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Exploring the relationships between altered body perception, limb position sense, and limb movement sense in complex regional pain syndrome

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## Highlights:

- Alterations of senses of limb position and movement are observed in CRPS
- They are not related to the alterations of the perception of the painful limb
- These two body representations should be assessed separately in rehabilitation

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**Title**

Exploring the relationships between altered body perception, limb position sense, and limb movement sense in complex regional pain syndrome.

**Running title:**

Body representations in CRPS

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**Author Contributions**

CM designed the study; CB, NG, AMP and MG performed data collection; CB, MG, CSM and CM analyzed and interpreted the data; CB and CM drafted the paper; all authors commented on the paper and approved the final version.

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**Abstract**

Chronic pain is often accompanied by patient reported distorted body perception and an altered kinesthesia (referring to the senses of limb position and limb movement), but the association between these deficits is unknown. Objectives: 1- to assess body perception, and the senses of limb position and limb movement in Complex Regional Pain Syndrome (CRPS); 2- to test whether these variables are related to each other and to pain intensity. Thirteen upper limb CRPS (mean pain intensity:  $4.2 \pm 2.4/10$ ) and 13 Controls were recruited. Body perception was self-reported with a questionnaire, while the senses of limb position (Task 1) and of limb movement (Task 2) were assessed with a robotic system combined with a 2D virtual reality display. Results show altered kinesthesia in CRPS compared to Controls (all  $p < 0.05$ ). Moreover, in the CRPS group, higher pain intensity was associated with lower performance in Task 2 ( $r = -0.6$ ,  $p < 0.05$ ). While alterations in participants' sense of limb position and limb movement were associated to each other ( $r = -0.7$ ,  $p < 0.01$ ), they were not related to the altered body perception (all  $p > 0.26$ ). Therefore, the results suggest that kinesthesia and body perception should be considered and evaluated separately in CRPS.

**Perspective:**

*Senses of limb position and movement rely on sensorimotor integration. Both are altered in complex regional pain syndrome. However, they are not related to the subjective perception of the painful limb. Therefore, they should be assessed separately in rehabilitation.*

**Keywords**

Complex regional pain syndrome (CRPS), Sense of limb movement, Sense of limb position, Body perception, Virtual reality

## 1. INTRODUCTION

Perceiving the size, shape, position and movement of our limbs is essential to help us interact adequately with our environment. An extensive literature shows that chronic pain conditions are often accompanied by various distortions in body perception, which can include changes in perception of the size, shape and temperature of the painful limb<sup>11,17,18,22,36</sup>. In addition, alterations of the sense of limb position (assessed with the limb in a static posture) have also been observed<sup>1,11,33</sup>. For example, individuals with Complex Regional Pain Syndrome (CRPS) were shown to overestimate the angular position of their painful wrist on active and passive movements but passive movement elicited the greatest disparity<sup>1</sup>. Moreover, alterations of the sense of position have been reported to be associated with the severity of motor deficits<sup>1,7</sup>. However, only one study has assessed the sense of limb movement during an active movement and showed that individuals with chronic low back pain tend to overestimate their trunk flexion compared to pain-free controls<sup>27</sup>. Importantly, in that study the flexion-extension movement was continuous to ensure that judgment relied on a continuous comparison between sensory inputs and motor output rather than on comparison of final (static) postures<sup>27</sup>.

The observed alterations of body perception and kinesthesia (i.e. the senses of limb position and limb movement<sup>26</sup>) in various chronic pain populations raises the question of whether the three variables are related. Surprisingly, no study has assessed such associations in chronic pain.

It is particularly relevant to study these potential associations in a CRPS population, as in CRPS, pain is accompanied by sensorimotor and autonomic dysfunctions, abnormal body perception<sup>10</sup> and alterations in the sense of limb position<sup>1,11</sup>. However, to the best of our knowledge no study has assessed the sense of limb movement during active movement in this population, despite the fact that motor deficits are frequently observed<sup>1,14,29</sup>. Therefore, the aim of this study was to assess body perception and kinesthesia in individuals with CRPS, and assess whether body perception, the sense of limb position and the sense of limb movement are related to each other.

The first specific objective was to assess a) sense of limb position, b) sense of limb movement during active movement, and c) body perception in CRPS patients. We hypothesised that the senses of limb position and movement would be altered compared to controls and to normative data. Body perception was self-reported using the Bath Body perception disturbances scale<sup>12</sup> and the senses of limb position and movement were objectively measured using a robotic system combined with virtual reality. The second specific objective was to test whether the three variables are related to each other, and to pain intensity.

## 2. MATERIAL AND METHODS

### 2.1. Participants

Thirteen patients with unilateral CRPS (diagnosed according to Budapest clinical criteria<sup>8</sup> by an anesthesiologist in the Center of expertise in chronic pain in Quebec City) and 13 healthy Controls matched for sex, age and self-reported laterality were recruited over a 1-year period in the Quebec City area. CRPS participants were recruited from the outpatient clinic at the Center of expertise in chronic pain in Quebec City. Controls were recruited from Laval University, Quebec City. Both CRPS type 1 and type 2 (referring respectively to the absence or presence of a

peripheral nerve injury) were included, given that in the Budapest criteria<sup>8</sup> the clinical diagnosis is similar for both types and the clinical utility of these subgroups is controversial<sup>8</sup>. Participants were excluded if they had motor impairments interfering with the task performance (which necessitated 80 degrees shoulder abduction and forward movements with an amplitude of 20 cm and the weight of the arm fully supported). Exclusion criteria for Controls were the presence of acute upper limb (UL) pain in the last three months or of chronic UL pain in the last year. Finally, the presence of non-corrected visual impairments was an exclusion criterion for both groups. Two CRPS patients were excluded from this study due to motor impairments and non-corrected visual deficits. All participants provided their written informed consent prior to the study, which was approved by the local ethical review board (Institut de réadaptation en déficience physique de Québec, Canada, n°2014-395) and conformed with the Declaration of Helsinki.

**Clinical characteristics in the CRPS group.** A brief history of each patient's condition was conducted and information about the circumstances and the timing of the CRPS onset, pain manifestations, pain treatments (pharmaceutical and non-pharmaceutical), and co-morbidities was obtained from a semi-structured interview. Patients were asked to indicate the anatomical location of their pain and rate their pain intensity over the last 24 hours on an 11 point numerical rating scale (NPRS) with 0 = no pain, 10 = worst pain imaginable.

## 2.2. Material and Procedure

CRPS patients and Controls participated in a single session lasting approximately two hours. For the CRPS group each session began with the assessment of their body perception with a questionnaire. The sense of limb position (Task 1) and the sense of limb movement (Task 2) were assessed successively in all groups with the KINARM Exoskeleton Lab<sup>TM</sup> (BKIN Technologies, Kingston ON, Canada), a robotized bilateral exoskeleton allowing movements of the shoulder (horizontal abduction-adduction) and the elbow (flexion-extension) joints in order to move participants' ULs in the horizontal plane (see Fig. 1). In Task 1, ULs were simply obstructed from view. In Task 2, the robot was interfaced with a 2D virtual environment allowing to replace the participant's UL by a virtual UL (presented with an appropriate perception of depth, Fig. 1b). Joint angular positions for both the shoulder and elbow joints were obtained from KINARM motor encoders and sampled at 1 kHz, and the position of the index finger was computed in real-time. Data processing was conducted via Matlab (MathWorks, R2011b).

*Insert Fig. 1 approximately here*

### 2.2.1. Task 1: The sense of limb position

This task assessed the sense of limb position at rest. The robot passively moved an UL to one of four predefined positions in the ipsilateral hemispace. The participant then had to reproduce the position with the other UL (i.e. the second UL being the mirror image of the first UL). Both ULs were obstructed from view (Fig. 3a).

This task is a KINARM Standard test (Arm position matching task<sup>32</sup>), that has previously been used to show alterations in the sense of limb position in stroke patients<sup>4</sup>. The four (non-visible) targets are spread on a 2x2 grid at 20 cm intervals on the ipsilateral hemispace. Each position is repeated six times in a pseudo-randomised order (total of 24 trials). Both ULs were tested in all participants in a random order.

Precision of the robot (position error = 1.5 mm) and reliability of the measures for this task (intraclass coefficient correlation=0.86,  $p<0.00001$ <sup>4</sup>) are very good.

### 2.2.2. Task 2: The sense of limb movement

Task 2 consisted of judging whether the movement made by a virtual UL (anchored to the participant's UL movement) was greater or smaller than the participant's actual movement. For each trial, the robot moved the UL to a starting position, and then a visual cue indicated to the participant that they needed to move their hand forward at a comfortable speed (see Video 1 in Supplementary Material). Across trials, the movement of the virtual UL displayed in real time was either smaller, greater or identical (no scaling) (Fig. 2) to their actual limb movement. Importantly, the actual and the virtual UL were always aligned at the beginning of a movement, and the virtual UL was disappearing before the end of a movement, constraining the participant to base his judgement on the movement and not on the final position. After each trial, participants had to report whether the virtual UL's movement was "greater" or "smaller" than their own movement (two-alternative forced choice paradigm).

For this task, only the painful limb was tested in the CRPS group, as testing both arms was too long and tiring for the CRPS participants. However, both arms were tested in the Controls in a random order.

*Insert Fig. 2 approximately here*

**Familiarization trials.** Before the experimental tasks described above, a 2-step familiarization procedure was performed. First, participants practiced forward movements at a comfortable speed without scaling of the virtual UL (5 trials). Secondly, the movement of the virtual UL was augmented 2.75 times (0.364 for smaller movements) and each trial was repeated twice. These scaling factors were greater than those used in the experimental trials and were used to make sure that the participant understood the task correctly.

**Experimental trials.** Participants were exposed to 13 scaling factors. The scaling was applied to the angular rotation of the elbow and the shoulder joints. The scaling factors ranged from 1.25 to 2.5 times the rotation angle of the elbow and shoulder joints (1.25, 1.5, 1.75, 2, 2.25, and 2.5) for the larger movements. The inverses of these factors (e.g.  $1/1.5 = 0.667$ ) were used for smaller movements. For the identical condition, the scaling was set to 1. Each scaling factor was repeated 8 times, for a total of 104 trials (performed in a pseudo-randomized order). No feedback on performance was provided to minimize potential learning.

### 2.2.3. Assessment of the body perception in the CRPS group

The body perception of the affected UL in CRPS participants was assessed using the French version of the Bath Body perception disturbances scale<sup>12</sup>. This scale was specifically developed for a CRPS population based on a qualitative study<sup>10</sup> assessing perceptual abnormalities of the painful limb, and included questions on the sense of disowning the body part, impairment of the perceived limb position, attention and hostile feelings to the painful limb (Fig. 5a). The question about the desire to amputate the painful limb and the drawing part of the questionnaire were not included. Participants were required to rate four questions from 0 to 10 on a Likert-scale (see Fig. 5a for the details) and to complete four 'yes'-'no' items in the fifth question in order to assess perturbations in the perception of the painful limb about size, temperature, pressure and weight. The English version has been shown to have a variable consistency from poor<sup>2</sup> to good<sup>2,13</sup> and an



adequate interrater reliability<sup>13</sup>. Translation of the questionnaire was performed using a forward and backward translation and the translated version was reviewed by an expert committee. However, no validation of the French version has been performed so far.

### 3.1. Outcome measures

**Task 1.** Mean absolute distance error in the X and Y axes across trials were obtained from Dexterit-E software (Arm position matching task<sup>32</sup>, version 3.4.2).

**Task 2.** The sense of limb movement was evaluated as in Roosink and collaborators<sup>27,28</sup>. First, results obtained with the two-alternative forced choice paradigm (greater = 1, smaller = 0) were plotted against the 13 scaling factors (log transformed to be on a linear scale). Second, a sigmoid curve (1), with initial values  $X_{Y0.50} = 0$ , with constraints  $Y_{MAX}=1$  et  $Y_{MIN}=0$ , and with a variable slope ( $m$ ) was fitted to the data (Prism 6 for Windows, Graphpad Software Inc., La Jolla, CA, USA).

$$(1): Y = Y(MIN) + \frac{Y(MAX)-Y(MIN)}{1+10^{(X(Y0.50)-X)m}}$$

Finally, three data points were interpolated from each curve ( $X_{Y0.25}$ ,  $X_{Y0.50}$ ,  $X_{Y0.75}$ ), and used to determine the point of subjective equivalence (PSE) (2) and the just noticeable difference (JND) (3).

$$(2): PSE = XY0.50$$

$$(3): JND = \frac{X(Y0.75) - X(Y0.25)}{2}$$

The PSE corresponds to the scaling factors for which the participant equally answered that the virtual UL's movement was "smaller" or "greater". In theory, the PSE is equal to 0, i.e. there is a 50% chance of responding "smaller" or "greater" when in fact no scaling has been applied. When the PSE = 0, there is no alteration of the sense of limb movement. A PSE > 0 indicates that the participant overestimates his/her own movement. A PSE < 0 indicates that the participant underestimates his/her own movement. The JND refers to the ability to discriminate between different levels of scaled feedback. The higher the slope and the smaller the JND, the better participants are able to discriminate between different levels of scaling factors.

The percentage of accurate responses was also calculated for each level of scaling, except for trials from the identical condition (i.e. no scaling). Measuring accuracy may appear redundant given that the PSE and JND were included as variables. However, in participants with a very low percentage of accurate responses, it can be impossible to fit a psychophysical curve, and therefore to calculate the PSE and JND. The percentage of accurate responses therefore allows analysis of all participants' data, including the most impaired participants.

Finally, the mean velocity between the beginning of the movement and the disappearance of the virtual UL was calculated for each participant in each trial. As participants were instructed to perform the task at a comfortable speed, individuals with CRPS could have moved more slowly than Controls due to their pain or fear of movement. As movement velocity could be a confounding variable, this aspect was controlled for in statistical analyses.

**Body perception.** A total score for the first four questions was computed corresponding to the sum of their numerical Likert ratings and then the total sum of the four responses in the fifth

question (yes-no questions: yes=1; no=0) was added. A greater score indicates greater disturbances in body perception, 44 being the maximum possible score.

### 3.2. Statistical analysis

Results are either reported as mean  $\pm$  SD or as median (min-max). Independent T-test (2-tailed) was used to compare groups for age. Descriptive analyses (mean  $\pm$  SD) were used for the Bath Body perception disturbance scale.

Errors in Task 1 were analysed using 2 [Group (CRPS or Controls)] X 2 [Error direction (X-axis or Y-axis)] repeated-measures analyses of variance (rmANOVA). Individual data from each participant were compared to age and sex-matched normative data available for that KINARM Standard test (based on a group of 461 healthy participants including 214 males and 247 females aged between 18 and 93).

For Task 2, analyses of covariance (ANCOVA) with the movement velocity in covariate were performed for the percentage of accurate responses, the PSE and the JND. Pearson coefficients were used to test whether body perception, the senses of limb position and limb movement were related with each other, and with pain intensity. Statistical analyses were performed with R (version 3.1.2).

## 4. RESULTS

### 4.1. Population

CRPS and Control groups were similar in terms of age (CRPS:  $56.1 \pm 9.2$  years, Controls:  $50.8 \pm 13.8$ ,  $p=0.31$ ), gender (10 women in each group) and laterality (11 right-handed in each group).

For the CRPS group, clinical characteristics and results (body perception score, sense of limb position and sense of limb movement) for each participant are reported in Table 1. All CRPS participants took analgesics and all but one (CRPS 4) was receiving physiotherapy and occupational therapy treatments.

*Insert Table 1 approximately here*

### 4.2. Task 1: The sense of limb position

As there was no statistical difference between the dominant and the non-dominant arm ( $t(12)=0.89$ ,  $p=0.40$ ) for the Controls and between the painful and the non-painful limb for the CRPS group ( $t(12)=1.5$ ,  $p=0.15$ ), statistical analyses were performed on the mean of both arms. Although this absence of difference for CRPS patients might be surprising at first sight, it needs to be kept in mind that this task is bilateral, one arm matching the position of the other.

Fig. 3a provides an example of the performance of two representative participants from each group. Fig. 3b shows the mean errors on the X and Y axes for each group. Errors were found to be larger in the CRPS ( $4.4 \pm 1.9$  cm) group compared to Controls ( $3.1 \pm 1.7$  cm,  $F(1,24)=5.1$ ,  $p=0.03$ ,  $\eta_p^2=0.19$ ), and to be larger in the X-axis ( $4.6 \pm 1.8$  cm) compared to the Y-axis ( $2.8 \pm 1.5$  cm,  $F(1,24)=54.4$ ,  $p<0.001$ ,  $\eta_p^2=0.68$ ). However, no significant interaction between the Group and the Errors direction was observed ( $F(1,24)=0.46$ ,  $p=0.51$ ).

The errors in the X and Y axes were also compared to normative data (age and sex-matched controls (Dukelow et al., 2010; Scott and Brown, 2013) for each participant (CRPS and Controls). Five participants of the CRPS group, but none of the Control group, obtained abnormal scores.

*Insert Fig. 3 approximately here*

#### 4.3. Task 2: The sense of limb movement

In Task 2, for the Control group, a significant difference was found between the dominant and the non-dominant arm for the percentage of accurate responses ( $p=0.04$ ) and for the JND ( $p=0.006$ ). No statistical difference was observed for the PSE ( $p=0.17$ ). Therefore, statistical analyses were performed on only one UL for the Control group. The UL included in the analysis for each control participant was selected in order to have a comparable proportion of dominant and non-dominant ULs in both groups. In the CRPS group 7 participants had CRPS in their dominant limb (6 participants non-dominant side affected).

On average, CRPS patients (mean  $\pm$  SD:  $0.34\pm 0.09$  m.s<sup>-1</sup>) were significantly slower on limb movement than Controls (mean  $\pm$  SD:  $0.45\pm 0.17$  m.s<sup>-1</sup>,  $t(24)=2.08$ ,  $p=0.047$ ). The movement velocity influenced neither the PSE ( $F(1,19)=1.1$ ,  $p=0.30$ ) nor the percentage of accurate responses ( $F(1,19)=1.9$ ,  $p=0.17$ ). However it was positively associated with the JND ( $F(1,19)=8.6$ ,  $p=0.009$ ,  $\eta_p=0.31$ ), meaning that it was harder to discriminate between levels of scaling when the movement was fast. To control for the potential impact of movement velocity on outcomes, it was included as a covariate in the statistical analyses.

**Percentage of accurate responses.** A trend for a difference in response accuracy was observed between groups ( $F(1,21)=4.15$ ,  $p=0.055$ ,  $\eta_p=0.18$ ). The percentage of accurate responses was  $78\pm 20\%$  for the CRPS group and  $88\pm 8\%$  for the Control group.

**Point of subjective equivalence (PSE) and just noticeable difference (JND).** For the CRPS group, two participants had to be excluded from these analyses because of the low percentage of their accurate responses (26% and 53%) precluded fitting the psychophysical curve. Interestingly, these two participants scored outside of the normative values in Task 1. As shown on the psychophysical curves in Fig. 4, the PSE was similar ( $F(1,21)=0.09$ ,  $p=0.76$ ) for the CRPS ( $0.05\pm 0.09$ ) and the Control ( $0.04\pm 0.07$ ) groups. However, the JND was higher (i.e. the slope was lower) for the CRPS ( $0.12\pm 0.05$ ) group compared to the Controls ( $0.11\pm 0.06$ ,  $F(1,21)=5.12$ ,  $p=0.035$ ,  $\eta_p=0.21$ ), meaning that the ability to discriminate between different levels of scaling was impaired in the CRPS group.

*Insert Fig. 4 approximately here*

#### 4.4. Body perception (Body perception disturbance scale)

As shown on Fig. 5b, there was a high variability between CRPS participants for the first four questions of the Body perception disturbance scale. For the fifth question (focusing on perceptual changes), participants reported changes in the size ( $n=6$ ), temperature ( $n=9$ ), pressure ( $n=8$ ) and weight ( $n=6$ ) of the painful limb. The total score of the questionnaire was  $16.3\pm 6.6$ . Note, however, that a *posteriori* analysis showed low internal consistency of the body perception disturbances scale in our study (Cronbach's alpha = 0.53; confidence interval (95%): 0.23-0.84).

*Insert Fig. 5 approximately here*

#### 4.5. Correlation analyses

The correlation coefficients between body perception, the senses of limb position and movement, and pain intensity for the CRPS and the control groups are presented in Table 2. A lower percentage of accurate responses in Task 2 (sense of limb movement) was strongly associated with a lower ability to discriminate between different levels of scaling factors (JND - Task 2,  $r=-0.94$ ,  $p<0.0001$ ) and with larger errors in Task 1 (sense of limb position,  $r=-0.71$ ;  $p=0.006$ ). As shown in Table 2, similar associations were also found to be significant in Controls (respectively  $r=-0.63$ ,  $p=0.018$  and  $r=-0.94$ ,  $p<0.0001$ ). Moreover, higher pain intensity in the CRPS group was associated with a lower percentage of accurate responses in Task 2 (sense of limb movement,  $r=-0.60$ ,  $p=0.027$ ). However, no significant correlations were observed between body perception and the senses of limb position and movement (see Table 2 for Pearson's coefficients and p-values).

*Insert Table 2 approximately here*

## 5. DISCUSSION

While previous CRPS studies have focused primarily on body perception and the sense of limb position, the two novel aims of this study were to investigate the sense of limb movement during active movement in CRPS and to identify any associations between body perception, the senses of limb movement and limb position, and pain in the CRPS affected limb. Our results show that the senses of limb position and limb movement are altered in CRPS compared with healthy Controls. Interestingly, while alterations in the senses of limb position and limb movement are associated, they are not related to the participants' perceptions of their painful limbs, as assessed by the Bath Body Perception Scale. As Task 1 required bilateral movements of the ULs (i.e. the painful limb was always involved), and Task 2 tested only the painful limb in the CRPS group, then our data do not allow us to assess the senses of limb position and limb movement in the non-painful limb. Our discussion will therefore only focus on our findings in the painful limb.

In accordance with previous studies that showed a deficit in proprioception<sup>1,11</sup> in people with CRPS, our data also demonstrated that limb position (Task 1) is altered in CRPS: CRPS patients made more errors than Controls in the arm position matching task. Moreover, we showed for the first time, alterations of the sense of limb movement during active movement (Task 2), which were characterized by a lower percentage of accurate responses and a poorer capacity to discriminate between different levels of scaled feedback in CRPS patients compared to Controls. Previous studies have suggested that perception of the body and its movements are biased in the presence of chronic pain, for example showing that the subjective body midline in CRPS is shifted toward the painful side<sup>34</sup> or that trunk flexion movements are overestimated in chronic low back pain<sup>27</sup>. In contrast with these observations, we did not find a perceptive bias in the assessment of kinesthesia in CRPS. Indeed, no interaction between Group and Error direction was observed in Task 1, which does not indicate a bias toward larger errors in the X-axis in the CRPS group relative to the Controls. Moreover, CRPS patients did not overestimate their own movements (as measured by the PSE in Task 2).

Interestingly, a lower percentage of accurate responses in Task 2 was associated with higher errors in Task 1, suggesting that the observed deficits in the senses of limb position and limb movement in CRPS rely on similar processes. Our results are in line with the idea that body representations are blurred in the presence of pain, as suggested by behavioural and neuroimaging studies that report motor and sensory cortical areas are altered in CRPS (for a literature review see Swart and collaborators<sup>35</sup>). Indeed, referred sensations<sup>15,16</sup>, alteration of the primary and secondary

somatosensory areas<sup>23</sup> and an expansion of the motor areas<sup>14</sup> of the painful limb are observed in CRPS. Interestingly, these alterations were shown to be positively related to the level of pain<sup>14,15,25</sup>, which is consistent with our observation that performance in Task 2 was negatively associated with pain intensity. Altogether these results suggest that alterations of sensorimotor cortical areas could explain both the deficits in the senses of limb position and limb movement during active movement in CRPS.

One important new finding from our data is that the alteration of kinesthesia in CRPS was not related to the reported alterations of body perception (e.g. perceived changes in the size, temperature, pressure and weight or changes in feeling of ownership of the painful limb), suggesting that these variables are generated by independent processes. This result can be interpreted in line with the classical model of body representation that suggests at least two distinct and independent body representations govern our motor action: the body image and the body schema<sup>21,30,37</sup>. While body image and body schema share similar somatosensory and parietal areas<sup>3,20,24</sup> and are often both impaired in pathological conditions<sup>24</sup>, they are relatively independent<sup>3,24,30,37</sup>. The body schema depends on online sensorimotor integration<sup>3,37,38</sup> and has been shown to be altered in CRPS<sup>31</sup>. Interestingly, the largest deficits in the sense of limb position in CRPS were found to be positively related to the amount of motor deficits<sup>1</sup>. Therefore, we would suggest that the observed alterations in the senses of limb position and limb movement reflect a deficit in the body schema in CRPS. On the other hand, body image, which refers to the “conscious awareness of one's own body”<sup>21</sup> seems to be related to the insula<sup>3</sup>, an area involved in emotional processing<sup>6</sup>, agency<sup>5</sup> and ownership<sup>9</sup>. In our study, alterations of body perception could be a part of a deficit in the body image. In CRPS, disturbances in the body perception are characterized by feeling the painful limb as a foreign body part, a pronounced disliking and denial of the painful limb and a high desire to amputate it<sup>10</sup>. Lewis and collaborators<sup>10</sup> suggest that such disturbances could interfere with the body schema and consequently with motor control. While an extensive literature shows that the body schema<sup>1,11,19,31</sup> and the body image<sup>10,18</sup> are altered in CRPS, we demonstrate for the first time that these alterations might be independent. However, more work is needed to clarify the mechanistic underpinnings.

Some limitations of the present study need to be highlighted. First, the sense of limb position in Task 1 was assessed using both upper limbs (one arm matching the position of the other), therefore it made it difficult to dissociate between the proprioception for the painful and the non-painful limb. However, the advantage of this task was the access to normative data which allowed us to compare to a wide group of age and sex matched controls<sup>4,32</sup>. Another limitation was that the CRPS participants were significantly slower in Task 2 compared to Controls, but an ANCOVA was used to statistically control for that difference. Moreover, it is important to mention that faster movements were related to lower performance, and therefore it is unlikely that the difference in velocity between both groups would explain the difference in performance. Rather, the velocity difference between the groups could have resulted in an underestimation of the deficit in CRPS patients. Furthermore, our ability to measure the performance in the most impaired patients was limited by the low percentage of accurate responses in Task 2. Two patients were excluded in Task 2. A larger range of scaling factors would be needed in order to be able to successfully fit psychophysical curves in these individuals. These two patients were those with the poorest performance in Task 1 and with the highest pain intensity. The limited sample size and the heterogeneity of the CRPS population makes it difficult to identify specific factors explaining why these CRPS participants had the poorest performance. No clear difference in their clinical profiles compared to the other CRPS participants was noted, but Table 1 describes the clinical characteristics and data for each CRPS participant to allow the reader to see the performance of

each CRPS participant as well as their clinical characteristics. Besides, high variability was observed in the Bath Body perception disturbances scale, suggesting that disturbances in body perception in CRPS are heterogeneous. Such inter-subject variability should normally facilitate the observation of correlations between variables, but no correlation was found for this specific variable. However, the metrological properties for the French version of this scale have not yet been established, and our sample size was limited. Moreover, in accordance with a previous study<sup>2</sup>, we found low internal consistency of the Bath Body perception disturbances scale suggesting that this scale is not consistent enough to measure alterations in body perception. Therefore, the lack of correlation for this variable needs to be interpreted very carefully as it might simply result from inability to reliably assess this construct in the study sample. However, as demonstrated by Lewis and collaborators<sup>10</sup>, the nature and the extent of body perception impairments in CRPS are highly variable across individuals. While other scales measuring body image mainly focus on the size and shape of the painful limb<sup>17,22</sup>, the Bath Body perception disturbances scale takes account of feelings and attention about the painful limb which might explain the low internal consistency. Finally, the pain intensity reported by CRPS patients was low compared to previous studies assessing body perception and sense of limb position in this population<sup>1,10,11</sup>. However, deficits in body perception and kinesthesia have been observed in our study, suggesting that alterations are present even in the less severe cases of CRPS.

## 5. CONCLUSIONS

The senses of limb position and limb movement during active movement are altered and associated in CRPS, suggesting a blurred representation but not a bias in the perception of the painful limb. The strong correlation found between both tasks suggests that the deficits observed rely on similar underlying processes. Interestingly, alterations of kinesthesia were not related to the participants' reported perceptions of the painful limb, suggesting independent processes in the alterations of the body schema and the body image in CRPS. From a clinical perspective, these data suggest that these two body representations should be evaluated separately in CRPS, and that interventions aiming to improve body image will not necessarily impact on body schema and vice-versa. However, more reliable assessment methods of the body image in CRPS are needed.

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Table 1: Clinical characteristics and results of the CRPS group.

CRPS patients	Clinical characteristics						Results				
	CRPS subtypes	Handedness	Affected side	Etiology	Time since diagnostic (months)	Pain intensity	Body perception	Sense of limb position	Sense of limb movement		
							Total BPDS	Mean error	Percentage of accurate response	PSE	JND
CRPS 1	Type II	Right	ND	Nerve compression	72	5	22	4.7	92	0.08	0.091
CRPS 2	Type I	Right	ND	Hand surgery	23	6.5	10	4.9*	53	-	-
CRPS 3	Type I	Right	ND	Fall	3	7	25	3.2	83	0.10	0.17
CRPS 4	Type I	Right	D	Hand surgery	3	3	11	3.4	79	-0.01	
CRPS 5	Type I	Right	ND	Wrist surgery	5	7	9	9.2*	26	-	-
CRPS 6	Type I	Left	ND	Hand surgery	4	4	22	7.1*	80	-0.01	0.19
CRPS 7	Type I	Right	D	Fall	3	0 <sup>a</sup>	8	3.9	92	0.03	0.09
CRPS 8	Type I	Right	D	Wrist surgery	7.5	2	13	2.3	86	0.16	0.08
CRPS 9	Type I	Right	ND	Wrist fracture	15	3	16	3.5	77	0.15	0.22
CRPS 10	Type I	Right	D	Fall	4	4	29	3.7	79	0.17	0.16
CRPS 11	Type I	Right	D	Hand surgery	1.5	1.5	12	4.2*	91	0.11	0.09
CRPS 12	Type I	Left	D	Hand fracture	4	8	18	5.3*	91	-0.09	0.10
CRPS 13	Type I	Right	D	Fall	4	3	17	1.8	95	-0.05	0.03
Mean±SD	-	-	-	-	12.7±20.6	4.2±2.4	16.3±6.6	4.4±2.1	78.7±19.2	0.056±0.09	0.12±0.06

CRPS: Complex regional pain syndrome; BPDS: Body perception disturbances scale; PSE: point of subjective equivalence; JND: Just noticeable difference; D: dominant; ND: non dominant. SD: Standard deviation. Asterisks indicate participants who obtained abnormal scores compared to age and sex-matched controls (Dukelow et al., 2010; Scott and Brown, 2013).

<sup>a</sup>One patient did not report pain during the last 24h, but typically experienced pain and reported a pain level of 4/10 by the end of the experience.

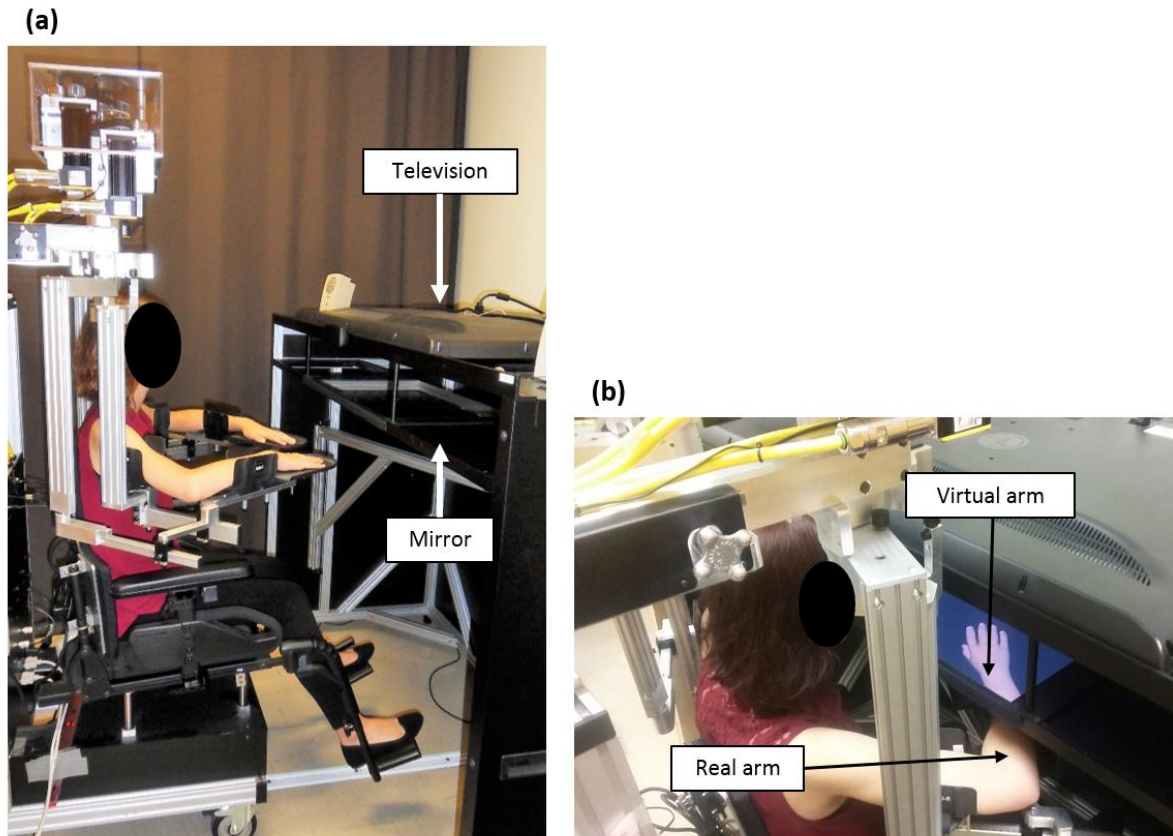
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**Table 2:** Pearson's coefficients (and p-values) between the body perception, the senses of limb position and movement and the level of pain in the CRPS group.

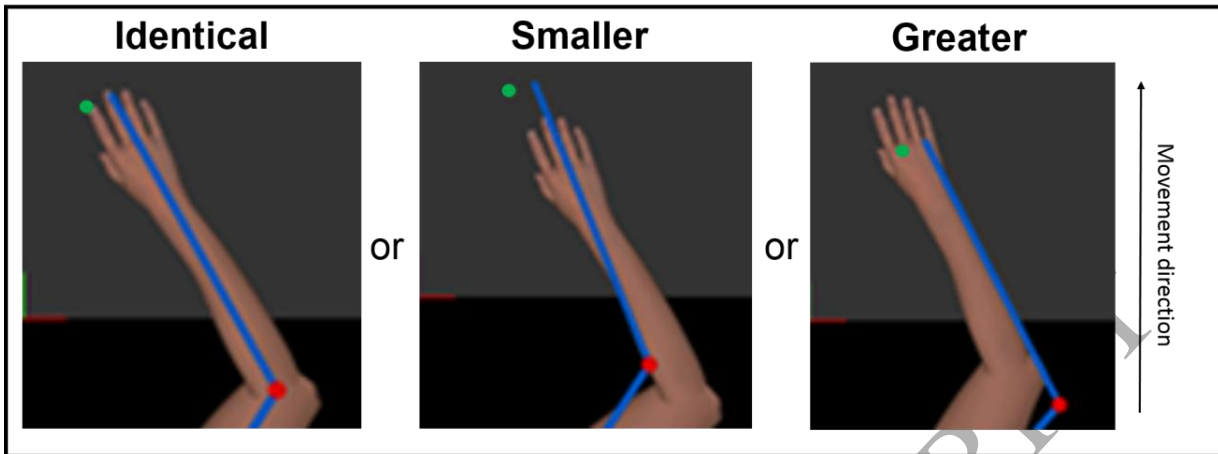
	Sense of limb position	Sense of limb movement		Body perception		
	Mean error	Accurate responses	PSE	JND	Total BPDS	Score
<b>CONTROL GROUP</b>						
Mean error		<b>-0.63</b> ( <b>p=0.018</b> )	0.15 (p=0.63)	0.57 (p=0.069)	-	-
Accurate response	<b>-0.71</b> ( <b>p=0.006</b> )		0.03 (p=0.92)	<b>-0.92</b> ( <b>p&lt;0.0001</b> )	-	-
PSE	-0.30 (p=0.36)	-0.40 (p=0.22)		-0.19 (p=0.56)	-	-
JND	0.32 (p=0.33)	<b>-0.94</b> ( <b>p&lt;0.0001</b> )	0.28 (p=0.39)		-	-
Body perception (total score BPDS)	-0.15 (p=0.61)	0.30 (p=0.26)	0.21 (p=0.53)	0.27 (p=0.41)		
Pain intensity	0.47 (p=0.15)	<b>-0.60</b> ( <b>p=0.027</b> )	-0.28 (p=0.85)	0.15 (p=0.47)	0.30 (p=0.31)	
<b>CRPS GROUP</b>						
BPDS: body perception disturbance scale. PSE: point of subjective equivalence. JND: just noticeable difference. CRPS: Complex regional pain syndrome. Pearson coefficient correlations (and p-values) are reported. Bold type indicates a significant correlation.						

### Figure captions

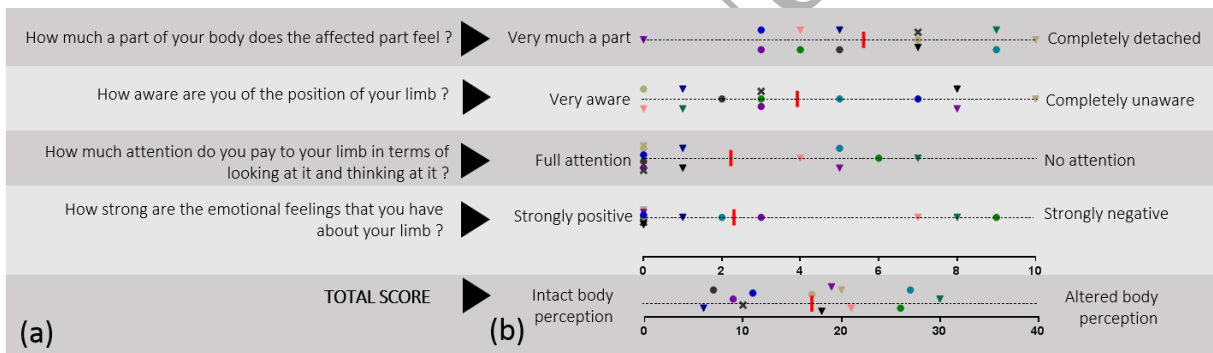
**Fig. 1: Experimental set up.** (a) The robotized exoskeleton is fitted to the anthropometric characteristics of the participant. (b) The 2D virtual environment consists in the projection of virtual upper limbs on a mirror (47'') thanks to a television. Upper limbs are fully supported by the exoskeleton and are obstructed from the participant's view.



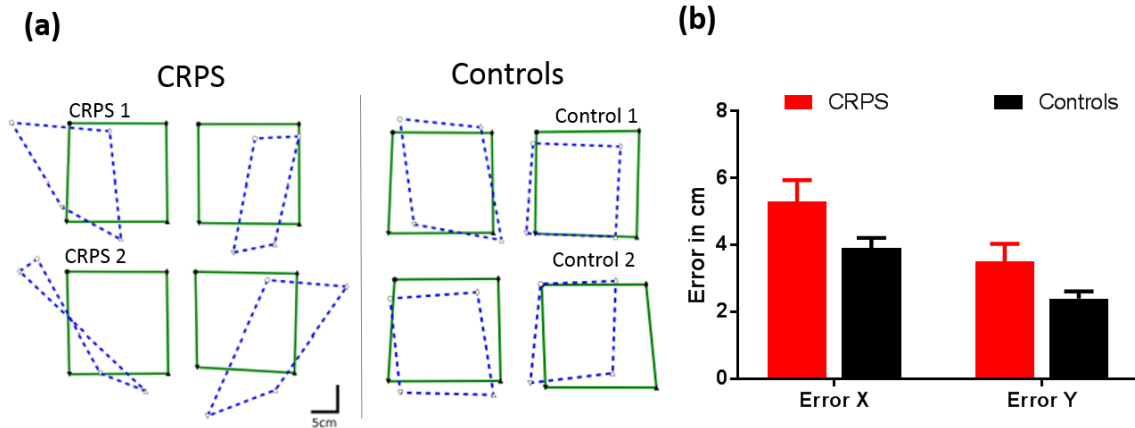
**Fig. 2: Scaling of movements of the virtual upper limb (UL) in Task 2.** The amplitude (and therefore the velocity) of the virtual UL was scaled in real-time to appear smaller or greater than the participant's movements. The size and the starting position of the virtual UL (35 degrees for the shoulder and 115 degrees for the elbow) were similar in all conditions. Participants were exclusively seeing the virtual UL. Blue bars, red and green dots depict respectively the actual position of the participant's UL, the position of the elbow joint and the computed position of the index.



**Fig. 3: Errors in Task 1. (a):** Individual data for two representative participants from each group (two CRPS and two Controls). The green squares represent the position of one UL moved passively by the robot and the superimposed blue dashed squares represent the matching positions with the contralateral UL. **(b):** Mean errors for the X and Y axes for the CRPS and control groups. Error bars represent the standard error of the mean.



**Fig. 4: Grand average psychophysical curves for CRPS (red line and dots) and Controls (black line and crosses).** Blue line indicates  $X_{0.50}$  (point of subjective equivalence) and the green lines the  $X_{Y0.25}$  and  $X_{Y0.75}$ . The full line represents the X points for the CRPS group and the dashed lines for the Controls. The PSE corresponds to the  $X_{Y0.50}$  points and the JND corresponds the difference between the  $X_{Y0.75}$  and  $X_{Y0.25}$  divided by 2.



**Fig. 5: Body perception disturbance scale.** (a): The four questions of the Body perception disturbance scale. (b): Individual data for the CRPS group (each dot corresponds to a CRPS participant). The vertical red bars represent the mean of the CRPS group.

