the close neural processing links between these modalities. Notably, research on macaque monkeys showed that several neurons in the SII region respond not only to visual stimuli but also to auditory stimuli, reinforcing the idea that SII functions as a multisensory hub rather than being exclusively somatosensory, as was traditionally thought[64].

Regions contributing to the role of skin temperature in body ownership may extend beyond the areas of direct tissue damage. Indeed, CLSM analysis revealed that lower hands temperature (found in HP+ DSO+ patients compared to the control groups) was primarily associated with interhemispheric disconnection in regions involved in multisensory integration critical for bodily self-awareness[40,65]. These regions include the inferior parietal lobe and areas adjacent to SI and

SII. This result may explain why unilateral alteration of the sense of ownership is associated with bilateral temperature change, as mentioned before. Thus, the close interconnections between the right and left parietal areas may underlie the decrease in bilateral hand temperature. Furthermore, this would make contact with the results obtained in the sole neuromodulatory study investigating the relationship between skin temperature and ownership, wherein rTMS over the right parietal cortex decreased temperature on both hands[42]. However, the stimulation did not interfere with the sense of ownership.

Our findings also revealed that an altered perception of thermal stimuli could be associated with disturbed ownership. Compared to the other two groups, patients with DSO presented with an impairment of both warm and cold stimuli detection on the left (affected) hand. When translating this neuropsychological finding from brain-damaged to neurotypical individuals, it suggests that thermosensation may be one source of information in the multisensory integration that underpins the sense of body ownership. The presence of thermoception deficits has been understudied in patients with disrupted ownership. Yet interestingly, DSO may occur with complaints of peculiar sensations regarding the affected limb (e.g., feeling of coldness)[48]. Our data validate this clinical observation using a more objective measure, i.e. a thermoception discrimination task rather than a self-report of spontaneous sensations. Furthermore, in an RHI experiment in healthy individuals, Crucianelli and Ehrsson[20] showed that the thermal stimulation synchronously felt on the own hand and seen on the rubber hand caused the same feeling of embodiment toward the rubber hand achieved via tactile stimulation. Interestingly, the use of both warm and cold stimulation induced the same embodiment effect. Thus, it is reasonable to hypothesise that afferent signals regarding temperature, which conventionally convey information about one of the features of the objects our hands encounter, also concurrently convey information about the ownership of the hand in contact with the object, regardless of the nature of the thermal stimulus (warm or cold).

When exploring the brain lesions related to thermoception deficits on the left hand, we found that the damage to the right Rolandic Operculum/Insula predicted a lower ability to discriminate cold and warm stimuli. HP+ DSO+ patients presented with significantly reduced thermoception on the left affected arm compared to the two control groups. Thus, although this study does not have the power to test these lesional hypotheses directly, the current data provide indications that this area may reflect the concomitant presence of thermoception deficits and disrupted body ownership. This hypothesis is further supported by the visual inspection of the lesion distribution across the three patient groups. Indeed, the majority of HP+ DSO+ patients (6 out of 8) presented a lesion at the resulting MNI peak (see Supplementary Fig. 3), while far fewer patients show such lesions in the other two groups (HP+ DSO−: 3 out of 7, HP− DSO−: 3 out of 19). Additionally, a visual inspection of the resulting VLSM map for thermoception, using the Jülich Brain Atlas parcellation[53], revealed that the resulting cluster was located more anteriorly compared to the Rolandic Operculum/Insula cluster associated with lower skin temperature. This observation aligns with the idea of a functional posterior-to-anterior gradient in the insula, where representations of bodily sensations become increasingly more integrated into contextual factors and conscious percepts[12]. According to the model of the 'sentient self', Craig suggested that the human insula contains a posterior to anterior structural progression linked to progressively more complex functions: (1) the primary cortical sensory representations of feelings from the body, (2) modules that integrate these representations with inputs from multiple other neural sources, and (3) an ultimate neural instantiation of all subjectively perceived feelings within a moving window of present time[12]. This integration in the more anterior portion of the insula, as a part of a network, may also participate in the maintenance of a coherent sense of ownership[44,46,58,61]. This idea is further corroborated by previous evidence on healthy and pathological populations demonstrating that the Insula regions, together with other specialised brain regions such as the supramarginal gyrus, thalamus, and prefrontal cortex, among others, support both thermoception accuracy[3] and body ownership[44,46,58,60,61,66–68]. Moreover, prior evidence has associated the Rolandic Operculum with thermal perception[69,70], as well as with the integration of interoceptive and exteroceptive signals that underpin bodily self-awareness[39,40]. A decreased thermoception ability on the left contralesional hand was also associated with disconnections in a right-lateralised thalamic-parietal hub, as shown via CLSM. As thermoception deficits on the left hand were significantly more present in the HP+ DSO+ group compared to others, it could be likely to hypothesise that signals from the body are integrated by direct cortico-subcortical communications in support of the construction of a coherent sense of ownership[46,58]. Previous evidence showed that skin thermosensory information is transmitted through the spinothalamic pathway to various cortical areas, including the parietal cortices[9], which typically subserve multisensory integration processes in bodily self-awareness[40,65]. Thus, in patients with DSO, brain lesions may have affected the integration between physiological signals from the body[13] and more abstract information about the representation of the self[14], thus ultimately preventing the emergence of a coherent bodily self-awareness.

Combining all the findings from this study, we provide insights into the role of skin temperature and thermoception in body ownership. This is particularly noteworthy, as behavioural studies in healthy individuals have not yet provided conclusive evidence on this complex issue. Causal evidence derived from classical neuropsychological behavioural assessments and lesion-symptom mapping offers significant theoretical advancements, highlighting the role of thermosensory signals in body ownership. It should also be noted that conflicting evidence between studies in healthy subjects and the current findings may be in part ascribable to methodological factors. For instance, the experimental paradigms used in studies in healthy individuals (e.g., multisensory illusion paradigms) manipulate ownership only temporarily. In contrast, neuropsychological studies focus on spontaneous and more enduring disruptions in body ownership caused by brain lesions. Furthermore, some of the present authors have documented that while disturbances of body ownership are linked to processes of multisensory integration, the integration of the modalities typically studied in the classic RHI paradigm (i.e. vision, proprioception, and touch) are not sufficient to explain spontaneously formed DSO[50]. Specifically, Martinaud et al.[50] demonstrated that while proprioceptive deficits tipped the balance of multisensory integration towards visual capture of a rubber hand following a specific pattern of right hemisphere lesions, patients with spontaneous DSO denied the ownership of their own hand despite such visual capture, showing a different lesional profile. They thus hypothesised that additional deficits in the somatosensory and/or interoceptive domains, such as those tested in the present study, may underlie these patients' experiences of their arm not feeling as they expect their own arm to feel. According to a Bayesian belief updating model (see also ref. 71), they proposed that these patients are unable to use somatosensory/interoceptive prediction errors to update their prior beliefs about their arm. Since then, DSO has been indeed linked to spontaneous somatosensory and interoceptive complaints about the feeling of the arm[48]. In the present study, we document objectively measured limb temperature alterations and thermoception deficits that may contribute to these specific failures in multisensory integration. The thermosensory system is highly flexible and can adapt to repeated internal and external temperature changes. Thus, it undergoes continuous updates, much like other pertinent information related to bodily self-awareness (e.g., limb position in space). The integration of these updates is crucial, and the potential failure of this process due to a brain lesion would prevent coherent representation, favouring the emergence of ownership

disorders. The lesion-symptom mapping results hinted at a role of the Rolandic Operculum/Insula, parietal areas, and the thalamus supporting the integration of the thermosensory information, which could be pertinent to body ownership. Indeed, these brain areas are also known to be involved, among the others, in the complex set of cortical and subcortical regions subserving a coherent sense of the self[40,58,61,65].

Our research also holds implications for the field of rehabilitation. Our findings pave the way for potential therapeutic interventions applicable to diverse patient populations experiencing disruptions of the sense of body ownership, such as the peripheral modulation of limb temperature. In a study with healthy individuals, temperature modulation appeared to have a bidirectional effect; cooling down participants' hands tended to increase the strength of the RHI while warming the hands prevented the embodiment of the artificial limb[72]. However, caution is warranted when generalising this finding, as it is based on a single study with a relatively small sample size. Interestingly enough, we have demonstrated in a previous work that the temporary restoration of body ownership in a case of chronic somatoparaphrenia leads to skin temperature increase in both the affected and the unaffected limbs[37]. Lastly, the neural systems we identified here could potentially serve as anatomical stimulation targets for non-invasive instrumental rehabilitation.

While this study offers meaningful insights, there are some limitations to consider when interpreting the findings. One of the primary limitations of this study is the relatively small sample size, which may have influenced the statistical power of both behavioural and lesion analyses. Nevertheless, to mitigate the impact of a limited number of participants, we implemented rigorous safeguards and robust analytical techniques. Although the limited sample size poses challenges, the significance of these findings in the context of an infrequent syndrome should not be underestimated. We believe that studying such condition provides valuable insights into the mechanisms of alterations in bodily self-awareness, offering a window into its underlying dysfunctions, essential for understanding how the body is represented in the healthy brain. As recently demonstrated, the DSO phenomenon may be more common than previously believed when assessed as part of routine clinical examinations, encompassing both its implicit and explicit manifestations[73]. Future research with larger cohorts will be needed to validate our findings and to better understand the neural and behavioural mechanisms underlying the relationship between thermosensory signals and body ownership. This can be achieved by directly testing the interaction between ownership and thermosensory disturbances, which was not possible in the current study due to our sample size. Moreover, VLSM methods have intrinsic limitations, particularly when relatively small samples are tested and a limited number of variables can be covaried[74,75]. It would also be interesting to monitor the baseline skin temperature and thermoception ability in the same sample of stroke patients from the acute to chronic phase, during which DSO usually spontaneously remits. This would help to better understand the relationship between these two functions. Additionally, the relationship between body ownership and thermosensory signals could be further studied by examining patients who have alterations in upper limbs thermosensation (e.g., Raynaud's syndrome) to assess whether they also present with ownership disorders. To conclude, despite the above-mentioned limitations, our study contributes to a deeper understanding of bodily self-awareness and its neural correlates, laying the groundwork for forthcoming investigations.

Methods

Participants

Forty-five patients were recruited at the Neurology and Stroke Unit of ASST 'Grande Ospedale Metropolitano Niguarda' in Milano (Italy). Consecutive admissions were screened for inclusion based on the following criteria: (1) right-hemisphere lesion confirmed by clinical neuroimaging (CT or MRI) and (2) right-handedness. Exclusion criteria comprised: (1) previous history of neurological or psychiatric illness, (2) <7 years of education, (3) medication with significant cognitive or mood side effects, and (4) language impairments that precluded the completion of the assessment. The Ethical Committee 'Milano Area C' approved the study. The study complied with the guidance provided in the Declaration of Helsinki (1964). Patients provided written informed consent to take part in the research. The study is part of a pre-registered project (registration https://doi.org/10.17605/OSF.IO/KH9A6). Skin temperature was measured in 40 patients (18 females, 22 males), while thermoception was measured in 34 patients (17 females, 17 males). The majority of patients had both measures (n = 29). Among the remaining patients, 11 had only skin temperature and 5 only thermoception measurements. This was mainly due to missing values or patients' fatigue that hindered the acquisition of one of the two measurements, which is typical of the acute phase of stroke. In both cases, the sample size is fully coherent with the infrequent clinical incidence of pathological alterations of ownership.

Clinical assessment

Global cognitive functioning. To ensure that the three groups did not differ in general cognitive abilities, patients underwent a brief neuropsychological assessment of global cognitive functioning using the Mini-Mental State Examination (MMSE)[76].

Neurological assessment. We used a standardised neurological assessment[77] to test hemiplegia and hemianesthesia[77,78]. Scores ranged from 0 to 3, and higher scores indicate higher levels of hemiplegia or hemianesthesia. A score of 3 indicates complete hemiplegia or hemianesthesia.

Extrapersonal and personal unilateral spatial neglect (USN). Extrapersonal USN was assessed using the Albert line cancellation test[79], for which a two or more target omissions difference between left and right hemispace was used as an indication of extrapersonal USN, and the Diller H cancellation test[80], for which patients were diagnosed as extrapersonal USN+ in case of four or more H omissions difference between left- and right-sided stimuli. A pathological performance in at least one of the above tests was considered a sign of extrapersonal USN. Personal USN was evaluated through the Comb/Razor test[81], in which patients were asked to simulate shaving, applying makeup, or combing their hair. The number of strokes made on each side of the face or head was recorded and converted into a personal USN index to classify patients as personal USN+ according to the test standardisation[82].

Anosognosia for hemiplegia. Anosognosia for the motor deficit was assessed by means of a five-point scale[77]: (0) the patient reports the strength deficit spontaneously or after a general question regarding their health problems; (1) the patient recognises the strength deficit only after a general question related to the limb; (2) the patient recognises the strength deficit only after a specific question regarding the strength and movement of the left limb; (3) the patient recognises the strength deficit in the left limbs only after it has been demonstrated to them by neurological manoeuvre; (4) the patient does not recognise the strength deficit even in after its demonstration. Only patients in the highest scoring category (case 4) were classified as having complete anosognosia for hemiplegia. This approach ensured a clear and robust distinction between severe anosognosia and milder or fluctuating unawareness, thereby maintaining the specificity of anosognosia for hemiplegia and ensuring reliable, representative results. Additionally, by employing a more refined methodology with stricter criteria, we mitigated the potential influence of confounding factors on the assessment of anosognosia for hemiplegia[83].

Proprioception. Since previous studies have demonstrated that limb proprioception is related to disruptions to the sense of body

ownership[47,84], and potentially also to deficits to the temperature regulation of the limb[19,31,52], we also assessed proprioception in the patients' groups. We used a modified version of the Rivermead Assessment of Somatosensory Performance (RASP), which is limited to the verbal description of the arm movement and its direction. Here, we evaluated the verbal description of the position (not the movement) and the perception of its position through imitation using the contralateral arm. In our proprioception task, the examiner moves the patient's affected/left arm into different positions. The patients have their eyes closed. The subject is asked to put the contralateral arm in the same position and to describe the arm position verbally. The six positions were: (1) arm extended forward with palm up; (2) arm raised up; (3) arm extended sideways at shoulder height; (4) arm along the body; (5) arm to the right side; (6) arm in military salute position. One point is scored for each correct position; otherwise, 0 (scores range: 0–6).

Disturbed sensation of ownership (DSO). The level of disownership was assessed on each of the four limbs using an existing assessment that involves asking four questions designed to measure right and left arm/hand−leg/foot recognition, feelings of belonging, and existence: Q1) 'Is this (pointing to the patient's body part) your own arm/hand−leg/foot?', Q2) 'Does it ever feel like this (patient's body part) arm/hand−leg/foot does not belong to you/is not really yours?', Q3) 'Do you ever struggle to know where your arm/hand−leg/foot is and feel you cannot find it?', and Q4) 'Does it ever feel like this arm/hand−leg/foot belongs to someone else?'. Patient responses to each question were recorded verbatim and scored by the experimenter using an existing scoring procedure[85], where higher scores indicated greater levels of disownership: 0 = no disownership, 0.5 = partial disownership, and 1 = disownership. Patients with a score >0 were considered DSO+[54]. In the examined sample, patients in the HP+ DSO+ group exhibited DSO exclusively for the left paralysed arm/hand. None of the patients displayed DSO solely for the legs/feet or in combination with the arms/hands. We did not investigate the precise boundary of the delusion. Thus, we measured the temperature not only from the hand but also from the lower part of the forearm, and from the ankle when considering the feet (see next paragraph).

Experimental assessment

Skin temperature. We used a handheld medical infrared thermometer to measure the patients' body parts temperature (TermoSkin 2.0, Meteda). Skin temperature was collected according to previous procedures[19,31,37,38], with three consecutive readings at each of seven points of interest on the patients' hands and feet (see Supplementary Fig. 4). The distance between points was adjusted according to each participant's hand size by calculating proportional measures. Once the points were identified on each body part, they were marked with a circle on the skin. After a period of 15 min, the temperature was measured with the patient's eyes closed. While the recording order (from points 1 to 7) was consistent, the body part measurement order was randomised across participants. We then averaged the three temperature readings for each of the seven points of the hands and feet separately, resulting in four scores representing the Celsius degrees average temperature for each patient's limb (i.e., hands and feet). Additional data on the validity and variance of the temperature measurements are also provided in the supplementary materials (Supplementary Fig. 6 and Table 3). Lastly, we relied on the clinical records to retrieve the patients' tympanic temperature on the day of testing to look for potential general between-groups differences in core body temperature.

Thermoception. The parameters of the experimental design for assessing perception of warm and cold stimuli were determined on a previously published procedure[19], which met the need to maximise the number of patients tested in a severe clinical state, such as those within a critical timeframe of 2 days post-stroke. Consequently, we opted for a straightforward experimental design prioritising clarity in task instructions and rapidity. This approach aimed to elicit the most reliable responses while mitigating the fatigue commonly observed in individuals during the acute phase of the disease within this clinical population. In this task, we used the same instrument for measuring body temperature, the TermoSkin 2.0, the surface of which is equipped with two flat metal surfaces used to assess the patients' thermal perception. Thermal discrimination was evaluated by placing alternately the two flat metal surfaces on the patient's skin. We regulated the flat surfaces differently, whereby the right metal plate was set at the temperature of each patient's hand central point (i.e., number 5; see Supplementary Fig. 4), namely, at the patient's limb temperature. In contrast, the left metal plate temperature was regulated according to the experimental condition (i.e., 'hotter' or 'colder' than the patient's limb temperature). The thermal discrimination task consisted of a series of pairs of thermal stimuli, 3 for the warm condition and 3 for the cold condition, administered in a block-design, following a standardised protocol previously applied to detect neuropathy[86,87]. In each pair, patients were first administered with a stimulus set at their limb temperature. Then, they were administered with either a stimulus warmer or a colder than the limb under evaluation, according to the current block. For the warm stimulation, the left metal plate temperature was set at +8 °C in the easy trial condition and at +6 °C in the medium trial condition. For the difficult trial condition, the temperature increase differed based on the participants' age: +5 °C (>70 years old), +4.4 °C (50–69 years old), or +3.5 °C (<50 years old)[86]. For the cold stimulation, the left metal plate temperature was set at −6 °C in the easy trial condition and at −4 °C in the medium trial condition. For the difficult trial condition, the temperature decrease differed based on the participants' age: −2.2 °C (>70 years old), −1.9 °C (50–69 years old), or −1.5 °C (<50 years old)[86]. While the order of the temperature trials was fixed within the condition and across patients according to a staircase procedure (starting from the easier trial with the higher temperature difference compared to the patient's skin−either cold or warm), the order of warm and cold blocks was counterbalanced across patients. Patients had their eyes closed and were asked whether the stimuli in each pair (one set at the patient's limb temperature and one regulated according to the condition/trial) were identical or not ('Are these two the same or different?'). We then calculated a score for each stimulus type (warm, cold) for each patient, considering both hits and trial difficulty. If the patient could perceive differences between stimuli at all three difficulty levels, the score used in the analysis would be 3. If they could perceive differences up to the medium difficulty, the score would be 2. If they could only perceive differences at the easy level, the score would be 1. If they could not perceive any differences, the score would be 0. All data were analysed using R version 4.2.2.

Lesion-symptom mapping

Voxel-based lesion-symptom mapping (VLSM). VLSM is a technique used in neuropsychology and cognitive neuroscience to identify the relationship between brain lesions and behavioural/physiological or cognitive impairments. It is a powerful method for pinpointing which brain regions are critical for specific functions by statistically comparing the patients' lesions to their performance on a specific task or physiological index on a voxel-by-voxel basis[88–90]. The VLSM methodology employs voxel-based procedures similar to those used in functional neuroimaging analysis, thereby bypassing some limitations of conventional lesion analysis methods. Unlike traditional approaches, VLSM does not group patients by lesion site or behavioural cut-off. Instead, it utilises continuous data on both behaviour and lesions[88]. MRI or CT scans for each patient were obtained as a component of routine post-stroke and were used for lesion mapping. The patients' lesions were drawn using a semi-automated mapping method via

Clusterize SPM toolbox[91–93] and subsequently normalised into the standard space (via Clinical toolbox[94]) and resliced. Then, the VLSM analyses were conducted on a voxel-wise basis using the MATLAB package NiiStat (https://github.com/neurolabusc/NiiStat). To precisely map the observed differences between groups' differential effects resulting from the data analyses on skin temperature measurement and thermoception task, we computed two separate indices and used them in the VLSM as dependent variables. In the case of skin temperature, we averaged the temperature raw score of both hands and adjusted it by using the GLM estimates for sex, and proprioception. In the case of thermoception, to mirror the between-group effect found in the behavioural analysis, we averaged the number of detected stimuli in the warm and cold stimulation, considering only the left hand.

A voxelwise approach was adopted considering the whole sample ($n = 40$ for temperature and $n = 34$ for thermoception). This methodological approach allowed us to overcome the problem of the numerosity of the HP+ DSO+ group by including all the available patients' lesion maps. In both cases, we adopted a one-tailed 0.05 alpha threshold with 10,000 permutations. The permutation-based correction was applied to maximise power while maintaining control of the FWER. The one-tailed hypothesis predicted that injured tissue only causes poorer performance, that is, lower skin temperature and lower thermoception ability. Thus, the direction of the results would indicate that a given lesion predicts lower skin temperature and decreased thermoception ability, a pattern we know from the behavioural models to be associated with the HP+ DSO+ group, which significantly differed from the other two groups. Only voxels lesioned in a minimum of 10 % of the sample were considered. All the analyses were corrected for lesion volume. The anatomical distribution of the statistical results was assessed using the Automated Anatomical Labelling map (template AAL[95]), which classifies the anatomical distribution of brain images in stereotactic space. The regional distribution of the white matter damage was also identified through the John Hopkins University (JHU) white matter labels template distributed with the software MRIcron. Only significant areas with more than ten voxels are discussed.

Connectome-based lesion symptom mapping (CLSM). As brain damage may extend well beyond the area of grey matter injury, a behavioural impairment may come from structural disconnections between regions pairs, caused by lesions to white matter tracts, which provide the scaffolding for brain functions[96,97]. The CLSM approach seeks to establish a statistical relationship between the strength of connections between brain regions (as defined by a standard brain atlas or discrete units as small as a voxel) and behavioural performance seen in patients with brain injury. The patients' lesions were drawn using a semi-automated mapping method via Clusterize SPM toolbox[91–93] and subsequently normalised into the standard space (via Clinical toolbox[94]) and resliced. Then, we analysed parcel-wise disconnectivity as provided by the Lesion Quantification Toolkit (LQT)[98]. This procedure allowed us to identify direct disconnections between grey matter regions in each patient. LQT created a structural connectivity matrix by combining the provided deterministic HCP842 tractography template[99] and an fMRI-based parcel atlas[100] with cortical and subcortical grey matter areas. The number of streamlines disconnected by the lesion between each pair of parcels was converted to a percentage of disconnected streamlines, resulting in symmetric 235-by-235 dysconnectivity matrices. Each value in this matrix denotes the percentage of disconnected streamlines between two given grey matter areas.

We analysed the patients' matrices through a mass-univariate analysis to identify associations between disconnections and lower skin temperature and reduced thermoception ability, separately, using custom scripting in MATLAB R2020b (provided in refs. 97,101), using the same indices as in the VLSM analyses. We loaded disconnection matrices into MATLAB and removed the diagonal and redundant elements below it. Many ROI-to-ROI disconnections were rarely or never present in the data, likely either because the whole sample's lesion anatomy did not include damage to the connection or because the connection was physiologically non-existent. Therefore, we identified the sum of all patients with a disconnection present (i.e., a disconnection score > 0) for each ROI-to-ROI connection. We removed all connections affected in less than 10% of the sample from the analysis. We then computed a GLM for each ROI-to-ROI connection with the dysconnectivity score as the independent variable and the temperature and thermoception indices as dependent variables in two separate analyses. Then, maximum statistic permutation ($n = 10{,}000$) was employed on permuted behavioural data and the original disconnection data with the same analysis strategy to assess the distribution of maximum statistics under the null hypothesis. To adopt a more conservative approach, we applied a one-sided corrected threshold for statistical significance at $p < 0.01$ by identifying the 99th percentile of permutation-derived maximum statistics. Results were visualised with the BrainNet Viewer[102] (http://www.nitrc.org/projects/bnv/).

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

The data generated in this study are available under restricted access as they contain information (age, gender, education level, hospital to which patients have been admitted) that could compromise research participant privacy/consent. Access can be obtained on request from the corresponding author (gerardo.salvato@unipv.it) who will answered within 2 weeks. Once access has been granted, data will be available for 1 week. Source data are provided with this paper.

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Author contributions

G.S.: conceptualisation, data curation, formal analysis, investigation, methodology, visualisation, writing—original draft, writing—review & editing; P.M.J.: conceptualisation, methodology, writing—original draft, writing—review & editing; M.Sellitto: writing—original draft, writing—review & editing; D.C.: data curation, investigation, writing—original draft; F.C.: data curation, investigation, writing—original draft; T.F.: data curation, formal analysis, visualisation, writing—review & editing; S.A.C.S.: data curation, investigation, writing—review & editing; M.P.: investigation, writing—review & editing; M.Sessa: writing—review & editing; M.G.: conceptualisation, methodology, writing—original draft, writing—review & editing; A.F.: conceptualisation, methodology, writing—original draft, writing—review & editing; G.B.: funding acquisition, methodology, resources, supervision, writing—original draft, writing—review & editing.

Competing interests

The authors declare no competing interests.

Additional information

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Correspondence and requests for materials should be addressed to Gerardo Salvato.

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