INTERPLAY BETWEEN BODY SCHEMA, VISUOSPATIAL PERCEPTION AND PAIN IN PATIENTS WITH SPINAL CORD INJURY

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Significance: Spinal cord injury is associated with alterations of lower body scheme as assessed with the laterality judgement task, which are directly related to pain intensity in patients with below-level neuropathic pain.

Abstract

Background: Changes in body representations (body image and/or body schema) have been reported in several chronic musculoskeletal pain syndromes, but rarely in patients with neuropathic pain and never in patients with spinal cord injury (SCI)-related pain.

Methods: We used implicit motor imagery (the laterality judgement task, and visuospatial body perception tests) in 56 patients with thoracic SCI with (*n* = 32) or without (*n* = 24) pain below the level of the injury, and in a group of matched healthy controls (*n* = 37). We compared the participants' reaction time and the accuracy with which they identified the laterality of hands and feet presented in various orientations. Visuospatial body perception was assessed with a series of tests referred to as the 'horizontal subjective body midline', and the umbilicus-reaching task, in which participants were asked to estimate the location of the umbilicus under different experimental conditions.

Results: Both groups of patients had longer reaction times for the identification of laterality for the feet than for the hands, but with no difference in accuracy. This longer reaction time was not correlated with spinal lesion severity, but was directly related to both average pain intensity and specific neuropathic pain components. The umbilicus-reaching task was affected in both groups of patients, with no effect of pain intensity. By contrast, the horizontal subjective body midline task was unaffected.

Conclusion: These results suggest an interplay between lower body scheme distorsions and pain in patients with spinal cord injury.

1- Introduction

More than half of the patients with spinal cord injury (SCI) suffer chronic neuropathic pain syndromes (Burke et al., 2017). The mechanisms of neuropathic pain, particularly for below-level pain, remain poorly understood, but may involve the reorganization of the somatosensory systems and changes in body representations related to the massive deafferentation associated with SCI (Jutzeler et al., 2015; Osinski et al., 2019).

In recent years, several studies have highlighted the interactions between pain and body representations (i.e. body image and/or body schema) (Moseley, 2005; Haggard et al., 2013; Tsay et al., 2015; Tabor et al., 2017). Distorted body image based on the way the body feels to its owner (Lotze and Moseley, 2007) have been reported in patients with phantom limb pain or CRPS (Lewis et al., 2010; Peltz et al., 2011; Gilpin et al., 2015). Body perception disturbances were also described in patients with SCI, but their relationships with pain are still uncertain (Evans, 1962; Fuentes et al., 2013).

The body schema, corresponding to an unconscious real-time dynamic representation of one's own body in space derived from somatosensory afferents and integrated into the motor systems for the control of action (Head and Holmes, 1911), is also altered in patients with chronic pain syndromes. Such alterations have been demonstrated, in particular, in studies based on the laterality judgment task (LJT). In this implicit motor imagery task, participants are asked to determine whether images of a body part (e.g. one hand or foot) correspond to the left or right side of the body, a task requiring an intact body schema (Parsons, 1987). Most of the studies that have used LJT to assess the relationships between pain and body schema were performed in patients with musculoskeletal pain syndromes (Breckenridge et al., 2019; Ravat et al., 2019). Other studies have reported alterations to the body schema in patients with neurological lesions, including patients with stroke, limb amputation, and SCI in particular (Curtze et al., 2010; Fiori et al., 2014; Nico et al., 2004; Sirigu et al., 1996), but the relationships between these alterations and neuropathic pain were not specifically investigated.

We addressed this question in patients with SCI-related pain. Our working hypothesis was that patients with SCI associated with below-level pain in the lower limbs would display distortions of the body schema affecting the lower body more

than the upper body because of the brain reorganization associated with the massive sensory deafferentation.

We tested this hypothesis, by using the LJT in patients with SCI with and without below-level pain and in a group of healthy volunteers. We compared the participants' reaction time and accuracy for determining the laterality of series of images of hands or feet presented in various orientations. We also used a series of tests referred to as 'subjective horizontal body midline (SHBM)' tests. These tests, adapted from the subjective vertical body midline test (SVBM) used to assess laterolateral spatial hemineglect (Sumitani et al., 2007), involved the estimation of the location of the umbilicus under different experimental conditions, as a means of assessing visuospatial aspects of body representation in SCI patients.

2- Methods

2.1 Subjects

The study sample consisted of two groups of patients with spinal cord injury (SCI), with and without below-level pain, and a third group of healthy controls (HC). The study was approved by the local institutional review board. Consecutive patients with SCI from the physical medicine and rehabilitation department (Raymond Poincaré University Hospital, Garches, France) were included prospectively in this study. The participants were carefully briefed about the experimental procedures and provided written informed consent for participation.

Eligible patients were French-speaking adults (aged 18 to 75 years) with a confirmed spinal cord injury, regardless of its origin (trauma, ischemia, tumor). Patients were consequently included if their neurological level of injury was between T2 and T9. This level was chosen because our objective was to compare body schema of lower versus upper body part and therefore upper limbs had to be free of impairment. In addition, as described in experimental procedure (see below) the umbilicus was used as target for evaluation of body schema of lower body part and therefore had to be located below the level of injury. Only patients with a lesion older than 18 months were included because below-level neuropathic pain appeared generally in first year following lesion (Siddall et al., 2003).

The first group consisted of patients with SCI and below-level neuropathic pain (SCI-P), defined as pain with neuropathic characteristics (i.e. a DN4 questionnaire score ≥ 4) (Bouhassira et al., 2005) in the region of sensory loss at least three segments below the level of the spinal injury. The second group consisted of patients with SCI, but without pain (SCI-noP). Exclusion criteria were the presence of other neurological conditions, other types of chronic pain, presence of at-level pain with an intensity higher than that of below-level pain, major depression, history of major psychiatric disease, severe cognitive deficits, difficulty in understanding the testing procedure.

Healthy volunteers, matched with the group of patients for age and sex, had no clinical history, clinical symptoms or signs of neurological disorders. None of the healthy volunteers were on medication at the time of testing or had been on medication during the month before testing.

2.2 Clinical evaluation

A standardized neurological examination was performed according to the recommendations of the American Spinal Injury Association Impairment Scale (Marino et al., 2003), to determine the most caudal level of the spinal cord with normal sensory and motor function and the severity of the lesion (complete or incomplete).

Patients with below-level neuropathic pain were asked to report their average pain intensity over the last seven days on a numerical rating scale extending from 0 to 10, using the question derived from the international spinal cord injury pain basic data set (Widerström-Noga et al., 2008). The Neuropathic Pain Symptom Inventory (Bouhassira et al., 2004) was used to assess the magnitude of five neuropathic dimensions: (i) superficial burning pain; (ii) deep pain (squeezing, pressure); (iii) paroxysmal pain (electric shock-like, stabbing pain); (iv) evoked pain (on brushing, cold, heat); and (v) paresthesia/dysesthesia (tingling, pins and needles) in the area of maximal pain. Each dimension was rated on a numerical scale (from 0 to 10). Depression and anxiety were evaluated with the Hospital Anxiety Depression Scale (Zigmond and Snaith, 1983).

2.3. Quantitative sensory testing

Quantitative sensory tests were performed on subjects comfortably installed in a bed, in a quiet room at a constant temperature (22°C). All the tests were performed bilaterally over the ischium area (S3 nerve territory) to assess the severity of the spinal lesion. The testing order was randomized and the assessments included the determination of vibration thresholds, mechanical and thermal (warm and cold) thresholds. Detection thresholds for mechanical static stimuli were assessed with calibrated von Frey hairs (0.008–300 g) (Somedic Sales AB©, Sweden), as previously described (Hatem et al., 2010). Subjects were asked to close their eyes

during the procedure. The von Frey filaments were applied (at least twice) in ascending and descending order of stiffness. Detection thresholds were defined as the lowest pressure perceived by the subject within 3 s of the stimulus. Mechanical pain thresholds were assessed with a pressure algometer (Algometer, SomedicSales©, Sweden) consisting of a pistol grip and a rod (1 cm^2) with a pressure-sensitive strain gauge at the tip, a display showing pressure (in kPa) and a scale indicating the rate of the pressure force increase, to ensure a fairly constant rate of pressure increase of approximately 50k Pa/s. The mean of three pain perception levels was calculated as the pressure pain threshold (PPT). Vibratory stimuli were applied with a Rydel–Seiffer-graded tuning fork (64 Hz, 8/8 scale), and vibration thresholds were determined as the mean of three measurements. Thermal sensations were assessed with a contact thermode (Somedic Sales AB), by the Marstock method (Fruhstorfer et al., 1976). The baseline temperature of the thermode was adjusted to the subject's skin temperature. Heat and cold detection and pain thresholds were measured according to the method of limits: stimuli of increasing or decreasing intensities were applied, and for each stimulus, the subjects pressed a button that reversed the thermal stimulation as soon as they detected a sensation of cold or warmth (indicating the detection thresholds) or as soon as the stimulation became painful (indicating the pain thresholds). Inter-stimulus intervals were 6–8 s for detection thresholds, 15–20 s for heat pain thresholds and 20–30 s for cold pain thresholds. The maximum temperature was set at 50°C to prevent tissue damage. The minimum temperature was set at 10°C for cold detection thresholds and 5°C for cold pain temperatures, to prevent cold injury. The thermal rate of change was 1°C/s for detection thresholds and 2°C/s for pain thresholds. Thresholds were calculated as the means of three successive determinations and are expressed as absolute values in degrees Celsius.

2.4. Body perception testing

2.4.1 Laterality judgement testing

Participants were asked to complete two series of laterality judgement tasks, one for the hands and one for the feet, using the Recognise App© (Neuro orthopaedic Institute (Australasia) Pty. Ltd, http://recognize.noigroup.com/recognize) on a computer tablet (Samsung Galaxy Tab2©). The laterality judgement task

involves deciding whether an image of the body part of interest (hand or foot) displayed in various positions on a monitor corresponds to the right or left limb. Participants were seated at a desk with their hands on each side of the tablet placed at about 50 cm of their eyes. The index finger of each hand was placed on buttons located on either side of the tablet. Pressing the button on one side of the tablet indicated a positive response for that side of the body (i.e. the right index was used to press the button if the participant wished to indicate that the image corresponded to a right hand or foot). Participants were asked to respond as quickly as possible to 30 visual stimuli for each body part (hand or foot). Each image measuring 13 x 13 cm, was randomly select from a bank of images and was displayed at the center of the screen. A maximum of 8 second was used to avoid time constrain which would affected participants' performance. The images database contained 80 images of right hands presented in 4 possible rotations (0°, 90°, 180°, 270°) which were flipped to create mirrored left hands for a total of 720 images. Foot image were created in the same way from 28 right foot images of a total of 224 images. The order of completion of the tasks was randomized for each participant. The outcomes of this task were accuracy (ACC), corresponding to the percentage of correct responses, and mean reaction time (RT) in seconds to answer. These two outcomes were analyzed statistically. As our working hypothesis was that patients have a larger LJT deficit (RT and/or ACC) for the feet than for the hands, we systematically calculated both the RT foot/hand ratio and ACC foot/hand ratio for each participant. Thus, RT ratio > 1 indicated longer RT (ie deficit) for the identification of feet laterality in comparison with hands lateratility. Regarding ACC, ratio < 1 indicated a lower accuracy (ie. decreased % of correct answers) for the identification of feet laterality in comparison with hands laterality.

2.4.2 Subjective horizontal body midline testing

We explored the possibility of inattention for the lower limb, often referred to as "neglect-like syndrome", through a series of tests in which participants were asked to estimate the position of the umbilicus under different conditions. These tests, referred to as the 'subjective horizontal body midline (SHBM)' task, were adapted from the subjective vertical body midline test used in previous studies for

investigating laterolateral spatial neglect (Kolb et al., 2012; Sumitani et al., 2007; Uematsu et al., 2009).

Four different tests were used:

- Subjective horizontal body midline test 1 (SHBM-1): This test aimed to assess the visuo-proprioceptive representation of the body with spatial references. It was performed in a window-less room, with the lights on. The subjects lay on a table 200 cm below the ceiling with their feet touching a wall. A pillow was placed on the participant's abdomen to prevent direct contact with the abdominal skin and an opaque board was placed under the chin so that the participants could not see their body during the task. The participants were asked to use a laser pointer placed in their dominant hand to indicate where the projection of their umbilicus would lie on the ceiling. The investigator explained the task by asking the participants to use the laser to indicate where they thought their umbilicus would touch the ceiling if they were lying face down on the ceiling. The hand holding the laser pointer was placed on the pillow over the abdomen and the participants were asked to move the laser to point at a tape graduated with non-digit symbols fixed to the ceiling, which meaning was not explained to the patients, to indicate the projection of their umbilicus.

- Subjective horizontal body midline test 2 (SHBM-2): This test was the same as SVHBM-1, as described above, except that it was performed in the dark. The aim of this task was to assess visuo-proprioceptive body representation without spatial references.

- Subjective horizontal body midline test 3 (SHBM-3): This test was similar to SHBM-2, except that the investigator moved the laser at a rate of about 20cm/s. Subjects were asked to indicate verbally when they thought that the laser was pointing at the projection of their umbilicus. This test was complementary to the two previous tests and aimed to assess visual body representation without proprioceptive or spatial references.

- Umbilicus-reaching task (URT): For this task, aiming to assess lower body representation more directly, the pillow placed over the abdomen was removed and the participants were asked to indicate the position of their umbilicus with the index

finger of their dominant hand, as close as possible to the abdominal skin without actually touching it.

For all these tasks, the absolute distance in the vertical axis (in mm) between the true projection (SVHBM 1-3) or the true location (URT) of the umbilicus and the estimates given by the subjects was measured, to assess the error in the responses. The true position of umbilicus was defined as the height of umbilicus (distance between the wall and umbilicus in the horizontal position). Each test was performed once under supervision of the same investigator blinded to the group allocation.

2.5 Statistical analyses

Results are expressed as means ± 1 SD. Group comparisons for clinical and demographic variables and comparisons of the results of LJT (both absolute values for RT and ACC for feet and hands, and relative values for feet and hands, i.e. the RT foot/hand ratio and ACC foot/hand ratio), SHBM (1-3), URT, and QST, were performed by two-way analysis of variance (ANOVA), with Fisher's *post hoc* least significant difference test. Fisher's exact test was used to compare proportions. Spearman's rank correlation coefficient was used to assess the correlations between LJT (reaction time and accuracy), SHBM 1-3 and URT results and pain intensity, NPSI total score and subscores and QST results. Effect sizes were calculated using the Cohen's d test. The primary outcomes were the comparison of LJT results between groups and their correlation with pain intensity. All other comparisons were exploratory. A p value < 0.05 was considered significant.

3. Results

3.1 Participants

This study included 93 participants: 32 SCI patients with below-level pain, 24 SCI patients without pain and 37 healthy controls. The demographic and clinical characteristics of the participants are summarized in table 1. The three groups were similar in terms of age ($p = 0.11$) and sex ratio ($p = 0.56$), and the two groups of patients were similar in terms of duration ($p = 0.32$) and severity (complete vs. incomplete) ($p = 1$) of the SCI, and anxiety and depression scores. Thirteen patients with pain received an analgesic treatment (table 1).

The results obtained for quantitative sensory testing (QST) are presented in table 2. All detection and pain thresholds in both groups of patients were significantly different from those in healthy controls, but none of these thresholds differed significantly between the SCI patients with and without pain.

3.2 Body perception

3.2.1 Laterality judgment test (LJT)

The absolute values for reaction time (RT) and accuracy (ACC) for the identification of the laterality of hands or feet did not differ between the three groups of participants (table 4). However, the foot/hand RT ratio (figure 1A) was significantly increased in both SCI patients with pain ($p < 0.01$; $d = 0.76$) and SCI patients without pain ($p < 0.01$; $d = 0.82$) in comparison with healthy volunteers, indicating a deficit in laterality judgement for feet relative to hands, but there was no significant difference between the two groups of patients. By contrast, the foot/hand ACC ratio did not differ ($p = 0.88$) between the patients and controls (figure 1B).

The increase in foot/hand RT ratio was moderately correlated with mean pain intensity (rho = 0.40; $p = 0.02$) in SCI patients with pain (figure 2A), with NPSI total score (rho = 0.38; $p = 0.04$) (figure 2B) and, more specifically, with two neuropathic pain dimensions assessed with this questionnaire: deep pain (rho = 0.39; $p = 0.03$) (figure 2C) and paroxysmal pain (rho = 0.40; $p = 0.03$) (figure 2D). These correlations were partly driven by outliers which were not excluded because they did not correspond to the same patients in the different analyses. By contrast, the RT

foot/hand ratio was similar in patients with complete or incomplete lesion (p = 0.34) and was not correlated with QST measurements (see appendix), suggesting that the relative increase in RT for foot laterality identification was not directly related to the severity of the spinal lesion. In patients with below-level pain, there was no correlation between RT foot/hand ratio and other clinical characteristics, including age (rho = 0.25, *p* = 0.60), duration of the lesion (rho = 0.09; *p* = 0.59), duration of pain (r= 0.20; p = 0. 27), anxiety (rho = 0.02, *p* = 0.09) and depression (rho = -0.34, *p* = 0.09) scores. The results were not significantly different between patients receiving or not an analgesic treatment (p = 0.28). The results were similar in patients without neuropathic pain showing no correlation between RT foot/hand ratio and age (rho = 0.17, p = 0.35), duration of the lesion (rho = 0.3, p =0.14), anxiety (rho = -0.19, p = 0.9) and depression (rho = 0.21, p = 0.17) scores.

3.2.2. *Subjective horizontal body midline tests (SHBM) and umbilicus-reaching task (URT)*

None of the SHBM tests used in this study (SHBM 1 to 3) gave results that differed between the patients and healthy controls or between the two groups of patients (table 3). By contrast, the error in the umbilicus localization task (URT) was significantly larger in both SCI patients with (p < 0.01; d = 1.64) or without (p < 0.01; d = 0. 99) pain than in controls (figure 3), but there was no significant difference between the two groups of patients (p = 0.80). The changes in URT were not related to pain intensity (rho = 0.20; p = 0.28). For QST measurements, we found only a trend towards a moderate correlation between error in URT and the vibration threshold measured, for the total patient population (rho= 0.45; p = 0.052).

4. Discussion

We detected selective alterations of lower body representation in SCI patients. Both patients with or without below-level pain presented with a relative longer reaction time (RT) for the identification of foot laterality than for hand laterality, which was directly related to both pain intensity and specific neuropathic pain components in patients with pain. These results suggest an interplay between central neuropathic pain and changes in the body representation associated with SCI.

It has repeatedly been shown in healthy volunteers that the time taken to decide whether an image of a limb corresponds to a right or left limb is proportional to the time it would take to move the actual limb physically (Parsons, 1987; Parsons, 2001) and that imagined movements induce similar changes in brain activation to actual movements (Jeannerod, 2001; Jeannerod and Decety, 1995; Lafleur et al., 2002). Thus, changes in LJT outcomes, in terms of RT and/or accuracy (ACC), are generally considered to reflect disturbances of body schema processing (Moseley, 2004; Parsons, 1987; Parsons, 2001). Alteration of LJT was reported in different chronic pain conditions (Breckenridge et al., 2019; Ravat et al., 2019), but few studies have included patients with neuropathic (phantom limb pain, plexus avulsion) (Moseley, 2006; Reinersmann et al., 2010) or mixed pain (carpal tunnel syndrome) (Schmid and Coppieters, 2012). In addition, these studies compared patients with neuropathic pain to healthy controls or patients with other chronic pain conditions. It was not, therefore, possible to determine whether the reported alterations in LJT were related to pain *per se* or to the neurological lesion.

We directly compared two populations of SCI patients with and without below-level pain. The two groups of patients displayed similar increases in RT for the identification of foot laterality relative to hand laterality. This suggests that the spinal cord lesion *per se*, independently of pain, is associated with changes in the body schema for the lower limbs, as reported in previous studies in SCI (Fiori et al., 2014; Ionta et al., 2016), in patients with other neurological lesions (Curtze et al., 2010; Nico et al., 2004; Sirigu et al., 1996) or after an acute local anesthesia (Silva et al. 2011). This relative increase in RT was similar in our patients with complete and incomplete spinal lesions and was not correlated with the magnitude of sensory deficits assessed with QST tools.

The LJT changes reported here were less significant than those reported in previous studies in patients with chronic pain (Breckenridge et al., 2019; Ravat et al., 2019). In fact, our patients had similar RT and ACC than healthy controls and presented only a relative alteration of the identification of foot laterality in comparison with hand. One possible explanation for this apparent discrepancy could be that patients with such a long lasting massive sensory deafferention developed compensatory mechanisms based on different strategies (eg visual or cognitive) during LJT explaining the partial maintenance of their performance, as this has been suggested in studies in SCI (Firori et al. 2014, Ionta et al., 2016) or locked-in syndrome patients (Conson et al., 2008), but also after acute regional anesthesia (Silva et al., 2011). However, the fact that the relative increase in RT in our patients was directly correlated, although moderately, with mean pain intensity, suggests specific interactions between below-level pain and body schema distortion in these patients. This was further supported by the direct moderate correlation also found with specific neuropathic pain symptoms, suggesting that the interplay involved was more specifically dependent on certain neuropathic pain mechanisms.

As in some of the previous studies on chronic pain syndromes (Moseley, 2004; Reinersmann et al., 2010, 2012; Schwoebel et al., 2001), we observed a dissociation between the two LJT outcome measures. Our patients presented an increase in RT with no significant change in ACC. These two measurements probably reflect different aspects of the processing of body representation. It has been suggested that ACC may reflect our ability to maneuver a body part mentally, whereas RT reflects the total time taken to select laterality, mentally maneuver a body part and make the final decision (Bray and Moseley, 2011). However, this interpretation remains a matter of debate, and changes in both these measurements are generally considered to reflect body schema disturbances (Breckenridge et al., 2019; Ravat et al., 2019). Other interpretations of LJT results have been considered, including the possibility that increases in RT are related to chronic underuse (associated with a form of pseudo-neglect) of the painful limb and/or to unspecific attentional bias induced by pain (Moseley, 2004). Our data are not consistent with these hypotheses. The motor deficits and functional impairment were similar in our SCI patients with and without pain. In addition, there was no correlation between the severity of the spinal lesion and the increase in RT. The relative increase in RT

concerned the foot, rather than the hand, ruling out the possibility of nonspecific attentional bias, which would have induced changes in LJT for both hands and feet.

It is difficult to speculate about the brain mechanisms underlying the interplay between pain and LJT in SCI patients. Structural, functional and neurochemical central changes have been reported in these patients (Gustin et al., 2010, 2014; Hatem et al., 2010; Henderson et al., 2011; Jutzeler et al., 2015; Nardone et al., 2013; Osinski et al., 2019*)*, but the relationships between brain changes and LJT or between LJT and pain have never been studied directly in patients.

One limitation of our study is that no conclusions can be drawn about the direction of the relationship between SCI-related pain and changes in body schema, but one cannot exclude that these interactions are bidirectional. This hypothesis could be tested in prospective studies focusing on the effects of graded motor imagery, which targets cortical reorganization and includes LJT (Moseley, 2006; Moseley and Flor, 2012) on both pain and body schema in these patients. Another limitation is that we did not assess the potential influence of biomechanical constraints reflecting the "difficulty" of LJT for the different images (related to the rotation angle and awkwardness of the position of the limb in each image), which is not available in the Recognize App. However, the fact that the absolute values of RT and ACC were similar between our three groups tend to confirm that the difficulty of the images did not significantly biased our results.

We also assessed the visuospatial perception of our patients, to check for possible changes in other aspects of body representation. We used a test derived from the vertical subjective body midline (SVBM) test, which has been used to assess hemispatial neglect in patients with stroke, but also in chronic pain syndromes (Christophe et al., 2016; Kolb et al., 2012; Reinersmann et al., 2012; Sumitani et al., 2007). In this test, patients are asked to locate their subjective vertical body midline, by looking at a laser dot moving horizontally on a screen placed in front of them and to stop the laser dot when it crosses the sagittal plane of their subjective vertical body midline. Impaired visuospatial perception was reported in some studies (Kolb et al., 2012; Reinersmann et al, 2012; Sumitani et al., 2007), but not in others (Christophe et al., 2016; Uematsu et al., 2009). We adapted this test to assess the subjective horizontal body midline (SHBM), corresponding to the transverse plane crossing the body at the level of the umbilicus. Our hypothesis was

that patients with SCI could have an altered visuospatial perception of their lower body inducing errors in the location of their umbilicus, which could be influenced by pain. As in SVBM tests, patients were tested in the light and in darkness. We also used two different tasks. In the first, patients moved the laser so as to point to the estimated location of the projection of their umbilicus, whereas, in the second, the laser dot was moved by the investigator and the patients verbally indicated where the dot should be stopped. We found no significant differences between our two groups of patients or between the patients and the controls for any of these tasks, suggesting that SCI is not associated with significant changes in visuospatial body perception as assessed with the tests used here. These results are consistent with those of some studies based on SVBM in CRPS (Christophe et al., 2016) or postherpetic neuralgia (Uematsu et al., 2009). However, we cannot exclude the possibility of methodological bias in our study. Indeed, our results were highly variable in the two groups of patients, but also in the healthy volunteers. This high degree of variability may reflect the difficulty of these tasks, as reported by several of our subjects, including healthy volunteers. One bias may result from the subjects being in a horizontal position during these tests. This position was chosen because most of the patients had severe motor deficits, but it may have introduced a bias due to a decrease in vestibular afferents, which play a key role in body representation (Lopez et al., 2012).

Finally, the umbilicus-reaching task was used to assess potential distortions of lower body representation more directly in SCI patients. The error in umbilicus localization was significantly larger in patients than in controls, but similar results were obtained for patients with and without below-level pain. Changes in the ability to point to specific body parts have been reported in CRPS (Reid et al., 2016), but never in SCI patients. The mechanisms underlying this task are probably complex and are still poorly understood (Reid et al., 2016). Although it should be interpreted with caution, the trend towards a correlation between the increase in vibration threshold and the error in URT observed in our patients suggest that these mechanisms may involve proprioceptive afferents. The lack of correlation with pain intensity also suggests that the changes in body representation assessed with this simple task are different from those assessed with the LJT.

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Author Contributions:

DB, VM and TO conceptualized the experiment and acquired funding. SMH provided input to the design of the study. TO collected data. DB and TO were involved in data analysis. DB and TO drafted the first version of the manuscript. All authors provided input to the final version of the manuscript.

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Figure legends

Figure 1: Comparison of laterality judgment task (LJT) between SCI patients with (SCI-P, black column) or without (SCI-noP, gray column) pain and healthy controls (HC, white column). A: The foot/hand ratio for LJT reaction time (RT) was significantly higher (** p<0.01) in patients than in healthy controls (HC), but there was no significant difference between the two groups of patients. B: The foot/hand ratio for LJT accuracy (ACC) did not differ between the three groups.

Figure 2: Correlation between changes in LJT and pain. A: Correlation (rho = 0.40; p = 0.02) between foot/hand ratio for reaction time (RT) and average pain intensity (numerical rating scale: NRS). B: Correlation (rho = 0.38; p = 0.04) between foot/hand ratio for RT and the total score for the Neuropathic Pain Symptom Inventory (NPSI). C: correlation (rho = 0.39; p = 0.03) between the foot/hand ratio for RT and the deep pain score of the NPSI. D: Correlation (rho = 0.40; p = 0.03) between the foot/hand ratio for RT and the paroxysmal pain score of the NPSI.

Figure 3: Comparison of umbilicus-reaching task (URT) results between SCI patients with (SCI-P, black column) or without (SCI-noP, gray column) pain and healthy controls (HC, white column). The error (in mm) in the localization of the umbilicus was significantly (** $p < 0.001$) larger for patients than for controls, but there was no difference between the two groups of patients.

	SCI-P (*n* = 32)	SCI-noP (*n* = 24)	HC (*n* = 37)
Age (years)	47.8 (±15.4)	41.4 (±13.9)	40.7 (±13.9)
Sex (m/f)	22/10	18/6	16/21
Duration of the lesion (years)	15.3 (±11.2)	16.0 (±12.7)	
Lesion severity n (%)	Complete = 18 (56.3%)	Complete = 14 (54.2%)	
ASIA-score	A = 18 B = 3 C = 4 D = 7	A = 14 B = 2 C = 2 D = 6	
HADS-anxiety	7.4 ± 4.7	5.9 ± 2.9	
HADS-depression	5.8 ± 3.4	4.9 ± 3.4	
Mean pain intensity	6.3 ± 2.2		
Pain duration (year)	11.4 ± 9.5		
Pain location	Bilateral : 28 Left : 2 Right : 2		
DN4 score	5.8 ± 1.2		
NPSI (total score)	33.4 ± 15.9		
NPSI (burning)	5.4 ± 2.9		
NPSI (deep pain)	3.5 ± 3.2		
NPSI (paroxysmal)	3.0 ± 2.8		
NPSI (evoked)	2.1 ± 2.4		
NPSI(paresthesia)	4.3 ± 2.6		
Pain medication n (%)	Pregabalin: 7 (21,9%) Opioids: 2 (6%) Gabapentin : 2 (6%)		

	Antidepressant: 2 (6%)

Table 1: Demographic and clinical characteristics of the participants SCI patients with (SCI-P) or without (SCI-noP) pain and healthy controls (HC)

	SCI-P (*n* = 32)	SCI-noP (*n* = 24)	HC (*n* = 37)
WDT (°C)	47.36 ± 4.34 ***	47.31 ± 5.19 ***	35.39 ± 1.18
CDT (°C)	14.10 ± 6.46 ***	13.61 ± 6.68 ***	30.48 ± 1.23
MDT (g)	182.08 ± 140.13 ***	177.97 ± 145.91 ***	0.79 ± 1.23
VDT	7.57 ± 0.99 ***	7.59 ± 0.91 ***	6.79 ± 0.77
HPT(°C)	48.31 ± 3.66 ***	48.86 ± 3.10 ***	43.96 ± 4.32
CPT(°C)	8.38 ± 5.58 ***	6.92 ± 4.60 ***	17.42 ± 6.96
PPT (kPA)	689.60 (±178.24) ***	712.91 ± 174.04 ***	534.07 ± 186.62

Table 2: Comparison of quantitative sensory testing results between SCI patients with (SCI-P) and without (SCI-noP) pain, and healthy controls (HC). All the measurements differed significantly between the patients, whether with (SCI-P) or without (SCI-NoP) pain, and the healthy controls (*** $p <$ 0.001), but there was no significant difference between the two groups of patients. WDT: warm detection threshold, CDT: cold detection threshold, MDT: mechanical detection threshold, VDT: vibration detection threshold, HPT: heat pain threshold, CPT: cold pain threshold, PPT: pressure pain threshold.

	SCI-P	SCI-noP	HC	Patients vs. HC
RT HAND	3.4 (1±.6)	3.4 (±1.7)	3.6 (±1.7)	ns
ACC HAND	87.4 (±10.4)	84.8 (±11.8)	88.0 (±10.4)	ns
RT FOOT	3.8 (±1.3)	3.9 (±1.7)	3.3 (±1.5)	ns
ACC FOOT	89.5 (±9.9)	87.8(±11.8)	90.5 (±10.2)	ns
SHBM-1	100.3 (±100.7)	80.4 (±60.7)	90.5 (±60.0)	ns
SHBM-2	100.6 (±90.8)	120.4 (±70.0)	130.2 (±120.3)	ns
SHBM-3	70.2 (±7.1)	80.8 (±60.6)	120.4 (±100.7)	ns

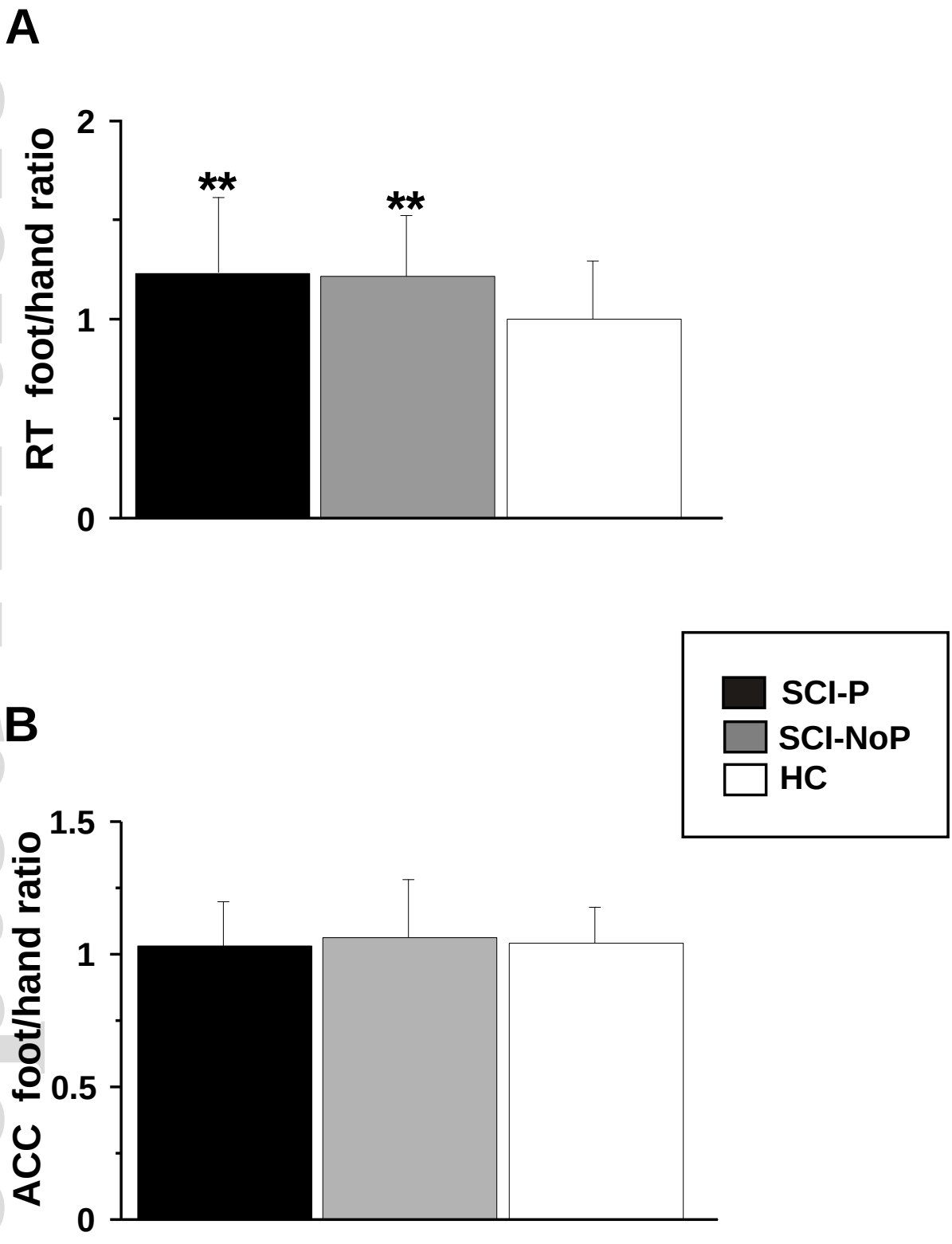
Table 3: Comparisons of body perception tests between SCI patients with (SCI-P) and without (SCI-noP) pain, and healthy controls (HC).

RT HAND: reaction time (s) for the identification of hand laterality; ACC HAND: accuracy (%) of hand image identification; RT FOOT: reaction time (s) for the identification of foot laterality; ACC FOOT: accuracy (%) of foot image identification

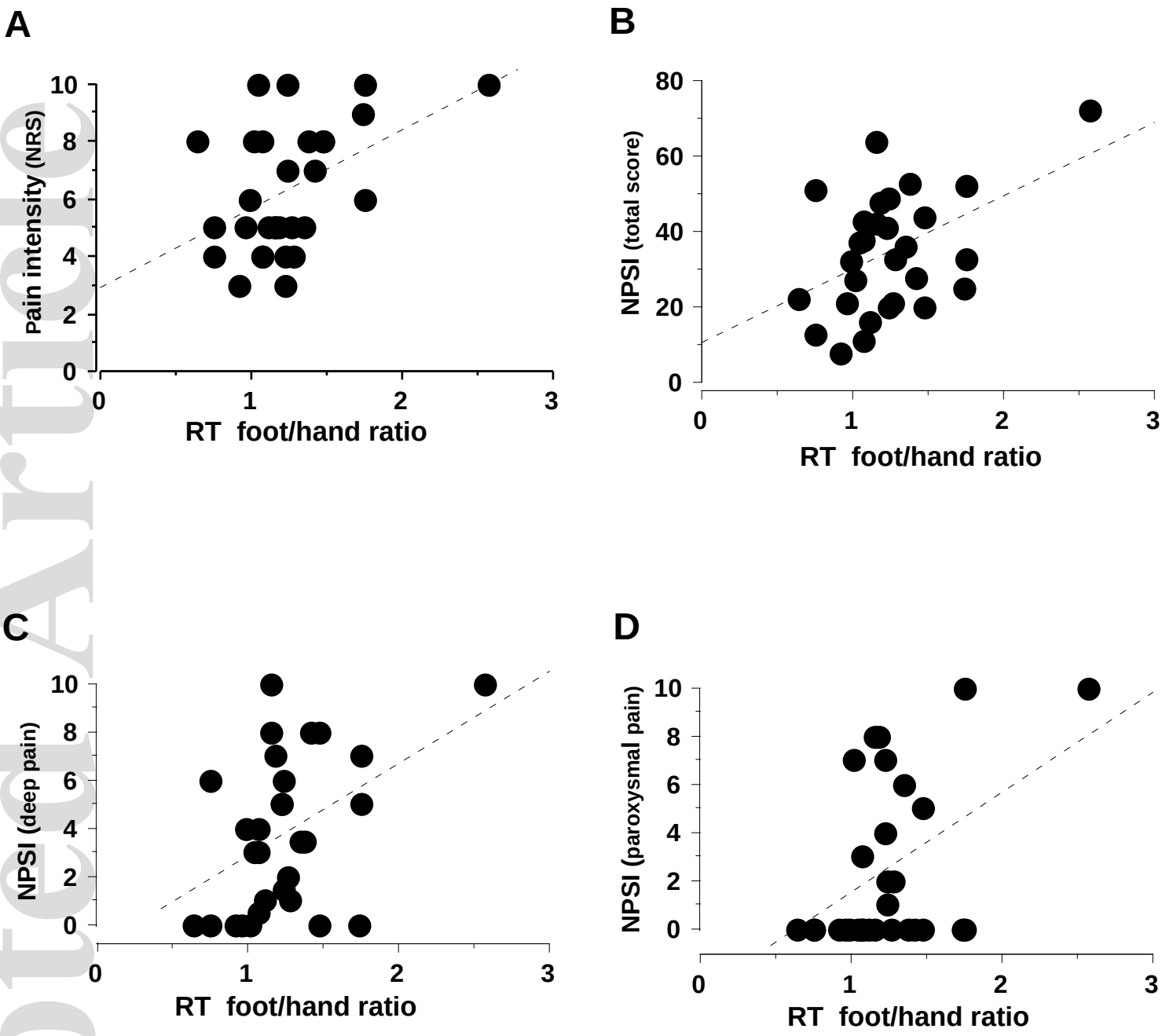
SHBM: subjective horizontal body midline test. The results indicate the error (in mm) between the estimated and true projection of the umbilicus under the different experimental conditions. SHBM-1: the participants had to indicate with a laser dot the projection of their umbilicus on the ceiling with lights on, SHBM-2: as for SHBM1 but with the lights off; SHBM-3: the laser dot was moved by the investigator and the participants had to indicate the projection of their umbilicus.

	RT foot/hand ratio	
	SCI-P	SCI-NOP
WDT	0.16	0.22
CDT	0.26	-0.23
MDT	0.02	0.14
VDT	0.08	0.14
HPT	0.13	0.28
CPT	0.24	0.11
PPT	-0.12	0.49

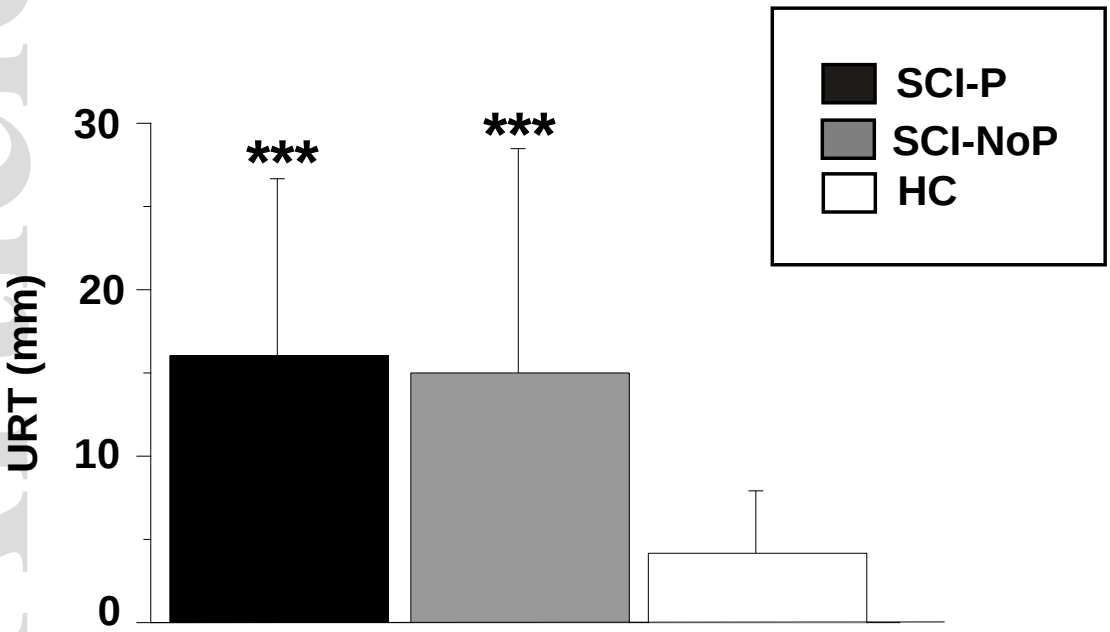
Table 4: Spearman rank coeficient (rho) for the correlations between foot/hand RT ratio and QST parameters in patients with (SCI-P) or without (SCI No-P) below-level pain. WDT: warm detection threshold, CDT: cold detection threshold, MDT: mechanical detection threshold, VDT: vibration detection threshold, HPT: heat pain threshold, CPT: cold pain threshold, PPT: pressure pain threshold.



Osinski et al., figure 1



Osinski et al. figure 2



Osinski et al., figure 3