



## Special Issue “Attention &amp; Motor Processes”: Research Report

# Ignoring space around a painful limb? No evidence for a body-related visuospatial attention bias in complex regional pain syndrome



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## ABSTRACT

**Background:** Complex Regional Pain Syndrome (CRPS) is a disorder of severe chronic pain in one or more limb(s). People with CRPS report unusual perceptions of the painful limb suggesting altered body representations, as well as difficulty attending to their affected limb (i.e., a ‘neglect-like’ attention bias). Altered body representations and attention in CRPS might be related, however, existing evidence is unclear. We hypothesized that if there were a body-related visuospatial attention bias in CRPS, then any attention bias away from the affected side should be larger for or limited to circumstances when the (impaired) body representation is involved in the task versus when this is not the case.

**Methods:** We included 40 people with CRPS, 40 with other limb pain conditions, and 40 pain-free controls. In half of the people with pain, their upper limb was affected, in the other half their lower limb. We administered computerized tasks of spatial attention, including free viewing of images, shape cancellation, temporal order judgement, and dot-probe. The degree to which different versions of each task involved body representation was manipulated by one or more of the following: (1) presenting stimuli nearer versus further away from the body, (2) using body related versus neutral stimuli, and (3) inducing mental rotation of body parts versus no mental rotation. In addition to perceptual judgements, eye movements were recorded as a sensitive index of spatial attention. Bayesian repeated measures analyses were performed.

**Results:** We found no evidence for a (body-related) visuospatial attention bias in upper limb CRPS. Secondary analyses suggested the presence of a body-related visuospatial attention bias away from the affected side in some participants with lower limb CRPS.

**Discussion:** Our results add to growing evidence that there might be no general visuospatial attention bias away from the affected side in CRPS.

Abbreviations: CRPS, complex regional pain syndrome; JND, just noticeable difference; PSS, point of subjective simultaneity; SOA, stimulus onset asynchrony.

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## 1. Introduction

CRPS is a disorder of severe chronic pain, autonomic dysregulation, and motor dysfunction in one or more limb(s) (Stanton-Hicks et al., 1995). Although CRPS can occur after physical injuries, the symptoms are disproportionate to the inciting trauma (Choi et al., 2008; de Mos et al., 2007; Veldman, Reynen, Arntz, & Goris, 1993). Aside from physical symptoms, people with CRPS report difficulty attending to their affected limb, show asomatognosia (i.e., the sense that the limb does not belong to them), and have disturbances in body representation (Galer, Butler, & Jensen, 1995; Lewis, Kersten, McCabe, McPherson, & Blake, 2007). Body representation is the mental knowledge regarding the size, shape, and position of the limb (Haggard & Wolpert, 2005, pp. 261–271; Longo, Azañón, & Haggard, 2010). People with CRPS commonly perceive their affected limb to be misshapen or a different size compared to reality, and there can be a mismatch between the true and perceived position of the limb (Lewis et al., 2007; Moseley, 2005). Impaired representation of the affected hand has been further evidenced by slower hand laterality recognition in CRPS compared to pain-free controls (Bultitude, Walker, & Spence, 2017; Moseley, 2004b; Ravat, Olivier, Gillion, & Lewis, 2019; Reinersmann et al., 2010; Schwoebel, 2001; Wittayer, Dimova, Birklein, & Schlereth, 2018; although not always replicated; Breimhorst et al., 2018; Reinersmann et al., 2012). A role of impaired body representation in the physical manifestation of CRPS is supported by observations that pain is alleviated by treatments targeting aspects of body representation, such as sensorimotor training, enhancing motor representations, and mirror visual feedback (Méndez-Rebolledo, Gatica-Rojas, Torres-Cueco, Alborno-Verdugo, & Guzmán-Muñoz, 2017; Moseley, 2004a; Pleger et al., 2005).

Over 75% of people with CRPS report ‘neglect-like symptoms’, such as that they feel their affected limb is not part of their body, and that they need to focus mental and visual attention in order to voluntarily move it (Galer et al., 1995; Galer & Jensen, 1999; Lewis et al., 2007). Neglect-like symptoms in CRPS are different from hemispatial neglect after stroke (Galer, Jensen, & Butler, 2013; Greenspan, Treede, & Lenz, 2012; Lewis et al., 2007), which is characterized by a visuospatial attention bias away from the contralesional side that cannot be explained by primary sensory or motor deficits (Heilman, Valenstein, & Watson, 2000). People with CRPS generally do not show deficits on conventional ‘pen-and-paper’ neglect tasks such as clock-drawing and line bisection (Christophe, Chabanat, et al., 2016; Förderreuther, Sailer, & Straube, 2004; Kolb, Lang, Seifert, & Maihöfner, 2012; Reid et al., 2016; Reinersmann et al., 2012; although see; Cohen et al., 2013; Robinson, Cohen, & Goebel, 2011). Some suggest the neglect-like symptoms in CRPS mainly affect movement (Galer et al., 2013; Punt, Cooper, Hey, & Johnson, 2013; Reid et al., 2018). Nevertheless, people with CRPS can show reduced motor performance and processing of tactile stimuli by whichever

limb (affected or unaffected) that is located in the *hemisphere* in which the affected limb normally resides (Moseley, Gallace, & Iannetti, 2012; Moseley, Gallace, & Spence, 2009; Reid et al., 2018; although not always replicated; De Paepe et al., 2020; Filbrich et al., 2017). This suggests that the bias is not restricted to the affected limb, but can involve the affected side of *space* (Legrain, Bultitude, De Paepe, & Rossetti, 2012).

Studies using experimental measures that are more sensitive than pen-and-paper tasks have found a subtle, purely visuospatial attention bias in CRPS. Visuospatial attention regards directing visual attention to a location in space. Bultitude et al. (2017) and Filbrich et al. (2017) used visual temporal order judgement tasks, in which two visual stimuli are briefly presented, one on either side of space, separated by different amounts of time. Participants are asked to judge the temporal order of the stimuli (e.g., which stimulus was perceived as being presented first). People with CRPS needed stimuli to appear earlier on the affected as compared to the unaffected side of space for them to be perceived as simultaneous, indicating a visuospatial attention bias away from the affected side. However, not all studies have found reduced visuospatial attention for the affected compared to the unaffected side (Christophe, Delporte, et al., 2016; Filippopoulos, Grafenstein, Straube, & Eggert, 2015; Halicka et al., 2020a). This emphasizes that if a visuospatial attention bias is present in CRPS, it is likely to be subtle, and sensitive measures are needed in order to capture it.

These inconsistencies in the presence and direction of a visuospatial attention bias in CRPS could potentially depend on whether body representation was involved in the task. Reid et al. (2016) proposed that visuospatial attention deficits in CRPS are confined to bodily representations, and people with CRPS will only show attention bias away from the affected side when the (impaired) body representation is also involved. For example, Filbrich et al. (2017) found a visuospatial attention bias away from the affected side when stimuli were presented close to the affected limb, within peripersonal space, but not when the hands were kept under the table or when the stimuli were presented further away and outside of peripersonal space. Furthermore, Reid et al. (2016) found that people with CRPS showed a visuospatial attention bias away from the affected side, but *only when body-related information was involved*. Specifically, people with CRPS were slower in making judgements on the lateralization of hands and feet presented in the affected side of space, but made normally-speeded judgements for hands and feet presented in the unaffected side. Additionally, people with CRPS showed no deviations on the conventional line bisection task, but showed deviations away from the affected side when they bisected lines that were overlaid on their arms and hands. Reid et al. (2016) proposed that people with CRPS do not have a deficit in spatial processing per se, but have a deficit in the integration of spatial processing with body representation, which they named “somatospatial inattention”. Further evidence was demonstrated by Bultitude et al. (2017),

who found that the degree of visuospatial attention bias away from the affected side shown by people with CRPS was predicted by a subjective measure of distortions in the representation of their affected limb.

One way to test whether body representation is important for visuospatial attention biases in people with CRPS is to administer visuospatial tasks that differentially involve the neural and cognitive processes that represent the body. The aim of the current study was to evaluate visuospatial attention bias in CRPS under circumstances that are more or less likely to recruit body representations. There are several ways to increase the likelihood that representations of the body are recruited for attentional tasks. For example, one can present information within versus outside of 'near' or reachable space: the visuospatial frames of reference (i.e., abstract coordinate systems linked to separate output systems which guide specific actions) in which interactions with the body are possible. Second, one can use body-part stimuli versus neutral (i.e., non-body) stimuli. Third, one can design the task so as to require mental rotation of body parts versus no mental rotation.

Different neuroanatomical structures are involved in processing sensory information that is presented closer to the body compared to information that is presented further away (Previc, 1998). Double dissociations of visuospatial neglect for near versus far space in stroke patients are well documented, with many reports of patients with only near space neglect and no far space neglect; and vice versa (Halligan & Marshall, 1991; Ten Brink, Biesbroek, Oort, Visser-Meily, & Nijboer, 2019; Van der Stoep et al., 2013). This shows that visuospatial attention can be selectively biased in near space or far space. Information that is presented in the space immediately surrounding the body is integrated with body information so that objects can be effectively avoided or manipulated (Graziano & Gross, 1998; Holmes & Spence, 2004; Reinersmann et al., 2013). If body representations are important for the manifestation or magnitude of visuospatial attention bias, then we would expect people with CRPS to show a visuospatial attention bias away from their affected side only, or to a larger extent, when information is presented within arms' reach versus outside arms' reach.

Another way of recruiting the body representation is by viewing body-part stimuli (e.g., pictures of body parts). The visual system differentiates between human and non-human images, and there is evidence for body- and body-part-selective brain areas called the extrastriate body area and the fusiform body area (de Gelder et al., 2010; Downing & Peelen, 2016; Minnebusch & Daum, 2009; Peelen & Downing, 2007; Schwarzlose, 2005). Evidence from behavioural (Funk, Shiffrar, & Brugger, 2005; Sebanz, Knoblich, & Prinz, 2003) and neuroimaging studies (Astafiev, Stanley, Shulman, & Corbetta, 2004; Grezes & Decety, 2001; Peelen & Downing, 2007; Stevens, Fonlupt, Shiffrar, & Decety, 2000) suggests that representations of one's own bodily actions share a neural substrate with processing visual representations of actions performed by others. The same neural overlap between one's own body representation and viewing another body is seen while viewing static pictures of body parts (Chan, Peelen, & Downing, 2004; Reed & Farah, 1995). We expect that in CRPS, viewing pictures of body parts (i.e., upper or lower limbs) will activate the same brain areas that are representing

their affected limb in a distorted manner. If body representations are important for the manifestation or magnitude of a visuospatial attention bias, then viewing body parts, but not neutral images, would result in a visuospatial attention bias away from the affected side.

Finally, presenting pictures of body parts in such a way that mental rotation is needed for a given task versus when it is not needed is thought to draw on the body representation by means of motor imagery, and require the aforementioned mechanisms to a greater extent (Parsons, 1987a, 1987b, 1994). Such mental rotation is thought to be required in tasks in which judgements about the laterality of pictured, rotated hands have to be made. If body representations are important for the manifestation or magnitude of a visuospatial attention bias, then people with CRPS should show a greater visuospatial attention bias away from the affected side when they complete tasks that involve mentally rotating pictures of body parts corresponding to their affected limb, than tasks that use the same stimuli but that do not require mental rotation.

To test these hypotheses, we adapted digitized tasks that are typically used to assess subtle visuospatial attention biases in stroke patients and healthy controls, with the aim of tailoring them to test for body-related visuospatial attention bias. In addition to perceptual judgements, we also recorded eye movements as they directly reflect patterns of visual exploration and could be more sensitive to a visuospatial attentional bias (Delazer, Sojer, Ellmerer, Boehme, & Benke, 2018). For example, the visuospatial attention bias in neglect is reflected as a reduction of fixations at the contralesional side compared to the ipsilesional side while exploring a scene (e.g., Datie et al., 2006; Hornak, 1992; Karnath & Niemeier, 2002; Sprenger, Kömpf, & Heide, 2002). Eye movements in CRPS have only been evaluated without recruiting the body representation, showing no bias (Filippopoulos et al., 2015). We used four sets of tasks to evaluate the presence of body-related visuospatial attention bias in CRPS. First, we administered a free viewing task, in which participants viewed pictures that did or did not contain body-part stimuli. Second, we used a cancellation task, a classic task used to measure visuospatial neglect (Halligan, Marshall, & Wade, 1989). Participants are presented with targets and distractors, and have to click on all targets. We used body-part versus neutral stimuli, and versions in which mental rotation of the stimuli was needed in order to perform the task. Third, we used a temporal order judgement task (Bultitude et al., 2017; Filbrich et al., 2017) with body parts versus neutral pictures. Finally, a modified dot-probe task was used, classically used to assess selective visuospatial attention biases for emotional stimuli (MacLeod, Mathews, & Tata, 1986). Participants had to detect a dot as quickly as possible. The dot was presented either on the left or right side of the screen and was preceded by two pictures in those left and right locations. These pictures were either body parts or non-body parts.

We administered these tasks in people with CRPS, people with other types of chronic limb pain, and pain-free controls. Most of the previous studies on visuospatial attention in CRPS did not compare performances of people with CRPS with people with other types of limb pain (Bultitude et al., 2017; Christophe, Delpote, et al., 2016; Filbrich et al., 2017; Filippopoulos et al., 2015; Halicka et al., 2020a), with a few

exceptions in which a lateralized bias for people with non-CRPS pain compared to people with CRPS was similar (Kolb et al., 2012; Reinersmann et al., 2010) or smaller (Reinersmann et al., 2012). Body representation disturbances are also reported in other chronic pain conditions, although to a lesser extent (Frettlöh, Hüppe, & Maier, 2006; Hirakawa, Hara, Fujiwara, Hanada, & Morioka, 2014; Michal et al., 2016). Therefore, we expect that if there would be a body-related visuospatial attention bias in people with other chronic pain conditions, this bias would be smaller than in people with CRPS. In addition, we separately assessed people with upper versus lower limb pain, to evaluate whether the proposed body-related visuospatial attention bias would be confined to or worse for upper or lower limb CRPS.

Our primary hypothesis was that people with CRPS would show a visuospatial attention bias away from the affected side that was larger for, or only evident in, conditions that were more likely to recruit body representation. Specifically, we predicted that people with CRPS would show a greater visuospatial attention bias: 1) when stimuli were presented near the affected side compared to conditions where stimuli were presented far from the affected side, 2) when body-part stimuli were used compared to when non-body-related stimuli were used, 3) and/or when mental rotation of the affected limb was required compared to when no mental rotation of the affected limb was required. In contrast, this visuospatial attention bias would be seen to a lesser extent in people with other types of chronic limb pain (if at all), and would not be seen in pain-free controls.

A secondary hypothesis was that there would be an interaction between any visuospatial attention bias and location of the body-part stimulus (i.e., on the affected or unaffected side of the screen). In the study of Reid et al. (2016), hand laterality recognition was slower for stimuli appearing in the affected side of space versus the unaffected side of space. Therefore, for the temporal order judgement task and dot-probe task, we included conditions in which we presented body stimuli in one side of space and neutral stimuli on the other side of space. We hypothesised that for people with CRPS presenting the body stimuli in the affected side of space would result in a larger visuospatial attention bias compared to when they were presented in the unaffected side.

Finally, another secondary hypothesis was that the severity of any potential body-related visuospatial attention bias would be positively related to the degree of body representation disturbances and/or pain, as measured by self-report scales.

## 2. Material and methods

The research was approved by the UK Health Research Authority and Research Ethics Committee (REC reference 18/LO/1430) and the Psychology Research Ethics Committee at the University of Bath (reference 18–251), in accordance with the Declaration of the World Medical Association ([www.wma.net/](http://www.wma.net/)). We report how we determined our sample size, all data exclusions, all inclusion/exclusion criteria, whether inclusion/exclusion criteria were established prior to data analysis, all manipulations, and all measures in the study. Before analysing

the data, we uploaded a preregistration on the Open Science Framework website (OSF; [https://osf.io/5dqjk/?view\\_only=d74b8a209fcf427b8e2c8484180829e3](https://osf.io/5dqjk/?view_only=d74b8a209fcf427b8e2c8484180829e3)).

### 2.1. Participants

We recruited people with CRPS, other chronic pain conditions (“pain controls”), and pain-free controls. All participants had to be aged between 18 and 85, have no visual deficits substantial enough to interfere with completing the tasks, have no history of neurological disorders (e.g., stroke) or epilepsy, and have an understanding of written and verbal English sufficient to understand the instructions.

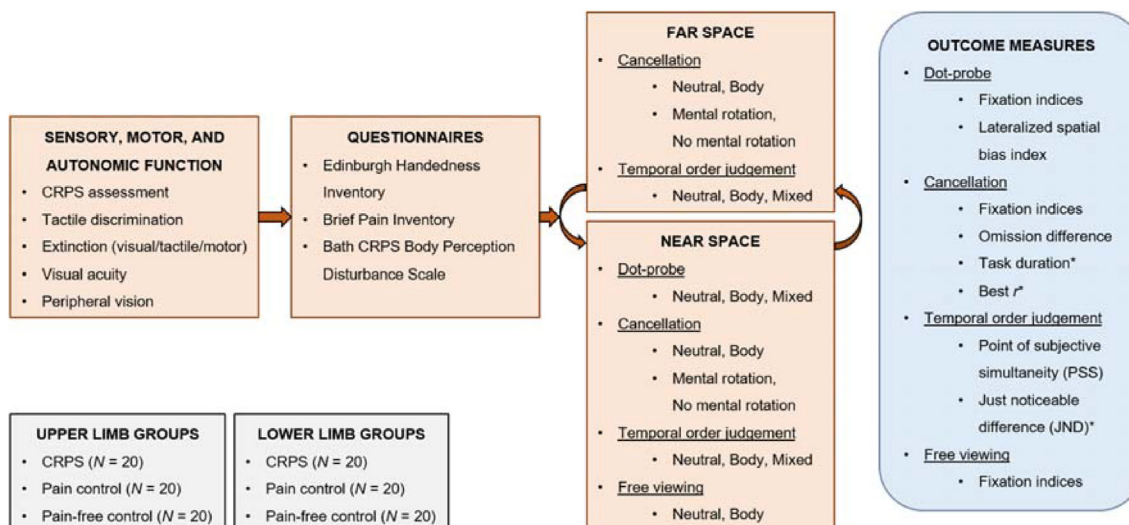
Participants with CRPS had to have received a diagnosis of CRPS type 1 or 2 affecting primarily an upper or lower limb for at least 3 months. On the day of testing, they had to meet the Budapest diagnostic clinical criteria for CRPS (Harden et al., 2010). The pain controls had to experience pain primarily affecting one upper or lower limb on most days in the past 3 months. On the day of testing, they could not meet the Budapest diagnostic clinical or research criteria for CRPS. The pain-free control group was matched with the CRPS group for sex, self-reported handedness, and age. They could not have a history of chronic pain in the past year (defined as pain experienced on most days for at least 3 months), and no pain on the day of testing. Pain-free controls were matched with a person with CRPS so as to determine which limb would be considered the ‘affected’ limb (left/right, upper/lower) in the analysis, and with respect to the used stimuli for tasks. For example, if a pain-free control was matched with a person with CRPS in their left hand, the left side was recoded as being the affected side in the analysis, and the right side was recoded as being the unaffected side. Participants were reimbursed £10 per hour for their time, along with travel and accommodation expenses where relevant.

We used G\*Power (version 3.1.9.2) to compute the minimal required sample size for our main repeated measures ANOVA's on visuospatial attention bias for the different tasks, with the between-subject factor Group (CRPS, pain control, pain-free control) and the within-subject factor Condition (body, neutral). With an alpha of .05 and a power of .80, it was estimated that at least a total of 42 respondents per upper/lower limb group was needed to detect a small effect size ( $f = .25$ ). We aimed to include 60 participants in the upper limb group, and 60 participants in the lower limb group. All participants gave written informed consent.

### 2.2. Clinical assessment and questionnaires

#### 2.2.1. Procedure

Fig. 1 lists all tasks, conditions, and outcome measures. All participants underwent a clinical assessment involving tests of sensory, motor, and autonomic functions, to diagnose and quantify CRPS according to the Budapest clinical criteria (Harden et al., 2010). The clinical examination of the CRPS signs is described in appendix A. To test for sensory deficits that could account for any differences between groups, we conducted several additional sensory tests (i.e., tactile discrimination; visual, tactile, and motor extinction; and visual acuity). Next, all participants filled out questionnaires to



**Fig. 1 – Tasks, conditions, and outcome measures.** All participants (i.e., CRPS, other pain, pain-free) performed all tasks. The order of distance (near/far space) was counterbalanced between participants. The fixation indices were only computed for the assessments in near space. The order of tasks was dot-probe, cancellation, temporal order judgement, and free exploration. For all tasks, the dominant hand was used unless this was too painful. We predicted that people with CRPS would show a greater visuospatial attention bias when stimuli were presented in near space compared to far space, when body-part stimuli were used compared to when neutral stimuli were used, and/or when mental rotation of the affected limb was required compared to when no mental rotation of the affected limb was required. \*These outcome measures (i.e., task duration, best  $r$ , and just noticeable difference) were secondary outcome measures and reflect other aspects of task performance than visuospatial attention bias. CRPS = complex regional pain syndrome.

assess handedness and body perception disturbances. Participants in the pain groups additionally filled out a questionnaire on pain severity and interference.

### 2.2.2. Sensory, motor, and autonomic function

We examined tactile discrimination thresholds on the index fingertips using a disk with tips that are spaced at intervals from 1 to 15 mm apart (Exacta, North Coast Medical), using a staircase procedure starting with a distance of 7 mm (Pleger et al., 2006).

We assessed visual, tactile, and motor extinction (with eyes open and closed) using confrontation tests. We used unilateral and bilateral finger movements, lights taps on the shoulder(s), and movements of the arm(s), to test visual, tactile, and motor domains respectively. Extinction was defined as missing one of the stimuli when they were presented simultaneously while accurately detecting the single stimuli.

Visual acuity was assessed using the Acuity letters subtest of the Freiburg Vision Test version 3.9.9a (Bach, 2007). Per eye, we reported the decimal visual acuity score ( $VA_{dec}$ ), ranging from 0 to 2.

Participants' binocular peripheral visual acuity was tested using Landolt C optotypes that were presented at a distance of 2°, 3°, 4°, 6°, 9°, and 13° left and right from the centre of the screen. The stimuli were scaled according to cortical magnification. Participants used the arrow keys to indicate the orientation of the gap. Per location, a Landolt C optotype was presented once per gap orientation (up, down, left, right), resulting in 48 trials. The accuracy (%) of responses was calculated for each location.

### 2.2.3. Questionnaires

All participants completed the Edinburgh Handedness Inventory, which measures the extent to which a person uses their left hand (score -100 to -40) or right hand (score 40 to 100) for everyday activities (Oldfield, 1971). People with upper limb pain filled out the scale a second time to indicate their memory of hand preference prior to the onset of the pain. We computed a “change in handedness” score (current handedness minus handedness before pain) to give a broad measure of the extent to which the daily use of their affected versus unaffected hands had changed.

For the participants with pain, pain severity and interference were assessed with a short-form of the Brief Pain Inventory (Cleeland & Ryan, 1994), using four questions on pain intensity and seven questions on pain interference, resulting in average scores ranging from 0 (lowest pain/interference) to 10 (highest pain/interference).

The Bath CRPS Body Perception Disturbance Scale was used to assess body perception disturbances in all participants (Lewis & McCabe, 2010). The questionnaire has seven items that cover different aspects of body perception disturbances (range 0–57). As this scale has not been validated, we computed correlations between items and only kept items with a corrected item-total correlation of  $>.5$ . Item 2 (“...how aware are you of the physical position of your limb?”) and item 3 (“...how much attention do you pay to your limb in terms of looking at it and thinking about it?”) had corrected item-total correlations of .39 and .05 respectively, and were removed. Cronbach's alpha of the remaining six items was .80. New total scores were computed with the remaining six items (range 0–37).

### 2.3. Experimental tasks and stimuli

#### 2.3.1. Procedure and apparatus

All participants performed the experimental tasks (i.e., free viewing, cancellation, temporal order judgement, and dot-probe). An overview of tasks and conditions is presented in Fig. 1. Tasks were administered in light and sound attenuated rooms. All tasks were administered in near space; the cancellation and temporal order judgement task were additionally administered in far space. The order of distances was counterbalanced between participants within groups. In near space, stimuli were presented on a 22-inch Dell P2217H monitor (~60 cm, i.e., within arms' reach) with a resolution of 1920 \* 1080 pixels and a 60 Hz refresh rate. Eye movements were recorded using a Tobii Pro X2-60 compact eye tracker (sampling rate of 60 Hz). Prior to each task a 9-point calibration procedure was conducted. In far space, stimuli were projected on a wall (~150 cm, "far" space, i.e., outside of arms' reach). The projection was 210 cm wide and 120 cm high and projected with a NEC U321H – DLP 1080P projector with a resolution of 1920 \* 1080 pixels and 60 Hz refresh rate. No eye movements were recorded for the far space conditions.

The cancellation and temporal order judgement tasks were programmed in MATLAB (version 9.5.0, R2018b) using the Psychophysics Toolbox extensions (Brainard, 1997), and the free viewing and dot-probe tasks in E-Prime 2.0 (E-Prime, 2004). All scripts and stimuli can be found at [https://osf.io/5dqjk/?view\\_only=d74b8a209fcf427b8e2c8484180829e3](https://osf.io/5dqjk/?view_only=d74b8a209fcf427b8e2c8484180829e3). For the temporal order judgement and dot-probe tasks, participants provided their responses (left or right) using congruently aligned buttons (i.e., the button on the left corresponded with the 'left' response, and vice versa) on a custom-built button box. The colour of the left and right buttons (red or yellow) was counterbalanced between participants within groups. Participants used their dominant hand, unless this was too painful, in which case they used their non-dominant hand. This was the case for five people with upper limb CRPS. Therefore, their matched pain-free controls ( $n = 5$ ) also used their non-dominant hand to provide responses. The entire research session lasted 2–3.5 h.

#### 2.3.2. Free viewing

Participants looked at a series of scenes for 10 sec each (Delazer et al., 2018). We presented neutral scenes (buildings/nature) and scenes of people where their lower limbs, upper limbs, or a mix of upper and lower limbs (five scenes per condition) were visible. A mirror-reversed copy of each scene was created to control for differences in saliency, visual crowding, and other visual features between the left and right side of the scene, resulting in 40 scenes in total (i.e., 4 conditions \* 5 scenes \* 2 copies per scene). Before each scene was shown, participants were instructed to look at a white fixation cross (.7°) presented against a grey background. A scene was presented as soon as the fixation cross was fixated. Participants were instructed to look at the images. It was explicitly mentioned that no other task was required. This task was administered in near space only.

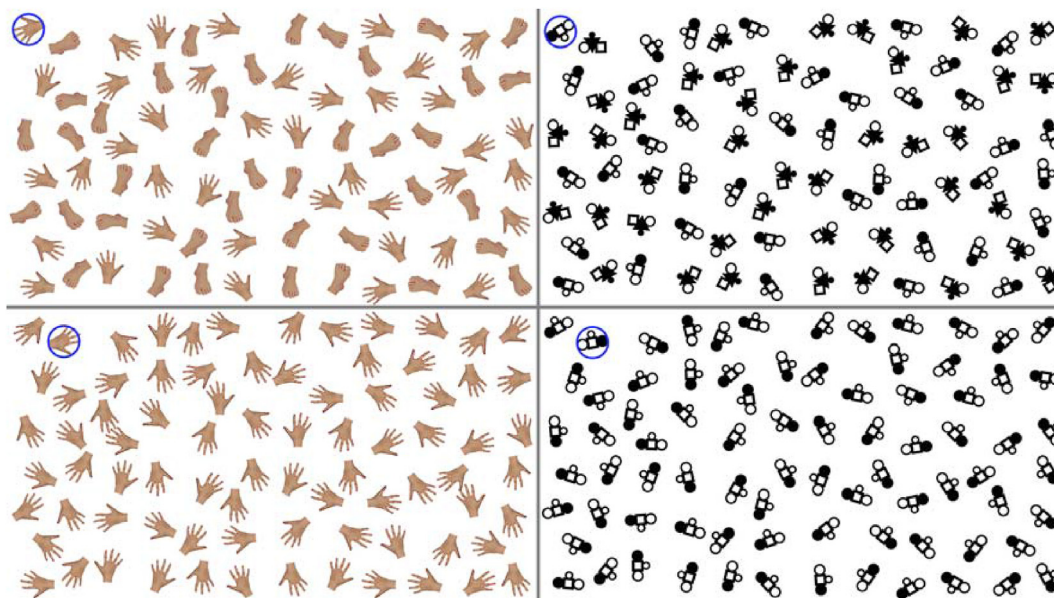
#### 2.3.3. Cancellation

Participants were asked to find and click on specific target items among distractors, using a computer mouse. There was unlimited time to perform the task. Stimulus conditions were non-body part objects (i.e., neutral target stimuli among neutral distractor stimuli) versus body parts. There were also two mental rotation conditions per stimulus type (mental rotation and no mental rotation). Thus, each participant completed four cancellation tasks (neutral with mental rotation, neutral without mental rotation, body parts with mental rotation, or body parts without mental rotation) per viewing distance (near or far). For the templates involving body parts, people with pain always had to look for the limb that matched their affected limb. (i.e., the targets were left or right feet for people with pain in the lower limb and left or right hands for people with pain in the upper limb; Fig. 2). For the templates that did not require mental rotation, the distractors were stimuli that could readily be distinguished from the target based on obvious features (e.g., when the target was a hand, the distractor was a foot). For templates that did require mental rotation, the distractors were the mirror image version of the target (e.g., when the target was a left hand, the distractor was a right hand). Looking for targets amongst mirror-image distractors necessitates mental rotation of each stimulus to distinguish between them. Pain-free controls were matched with a person with CRPS regarding which limb they had to look for, and the side of this limb (i.e., left or right) was treated as being the affected side in the analyses.

We computed the omission difference score by subtracting the number of omissions on the unaffected side from the number of omissions on the affected side. As there were 20 targets per side, the omission difference score ranged from –20 to 20. A positive score indicates that more targets were missed at the affected versus unaffected side. Secondary outcome measures were measures of search speed and organization. We computed task duration in seconds. Furthermore, we computed best  $r$  as a measure of whether participants searched consistently in the same direction (i.e., from left to right, or from top to bottom, or vice versa) in accordance with previous studies on stroke patients (Dalmajer, Van der Stigchel, Nijboer, Cornelissen, & Husain, 2014; Mark, Woods, Ball, Roth, & Mennemeier, 2004). Specifically, to attain best  $r$ , we calculated the Pearson correlation coefficient ( $r$ ) from the linear regression of the  $x$ - or  $y$ -values of all marked locations relative to the order in which they were clicked on by the participant. The highest absolute correlation of these two (best  $r$ ) was selected to represent the degree to which calculations were pursued orthogonally. Best  $r$  ranges from 0 (inconsistent search) to 1 (consistent search).

#### 2.3.4. Temporal order judgement

Participants were asked to fixate a central cross (white, .6°) that was presented throughout the task against a grey background. After fixation was detected there was a random delay of between 500 and 1000 msec. Then, two images (each 8° \* 8° in size) were shown for 1000 msec with the inner edge of the rectangle appearing 6° to the left or right of fixation, one appearing before the other. Participants were instructed to look at the central fixation cross only, and any trials in which



**Fig. 2 – Example templates for the cancellation task. In the two left templates the left hand is the target stimulus; in the two right panels a neutral object is the target stimulus. The target stimulus is indicated by a blue circle, which looks the same as the circle that appeared at any clicked location. The upper panels show stimuli for the no-mental rotation conditions; the lower panels show stimuli for the mental rotation condition. The same neutral stimuli (on the right) were used for all participants, whereas the body stimuli were adjusted so that the target matched their affected side (left/right) and extremity (upper/lower).**

they looked at one of the images were deleted and repeated at the end of the task. Half of the participants had to indicate which image appeared first (forced choice left or right), the other half had to indicate which image appeared second (forced choice left or right; answers were re-coded). This was randomized and counterbalanced across participants, within groups. We used five stimulus onset asynchronies (SOA's) per side that came first (left or right), which were chosen so as to fit with the screen refresh rate: 17, 34, 68, 118, and 237 msec. We used 8 stimulus pairs per condition, and each stimulus pair was presented twice per SOA, so that each image was presented equally often on the affected and unaffected side. This resulted in 160 trials per condition (10 SOAs \* 8 stimulus pairs \* 2 image positions).

Conditions were body part images (with upper or lower limbs, depending on the affected limb for pain patients, and on the affected limb of the matched patient for pain-free controls), neutral images (fruit/vegetables), mixed images with the body image on the affected side, and mixed images with the body image on the unaffected side. The mixed conditions were added for a secondary analysis. See appendix B for the stimulus selection and validation. The task in near and far space contained two stimulus conditions (neutral–neutral, body–body), resulting in 320 trials. In near space, there were two additional conditions with mixed images (body-neutral, neutral-body), resulting in 640 trials in total for the task in near space. We did not add these conditions to the task in far space to reduce testing time. The order of conditions was randomized within each task. Before start of the task, participants performed at least five practise trials using an SOA of 237 msec, or as many practise trials as

needed until they understood the task. Feedback on the correctness of the response was provided following each practise trial, but no feedback was given during the main task.

Our primary outcome measure was the point of subjective simultaneity (PSS), which is the amount of time (in milliseconds) one stimulus has to precede or follow the other in order for the two stimuli to be perceived as occurring simultaneously. We computed the PSS in such way that a negative value indicates that the image on the affected side needed to appear earlier than the image on the unaffected side to be reported as simultaneous, hence a visuospatial attention bias away from the affected side. A value of zero would indicate no bias. Our secondary outcome measure was the just noticeable difference (JND). The JND provides a measure of the smallest interval needed to reliably indicate the temporal order in which the two stimuli were presented, giving a measure of temporal acuity. A higher JND represents lower temporal acuity, i.e., larger time intervals are needed to reliably indicate the order of the stimuli.

### 2.3.5. Dot-probe

In the classic dot-probe paradigm, selective attention for one concurrently presented stimulus versus another is measured (MacLeod et al., 1986). We used a modified version of the task in which either two similar or two different stimuli were presented in one trial, while measuring the visuospatial attention bias for one side versus the other (affected vs unaffected). Furthermore, participants were allowed to make eye movements (Waechter, Nelson, Wright, Hyatt, & Oakman, 2014).

Participants were instructed to fixate a central cross (white, .5°) presented against a grey background and to subsequently look at the images however they wished. A trial started when participants fixated the cross. The fixation cross stayed on the screen for 1000 msec after participants fixed on it. Next, the cross disappeared, and two images were shown for 2000 msec. We chose this relatively long stimulus duration because previous research has shown that fixation indices are more reliable over a longer period of time (Waechter et al., 2014). The images (each 6° \* 6° in size) were presented with the inner edge of the rectangle appearing 3° to the left or right of fixation. Immediately following the offset of the images, a probe (white dot, 0.5°) was presented on either the left or right of the screen at the same location as the centre of one of the previously shown images. Participants were required to report the side of the probe (left or right) as fast as possible. The probe remained on screen until a response was made, which ended the trial.

For the main analysis there were two conditions: a neutral condition (with two different neutral images) and a body condition (with two different body images). There were 8 image pairs per condition (appendix B; Supplementary Figure 1). Each pair was presented four times: once per probe location (i.e., a probe following the left or the right image), and once per image location (i.e., one of the images was either presented at the left or right side), resulting in 32 unique trials per condition. For a secondary analysis, we added a mixed condition in which a body and neutral image were presented within the same trial. There were 8 mixed image pairs. Each pair was presented once per image position (left or right), and probe location (left or right), resulting in 32 unique trials. Participants completed 192 trials in total, divided into two blocks of 96 unique trials each. Trials were presented in a randomized order within blocks. Participants took a self-paced rest between blocks. Eight practise trials were created using four additional neutral stimuli. Feedback on the correctness of the response was provided following each practise trial, but no feedback was provided during the main task.

Trials (averaged across the neutral, body, and mixed conditions) in which participants gave an incorrect response (CRPS upper: .62%, lower: .83%; pain control upper: .52%, lower: .52%; pain-free control upper: .31%, lower: .26%), responded faster than 200 msec (none of the trials), or slower than 3 standard deviations from the participant's mean (CRPS upper: 1.17%, lower: .86%, pain control upper: .94%, lower: 1.01%; pain-free control upper: 1.12%, lower: .78%) were excluded.

For each included trial, we computed the response time (RT) for pressing the button in response to the probe. Instead of calculating a traditional attentional bias index from just the mixed image trials, we calculated an alternative index. This was because we were interested in whether there was visuospatial attention bias away from the affected side of space, which would result in faster responses to probes that appeared at the unaffected side as opposed to the affected side. As a measure of visuospatial attention bias, we computed the lateralized spatial bias index for each condition (i.e., neutral, body, mixed conditions). First, for each condition, we computed the average

RT for trials where a probe appeared on the affected side ('RT probe affected side'), and the average RT for trials where a probe appeared on the unaffected side ('RT probe unaffected side'). This could either be the left or right, depending on the affected side. For pain-free controls there was no affected side, and data was recoded based on the side that was affected in the person with CRPS who they were matched with (see '2.1. Participants'). Second, for each condition, we computed the lateralized spatial bias index, which indicated the average RT for trials with a probe on the unaffected side relative to the RT for trials with a probe on the affected side [lateralized spatial bias index = RT probe unaffected side / (RT probe unaffected side + RT probe affected side)]. A value below .5 indicates faster responses to target probes at the unaffected versus affected side, hence a lateralized visuospatial attention bias away from the affected side.

### 2.3.6. Fixation indices

For all tasks, eye-tracking data was analysed if the calibration was reliable and if drift checks (i.e., detecting a fixation at the central fixation cross) could be performed at the start of each trial. We used the I-VT Fixation Filter (Olsen, 2012) in Tobii Studio (version 3.4.8) to filter the eye tracking data and identify fixations. We used MATLAB to compute fixation indices. The first fixation was defined as the first time a fixation was made at least 100 msec after stimulus onset and was located on one of the stimuli. For the dot-probe task, participants were not included in the eye-tracking analysis if they made no eye movements in more than 20% of trials for one or both of the conditions (neutral or body). For all tasks, except the temporal order judgement task, we computed the following fixation indices per condition (Waechter et al., 2014):

- Fixation frequency ratio: the average number of fixations on the affected side relative to the unaffected side as a proportion (number of fixations on the affected side/total number of fixations).
- Viewing time ratio: the time participants spent fixating on the affected side relative to the unaffected side as a proportion (viewing time on the affected side/total viewing time).

For the dot-probe task, we computed the following additional fixation indices:

- First fixation ratio: the proportion of the first fixations on the affected side relative to the unaffected side (number of first fixations on the affected side/total number of first fixations).
- Latency ratio: the average time taken to make the first fixation towards the affected side relative to the unaffected side (average latency of first fixations on the unaffected side/average latency of all first fixations).

Values below .5 indicate more fixations, longer viewing time, more first fixations, and shorter latencies for the first fixations on the unaffected versus affected side, indicating a visuospatial attention bias away from the affected side.



## 2.4. Statistical analyses

We reported Bayes Factors (BF) using the Savage-Dickey density ratio method, which can be interpreted as the weight of evidence for one hypothesis over another (Wagenmakers, Lodewyckx, Kuriyal, & Grasman, 2010; Wagenmakers, Marsman, et al., 2018). Specifically, we reported  $BF_{10}$ , the evidence in favour of the alternative hypothesis. We interpreted a BF of 1–3 as providing anecdotal, 3–10 moderate, 10–30 strong, 30–100 very strong, and >100 extreme evidence (Wagenmakers, Love, et al., 2018) (Fig. 3).

Data were analysed using JASP version .12.2 (JASP, 2020; Wagenmakers, Love, et al., 2018). We used the default settings for ANOVA designs to set the prior distribution (Rouder, Morey, Speckman, & Province, 2012). The Bayes Factor of the interaction effect was computed by selecting the option ‘Effects/Across matched models’ in JASP, providing  $BF_{incl}$ .

All data and output files can be found at [https://osf.io/5dqjk/?view\\_only=d74b8a209fcf427b8e2c8484180829e3](https://osf.io/5dqjk/?view_only=d74b8a209fcf427b8e2c8484180829e3).

### 2.4.1. Demographic and clinical characteristics

The upper and lower limb groups were analysed separately. We provided descriptive data on demographic and clinical characteristics and compared groups (i.e., CRPS, pain controls, pain-free controls) using Bayesian one-way ANOVA's and Bayesian contingency tables with the Poisson sampling scheme (Jamil et al., 2017).

### 2.4.2. Visuospatial attention bias

For the cancellation task, the ‘mental rotation’ and ‘no mental rotation’ conditions were analysed separately. For the temporal order judgement and dot-probe task, our main question focused on the trials where the same image pairs were shown. This was to see whether people with CRPS would show a visuospatial attention bias away from their affected side, and

whether this bias would be larger or restricted to conditions in which body images were shown as opposed to conditions in which neutral images were shown. We performed Bayesian repeated measures ANOVA's with Group (CRPS, pain controls, pain-free controls) as between subject factor and Condition (neutral, body) as within subject factor. For the temporal order judgement and cancellation tasks, Distance (near, far) was included as an additional within subject factor. Dependent variables were the primary and secondary outcomes of the temporal order judgement (PSS, JND), dot-probe (fixation frequency ratio, viewing time ratio, first fixation ratio, latency ratio, lateralized spatial bias index), cancellation (fixation frequency ratio, viewing time ratio, omission difference score, task duration, best  $r$ ), and free viewing tasks (fixation frequency ratio, viewing time ratio). Post-hoc pairwise comparisons were reported if there was more evidence in favour of the alternative hypothesis than the null hypothesis (i.e., with  $BF \geq 3$ ); and/or when there was a trend.

In a secondary set of analyses, we analysed the mixed body-neutral conditions from the temporal order judgement and dot-probe tasks to determine whether any visuospatial attention biases were enhanced or reduced according to whether the body stimulus was presented in the affected versus the unaffected side. We performed Bayesian repeated measures ANOVA's with Group (CRPS, pain controls, pain-free controls) as between subject factor and Side of body image (body image at affected side, body image at unaffected side) as within subject factor. Dependent variables were the primary outcomes of the temporal order judgement (PSS) and dot-probe tasks (lateralized spatial bias index).

### 2.4.3. Relationships between visuospatial attention bias, body perception disturbances, and pain

For each of the CRPS groups, we assessed the relationships between all measures that indicated visuospatial attention bias and scores on the Bath CRPS Body Perception Disturbance Scale, and the Brief Pain Inventory. We computed non-parametric, Bayesian Kendall's tau ( $\tau$ ) correlational analyses.

$BF_{10}$ range	Interpretation
>100	Extreme evidence for $H_1$
30–100	Very strong evidence for $H_1$
10–30	Strong evidence for $H_1$
3–10	Moderate evidence for $H_1$
1–3	Anecdotal evidence for $H_1$
1	No evidence
1/3–1	Anecdotal evidence for $H_0$
1/10–1/3	Moderate evidence for $H_0$
1/30–1/10	Strong evidence for $H_0$
1/100–1/30	Very strong evidence for $H_0$
<1/100	Extreme evidence for $H_0$

**Fig. 3 – Legend for the interpretation of the Bayes Factors (BF).  $H_1$  refers to the alternative hypothesis (i.e., groups or conditions differ from each other) and  $H_0$  refers to the null hypothesis (i.e., groups or conditions do not differ from each other). The figure is based on Table 1 in Wagenmakers, Love, et al. (2018).**

## 3. Results

### 3.1. Upper limb

#### 3.1.1. Demographic and clinical characteristics

The upper limb pain control group was younger than the other groups (Table 1). There was no evidence for differences between groups regarding sex, handedness, two-point discrimination, and visual acuity of the left eye. The people with upper limb CRPS had higher CRPS severity scores and body perception disturbance scores; and lower visual acuity of the right eye than the other groups. The upper limb pain control group had higher CRPS severity scores and body perception disturbance scores than the pain-free control group. None of the participants showed visual, tactile, or motor extinction. There was no evidence for differences in change of handedness, affected side (left or right), and pain duration between the upper limb CRPS and pain control groups. The upper limb CRPS group obtained higher scores on the Brief Pain Inventory than the upper limb

**Table 1 – Demographic and clinical characteristics for the upper limb participants, means (SD) and frequencies (%), split per group. A  $BF_{10} > 3$  (shaded in blue) is evidence in favour of the alternative hypothesis, a  $BF_{10} < 1/3$  is evidence in favour of the null hypothesis (shaded in red). See Fig. 3 for the full legend.**

	CRPS ( <i>N</i> = 20)	Pain control ( <i>N</i> = 20)	Pain-free control ( <i>N</i> = 20)	$BF_{10}$
Age, years	53.75 (11.32) <sup>2</sup>	34.80 (15.87) <sup>1,3</sup>	53.30 (10.19) <sup>2</sup>	2325.82
Sex, % female	18 (90.0%)	15 (75.0%)	18 (90.0%)	.63
Self-reported handedness, % right	17 (85.0%)	19 (95.0%)	17 (85%)	.02
Edinburgh Handedness Inventory (pre injury)	53.00 (71.13)	85.15 (16.55)	68.45 (60.66)	.48
Change in handedness	-14.45 (92.95)	-8.00 (19.50)	-	.32
Affected side, % right	10 (50.0%)	10 (50.0%)	-	.72
Pain duration, years	7.21 (4.41)	4.98 (6.45)	-	.59
Brief Pain Inventory, 0-10	5.32 (2.45) <sup>2</sup>	3.19 (1.73) <sup>1</sup>	-	12.84
CRPS severity score, 0-16	11.10 (2.31) <sup>2,3</sup>	3.35 (2.16) <sup>1,3</sup>	.50 (.51) <sup>1,2</sup>	5.69 * 10 <sup>21</sup>
Bath CRPS Body Perception Disturbance Scale, 0-37	18.90 (9.89) <sup>2,3</sup>	10.25 (5.27) <sup>1,3</sup>	2.80 (2.69) <sup>1,2</sup>	5.53 * 10 <sup>6</sup>
Two-point discrimination, mm				
- Affected side*	3.20 (2.88)	2.56 (1.01)	2.77 (.70)	.22
- Unaffected side	3.11 (1.60)	2.49 (1.16)	2.71 (.78)	.36
Decimal visual acuity score, 0-2				
- Left eye	1.35 (0.37)	1.30 (.42)	1.42 (.46)	.18
- Right eye	1.00 (0.38) <sup>2,3</sup>	1.43 (.47) <sup>1</sup>	1.36 (.39) <sup>1</sup>	.53

Abbreviation: CRPS, complex regional pain syndrome. There is moderate to extreme evidence ( $BF_{10} > 3$ ) that the group differs from <sup>1</sup>CRPS, <sup>2</sup>pain controls, <sup>3</sup>pain-free controls. \* Three participants with CRPS found the two-point discrimination task too painful on the affected limb, so we only report data of 17 people with CRPS.

pain control group. The three groups did not differ regarding binocular peripheral vision (appendix C; Supplementary Figure 2).

### 3.1.2. Experimental tasks

The means on the primary outcome measures for the upper limb groups are depicted in Table 2, split per task and condition. Graphs for all outcome measures are depicted in appendix C (Supplementary Figures 3–8). Across tasks, there was moderate to strong evidence for the observation that the CRPS, pain control, and pain-free control groups did not differ from each other regarding visuospatial attention bias. In addition, there was moderate to strong evidence against any changes in visuospatial attention bias depending on whether

the tasks were conducted in near versus far space, involved body versus neutral stimuli, or involved mental rotation. For the fixation frequency ratio in the free viewing task, and all fixation indices in the cancellation task without mental rotation and the dot-probe task, there was only anecdotal evidence in favour of the null hypothesis regarding the main effect of Group, and/or the interaction effect of Group \* Condition. Therefore, no conclusions can be drawn based upon these results. However, the Bayes factor for the interaction effect of Group \* Distance for the PSS, derived from temporal order judgement task, was 2.71, which is close to our set threshold of 3. To further explore whether the PSS values in the CRPS group significantly differed from 0, we conducted Bayesian one-sample t-tests for the values attained at each

**Table 2 – Mean scores (95% CI) per task and condition, for the upper limb participants, split per group. A  $BF_{10} > 3$  is evidence in favour of the alternative hypothesis, a  $BF_{10} < 1/3$  is evidence in favour of the null hypothesis (shaded in red). See Fig. 3 for the full legend. The fixation indices (i.e., fixation frequency, viewing time, first fixation, latency) range from 0 to 1, values below .5 indicate a bias away from the affected side (i.e., more fixations, longer viewing time, more first fixations, and shorter latencies for the first fixations on the unaffected vs affected side). The omission difference score ranges from –20 to 20, positive scores indicate a bias away from the affected side (i.e., more targets were missed at the affected vs unaffected side). The point of subjective simultaneity (PSS) is depicted in ms, negative values indicate a bias away from the affected side (i.e., the image on the affected side needed to appear earlier than the image on the unaffected side to be reported as simultaneous). The lateralized spatial bias index ranges from 0 to 1, values below .5 indicate a bias away from the affected side (i.e., faster responses to target probes at the unaffected vs affected side).**

		CRPS		Pain control		Pain-free control		$BF_{10}$				
		N	Mean (95% CI)	N	Mean (95% CI)	N	Mean (95% CI)	Group	Condition	Group * Condition	Distance	Group * Distance
<b>Free viewing</b>												
Fixation frequency ratio	Neutral	19	.47 (.41-.54)	17	.50 (.46-.55)	14	.47 (.41-.53)	.34	.21	.17		
	Body	19	.48 (.44-.52)	17	.49 (.46-.52)	14	.47 (.44-.50)					
Viewing time ratio	Neutral	19	.49 (.41-.56)	17	.51 (.46-.57)	14	.47 (.41-.53)	.30	.25	.20		
	Body	19	.48 (.43-.53)	17	.49 (.46-.52)	14	.47 (.44-.40)					
<b>Cancellation – no mental rotation<sup>1</sup></b>												
Omission difference	Near, neutral	18	.28 (-.20-.75)	20	.05 (-.13-.23)	20	.15 (-.08-.38)	.15	.41	.38	.28	.08
	Near, body	18	-.22 (-.59-.14)	20	.15 (-.02-.32)	20	.20 (-.09-.49)					
	Far, neutral	18	0 (-.24-.24)	20	.05 (-.05-.15)	20	.15 (-.16-.46)					
	Far, body	18	-.06 (-.17-.06)	20	-.05 (-.15-.05)	20	.05 (-.05-.15)					
Fixation frequency ratio	Neutral	17	.48 (.44-.52)	19	.52 (.49-.54)	14	.51 (.49-.54)	.58	.24	.23		
	Body	17	.49 (.46-.51)	19	.50 (.47-.53)	14	.51 (.48-.54)					
Viewing time ratio	Neutral	17	.48 (.44-.52)	19	.51 (.48-.55)	14	.51 (.47-.54)	.40	.28	.22		
	Body	17	.48 (.46-.51)	19	.50 (.46-.53)	14	.50 (.47-.53)					
<b>Cancellation – mental rotation<sup>1</sup></b>												
Omission difference	Near, neutral	18	.11 (-0.48-.70)	19	-.21 (-.68-.26)	20	.35 (-2-.90)	.08	.63	.44	.15	.14
	Near, body	18	-.44 (-1.53-.64)	19	-.21 (-.99-.57)	20	-.20 (-1.84-1.44)					
	Far, neutral	18	.50 (-0.05-1.05)	19	-.05 (-.43-.32)	20	-.15 (-.76-.46)					
	Far, body	18	-.72 (-1.62-.18)	19	.16 (-.36-.67)	20	-.20 (-.92-.52)					
Fixation frequency ratio	Neutral	17	.50 (0.46-.53)	19	.50 (0.48-.52)	14	.51 (.47-.56)	.25	.21	.56		
	Body	17	.50 (0.47-.54)	19	.51 (0.48-.54)	14	.49 (.46-.52)					
Viewing time ratio	Neutral	17	.49 (0.46-.52)	19	.49 (0.47-.52)	14	.51 (.47-.55)	.20	.23	.27		
	Body	17	.49 (0.46-.52)	19	.49 (0.47-.52)	14	.49 (.46-.52)					
<b>Temporal order judgement<sup>2</sup></b>												
PSS	Near, neutral	18	13.69 (-12.17-39.55)	20	-1.59 (-20.45-17.28)	20	0.79 (-11.02-12.6)	.28	.14	.10	.30	2.71
	Near, body	18	12.01 (-5.06-29.09)	20	-.49 (-21.38-20.41)	20	-1.59 (-14.38-11.19)					
	Far, neutral	18	-4.26 (-22.92-14.41)	20	6.55 (-9.90-22.99)	20	-5.96 (-18.91-6.99)					
	Far, body	18	4.74 (-9.36-18.83)	20	3.95 (-14.03-21.93)	20	-4.43 (-18.51-9.65)					
<b>Dot-probe</b>												
Lateralized spatial bias index	Neutral	20	.49 (.48-.50)	20	.50 (.50-.51)	20	.49 (.48-.50)	2.87	.19	.15		
	Body	20	.49 (.48-.50)	20	.50 (.49-.51)	20	.49 (.48-.50)					
Fixation frequency ratio	Neutral	15	.51 (.44-.48)	18	.46 (.39-.53)	15	.47 (0.38-.55)	.59	.24	.83		
	Body	15	.52 (.47-.58)	18	.48 (.41-.56)	15	.44 (.36-.51)					
Viewing time ratio	Neutral	15	.53 (.44-.61)	18	.45 (.38-.53)	15	.43 (.34-.53)	.71	.24	.55		
	Body	15	.52 (.45-.59)	18	.49 (.42-.56)	15	.42 (.33-.51)					
First fixation ratio	Neutral	15	.53 (.44-.62)	18	.47 (.37-.57)	15	.42 (.29-.54)	.63	.54	.25		
	Body	15	.49 (.38-.60)	18	.46 (.36-.56)	15	.40 (.29-.51)					
Latency ratio	Neutral	15	.5 (0.46-.55)	18	.50 (.47-.54)	15	.49 (.44-.54)	.25	.40	.22		
	Body	15	.52 (.48-.57)	18	.50 (.47-.53)	15	.51 (.46-.56)					

Abbreviations: CRPS, complex regional pain syndrome; PSS, point of subjective simultaneity. Group sizes differ because no valid eye tracking data was obtained for all tasks and participants. <sup>1</sup>One participant with CRPS in an upper limb was too tired to complete the cancellation task in far space. Another participant with CRPS was not able to use a computer mouse with either hand. They were excluded from the analysis. For one upper limb pain control, data from the mental rotation condition in far space was not saved, and this person was excluded from the analyses of the mental rotation condition. <sup>2</sup>Two people with upper limb CRPS were too tired to complete the temporal order judgement task in far space and were excluded from the analysis. Eye-tracking was valid in 12 people with upper limb CRPS, 13 upper limb pain controls, and 12 pain-free controls. For the remaining participants, fixations were not verified, or were only verified in a part of the task. We included all participants in the following analyses, and when we analysed performance of participants with valid eye-tracking data, results were comparable.

distance in the CRPS group. There was moderate evidence that the PSS did not differ from 0 in far space ( $BF_{10}$  body: .30,  $BF_{10}$  neutral:0 .27). The evidence regarding the PSS in near space was inconclusive ( $BF_{10}$  body: .69,  $BF_{10}$  neutral: 1.62).

A similar pattern of evidence against the alternative hypothesis was seen for the secondary analyses in which the

mixed (neutral and body) conditions of the temporal order judgement task and dot-probe task were compared (results are described in appendix C; Supplementary Figure 9 and Supplementary Table 1).

Analyses of secondary outcome measures for the cancellation task (i.e., task duration and best  $r$ ), and the temporal

**Table 3 – Demographic and clinical characteristics for the lower limb participants, means (SD) and frequencies (%), split per group. A  $BF_{10} > 3$  (shaded in blue) is evidence in favour of the alternative hypothesis, a  $BF_{10} < 1/3$  is evidence in favour of the null hypothesis (shaded in red). See Fig. 3 for the full legend.**

	CRPS ( <i>N</i> = 20)	Pain control ( <i>N</i> = 20)	Pain-free control ( <i>N</i> = 20)	$BF_{10}$
Age, years	46.25 (11.75)	42.70 (19.77)	44.50 (14.85)	.16
Sex, % female	16 (80.0%)	11 (55.0%)	15 (75.0%)	1.76
Self-reported handedness, % right	16 (80.0%)	20 (100%)	17 (85.0%)	.20
Edinburgh Handedness Inventory (pre injury)	60.50 (62.39)	72.30 (34.60)	59.40 (63.06)	.17
Affected side, % right	9 (45.0%)	10 (50.0%)	-	.75
Pain duration, years	8.31 (11.13)	8.25 (11.14)	-	.31
Brief Pain Inventory, 0-10	7.01 (1.56) <sup>2</sup>	4.10 (1.92) <sup>1</sup>	-	2584.06
CRPS severity score, 0-16	12.35 (2.06) <sup>2,3</sup>	5.25 (2.29) <sup>1,3</sup>	0.65 (1.14) <sup>1,2</sup>	$5.77 * 10^{22}$
Bath CRPS Body Perception Disturbance Scale, 0-37	23.80 (7.45) <sup>2,3</sup>	10.70 (4.51) <sup>1,3</sup>	3.60 (2.95) <sup>1,2</sup>	$3.64 * 10^{13}$
Two-point discrimination, mm				
- Affected side	2.81 (1.20)	2.73 (1.11)	2.60 (.76)	.16
- Unaffected side	2.73 (.81)	2.83 (1.25)	2.42 (.72)	.28
Decimal visual acuity score, 0-2				
- Left eye	1.11 (.56) <sup>2,3</sup>	1.53 (.43) <sup>1</sup>	1.48 (.31) <sup>1</sup>	6.71
- Right eye	1.23 (.37)	1.43 (.43)	1.39 (.34)	.41

Abbreviation: CRPS, complex regional pain syndrome. There is moderate to extreme evidence ( $BF_{10} > 3$ ) that the group differs from <sup>1</sup>CRPS, <sup>2</sup>pain controls, <sup>3</sup>pain-free controls.

order judgement task (i.e., the just noticeable difference) are described in appendix C (Supplementary Figures 10–12 and Supplementary Table 2).

Results of the secondary correlational analyses between the experimental outcome measures and the body perception disturbance (measured with the Bath CRPS Body Perception Disturbance Scale) and pain intensity (measured with the Brief Pain Inventory) are depicted in appendix C (Supplementary Table 3). There was no evidence for any of the correlations showing a relationship between visuospatial bias and body perception disturbances or pain intensity.

### 3.2. Lower limb

#### 3.2.1. Demographic and clinical characteristics

There was no evidence for differences between groups regarding age, sex, handedness, two-point discrimination,

and visual acuity of the right eye (Table 3). The people with lower limb CRPS had higher CRPS severity scores and body perception disturbance scores; and lower visual acuity of the left eye than the other groups. The lower limb pain control group had higher CRPS severity scores and body perception disturbance scores than the pain-free control group. None of the participants showed visual, tactile, or motor extinction. There was no difference in pain duration or the affected side (left or right) between the lower limb CRPS and pain control groups. The lower limb CRPS group obtained higher scores on the Brief Pain Inventory than the lower limb pain control group. The three groups did not differ regarding binocular peripheral vision (appendix D; Supplementary Figure 13).

#### 3.2.2. Experimental tasks

The means on the primary outcome measures for the lower limb groups are depicted in Table 4, split per task and

**Table 4 – Mean scores (95% CI) per task and condition, for the lower limb participants, split per group. A  $BF_{10} > 3$  is evidence in favour of the alternative hypothesis (shaded in blue), a  $BF_{10} < 1/3$  is evidence in favour of the null hypothesis (shaded in red). See Fig. 3 for the full legend. The fixation indices (i.e., fixation frequency, viewing time, first fixation, latency) range from 0 to 1, values below .5 indicate a bias away from the affected side (i.e., more fixations, longer viewing time, more first fixations, and shorter latencies for the first fixations on the unaffected vs affected side). The omission difference score ranges from –20 to 20, positive scores indicate a bias away from the affected side (i.e., more targets were missed at the affected vs unaffected side). The point of subjective simultaneity (PSS) is depicted in ms, negative values indicate a bias away from the affected side (i.e., the image on the affected side needed to appear earlier than the image on the unaffected side to be reported as simultaneous). The lateralized spatial bias index ranges from 0 to 1, values below .5 indicate a bias away from the affected side (i.e., faster responses to target probes at the unaffected vs affected side).**

		CRPS		Pain control		Pain-free control		$BF_{10}$		Group * Condition	Distance	Group * Distance
		N		N		N		Group	Condition			
<b>Free viewing</b>												
Fixation frequency	Neutral	17	.44 (.37-.51)	16	.49 (.42-.56)	18	.50 (.47-.54)	.30	.36	.57		
	Body	17	.49 (.45-.53)	16	.51 (.47-.54)	18	.49 (.47-.51)					
Viewing time ratio	Neutral	17	.43 (.36-.51)	16	.48 (.41-.56)	18	.50 (.46-.53)	.45	.40	.81		
	Body	17	.48 (.44-.52)	16	.50 (.47-.54)	18	.49 (.47-.51)					
<b>Cancellation – no mental rotation</b>												
Omission difference	Near, neutral	20	-.05 (-.41-.31)	20	.20 (-.13-.53)	20	-.20 (-.67-.27)	.07	.15	.84	.18	.48
	Near, body	20	.35 (.08-.62)	20	-.10 (-.40-.20)	20	.05 (-.23-.33)					
	Far, neutral	20	-.15 (-.46-.16)	20	(-.15-.015)	20	.20 (-.27-.67)					
	Far, body	20	(-.21-.21)	20	(-.10(-.24-.04)	20	(-.15-.15)					
Fixation frequency	Neutral	16	.48 (.45-.51)	16	.50 (.46-.53)	19	.49 (.47-.52)	.30	.44	.46		
	Body	16	.49 (.47-.52)	16	.49 (.46-.52)	19	.52 (.49-.55)					
Viewing time ratio	Neutral	16	.49 (.45-.52)	16	.50 (.46-.54)	19	.50 (.47-.53)	.24	.52	.18		
	Body	16	.51 (.48-.53)	16	.50 (.47-.54)	19	.51 (.48-.54)					
<b>Cancellation – mental rotation</b>												
Omission difference	Near, neutral	20	-.05 (-.85-.75)	20	-.10 (-.72-.52)	20	-.05 (-.59-.49)	.56	.14	.18	.31	.28
	Near, body	20	-.35 (-1.33-.63)	20	.25 (-.48-.98)	20	.10 (-1.13-1.33)					
	Far, neutral	20	-.65 (-1.22-.08)	20	-.15 (-.56-.26)	20	.05 (-.42-.52)					
	Far, body	20	-1.15 (-1.94--0.36)	20	0 (-.57-.57)	20	.15 (-.69-0.99)					
Fixation frequency ratio	Neutral	16	.51 (.47-.54)	16	.51 (.48-.55)	19	.50 (.47-.53)	.21	.22	.23		
	Body	16	.52 (.48-.55)	16	.50 (.47-.53)	19	.49 (.46-.53)					
Viewing time ratio	Neutral	16	.49 (.46-.52)	16	.51 (.49-.53)	19	.49 (.46-.52)	.26	.53	.37		
	Body	16	.52 (.49-.55)	16	.51 (.48-.53)	19	.5 (.47-.52)					
<b>Temporal order judgement<sup>1</sup></b>												
PSS	Near, neutral	15	1.61 (-20.97-24.19)	20	2.15 (-13.43-17.73)	15	-7.67 (-25.21-9.87)	.47	.28	.16	.24	1.12
	Near, body	15	-4.81 (-24.09-14.46)	20	1.28 (-16.78-19.35)	15	-1.47 (-19.65-16.71)					
	Far, neutral	15	-8.12 (-33.2-16.96)	20	3.20 (-12.96-19.35)	15	-17.18 (-40.6-6.25)					
	Far, body	15	-3.54 (-24.92-17.84)	20	9.11 (-8.29-26.50)	15	-10.42 (-31.62-10.78)					
<b>Dot-probe<sup>2</sup></b>												
Lateralized spatial bias index	Neutral	20	.49 (.47-.51)	18	.50 (.49-.51)	20	.5 (.49-.51)	.56	.54	.14		
	Body	20	.49 (.47-.51)	18	.50 (.5-.51)	20	.5 (.49-.51)					
Fixation frequency ratio	Neutral	15	.49 (.41-.57)	13	.50 (.42-.58)	16	.49 (.44-.53)	.47	.28	.73		
	Body	15	.48 (.43-.54)	13	.53 (.46-.60)	16	.48 (.43-.53)					
Viewing time ratio	Neutral	15	.50 (.42-.59)	13	.48 (.40-.56)	16	.51 (.45-.56)	.44	.35	8.77		
	Body	15	.49 (.43-.55)	13	.53 (.45-.62)	16	.50 (.44-.56)					
First fixation ratio	Neutral	15	.49 (.35-.62)	13	.47 (.36-.59)	16	.44 (.33-.55)	.51	.22	.18		
	Body	15	.48 (.37-.60)	13	.47 (.37-.57)	16	.44 (.35-.53)					
Latency ratio	Neutral	15	.49 (.45-.54)	13	.52 (.49-.56)	16	.50 (.45-.55)	.53	.47	.23		
	Body	15	.49 (.45-.53)	13	.52 (.49-.55)	16	.48 (.44-.52)					

Abbreviations: CRPS, complex regional pain syndrome; PSS, point of subjective simultaneity. Group sizes differ because no valid eye tracking data was obtained for all tasks and participants. <sup>1</sup>Three people with lower limb CRPS and four pain-free controls did a version of the temporal order judgement task with fewer trials, and were not included in the analyses. No discernible pattern was present across the different temporal offsets in the responses of two people with lower limb CRPS in the far space condition, and one pain-free control in the near space condition, and the cumulative Gaussians could not be fitted to these data. This suggests that participants performed poorly for all SOA's, even for the relatively long SOA's. Their responses were excluded. Therefore, we analysed data of 15 people with CRPS, 20 pain controls, and 15 pain-free controls. Of the included participants, eye-tracking was valid in 12 people with CRPS, 15 pain controls, and 12 pain-free controls. For the remaining participants, fixations were not verified, or were verified only in a part of the task. We included all participants in the following analyses, and when we analysed performance of participants with valid eye-tracking data, results were comparable. <sup>2</sup>One participant in the lower limb pain control group experienced cramps in the hand when pressing the buttons and could not perform the task, and for one participant in the lower limb pain control group data was not saved. Therefore, we had data from 18 participants in the lower limb pain control group.

condition. Graphs of all outcome measures are depicted in appendix D (Supplementary Figures 14–19). Across tasks, there was mostly moderate to strong evidence for the observation that the CRPS, pain control, and pain-free control

groups did not differ from each other regarding visuospatial attention bias. In addition, there was moderate to strong evidence against any changes in visuospatial attention bias depending on whether the tasks were conducted in near

versus far space, involved body versus neutral stimuli, or involved mental rotation. For the fixation indices in the free viewing task, the cancellation task and the dot-probe task, there was only anecdotal evidence in favour of the null hypothesis regarding the main effect of Group, and/or the interaction effect of Group \* Condition. Therefore, no conclusions can be drawn based upon these results. The only exception on these null results was the dot-probe task: there was moderate evidence for an interaction between Group and Condition. Pain controls showed a visuospatial attention bias away from the affected side in the neutral condition, and towards the affected side in the body condition.

Results for the secondary analyses of the mixed (neutral and body) conditions of the temporal order judgement task and dot-probe task are described in [appendix D \(Supplementary Figure 20 and Supplementary Table 4\)](#). There was no evidence for differences between groups or conditions for the temporal order judgement task. For the mixed conditions of the dot-probe task, there was moderate evidence for an interaction between Group and Side of the body image. Consistent with our expectations, the CRPS group showed a visuospatial attention bias away from the affected side compared to the other groups, but only in the condition where the body image was at the affected side.

Analyses of secondary outcome measures for the cancellation task (i.e., task duration and best  $r$ ), and the temporal order judgement task (i.e., the just noticeable difference) are described in [appendix D \(Supplementary Figures 21–23 and Supplementary Table 5\)](#).

Results of the secondary correlational analyses between the experimental outcome measures and the body perception disturbance (measured with the Bath CRPS Body Perception Disturbance Scale) and pain intensity (measured with the Brief Pain Inventory) are depicted in [appendix D \(Supplementary Table 6\)](#). For most of the correlations, there was no evidence showing a relationship between visuospatial bias and body perception disturbances or pain intensity. However, on the temporal order judgement task there was moderate evidence for a negative relationship between the PSS for the body condition in near space with body perception disturbances. The greater the body perception disturbance, the more negative the PSS, indicating a bias away from the affected side. In addition, on the cancellation task there was strong evidence for a positive relationship between the omission difference score for the body condition in near space with pain intensity. The higher the pain intensity, the higher the omission difference score, indicating a bias away from the affected side.

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## 4. Discussion

The aim of the current study was to evaluate visuospatial attention bias in CRPS in tasks that are designed to recruit body representation to different degrees. We hypothesized that, compared to people with other limb pain and pain-free controls, people with CRPS would show a visuospatial attention bias away from their affected side, and that this would be specific to or stronger when stimuli were presented near the affected side versus further away from the affected side, when

body-part stimuli were used versus when neutral stimuli were used, and/or when mental rotation of the affected limb was required versus when no mental rotation was required. In addition, we expected visuospatial attention would be biased away from body-related stimuli when they were presented on one side of space and paired with neutral stimuli in the other side of space. Finally, we hypothesized any observed body-related visuospatial attention bias to be positively related to body representation disturbances and pain intensity. We did see impaired body representation and high levels of pain in people with CRPS. However, in our main analyses, we found no evidence for a body-related visuospatial attention bias away from the affected side in people with CRPS on any of our primary outcome measures. Indeed, although we used tasks adapted from known sensitive measures of visuospatial attention, for the majority of comparisons that we ran as part of our main analyses, our results indicated anecdotal to strong evidence against any visuospatial attention bias – body-related or not. In addition, these results generalize to people with other types of chronic limb pain, as we found evidence against differences between people with and without pain in a limb regarding visuospatial attention bias.

With regard to our secondary comparisons assessing the interaction between any visuospatial attention bias and the location of the body-part stimuli, on the dot-probe task we found moderate evidence that people with lower limb CRPS showed a bias away from their affected side compared to the other groups when a body stimulus was presented at their affected side. Furthermore, with regard to our correlational analyses, in the lower limb CRPS group, people who obtained higher pain scores showed a stronger visuospatial bias away from the affected side as measured with the cancellation task. People in the lower limb CRPS group who obtained higher body perception disturbance scores showed a stronger visuospatial bias away from the affected side as measured with the temporal order judgement task; only for the body conditions in near space. These findings suggest that, even though the evidence was inconsistent across tasks, a body-related visuospatial attention bias might be present in some people with lower limb CRPS, and might be related to pain intensity and/or body perception disturbances. Nevertheless, we found evidence in favour of visuospatial biases on only a small number of our secondary analyses in the lower limb CRPS group, and none at all on our main analyses for either upper or lower limb CRPS. Therefore, we can conclude that on a group level, there is no evidence for a visuospatial attention bias.

These results are consistent with other studies that have reported no evidence for a visuospatial attention bias in CRPS ([Filippopoulos et al., 2015](#); [Halicka et al., 2020a](#)). However, they contradict other previous findings, including where similar tasks were used (i.e., the temporal order judgement task; [Bultitude et al., 2017](#); [Filbrich et al., 2017](#)). Previously, a role of visuospatial attention in CRPS has been suggested by three studies showing symptom relief from a treatment called prism adaptation that is known to alter spatial attention and spatial representations in brain-lesioned patients and healthy controls ([Bultitude & Rafal, 2010](#); [Christophe, Chabanat, et al., 2016](#); [Sumitani, Rossetti, et al., 2007](#)). However, these studies were unblinded and uncontrolled, and the only double-blinded, randomized, clinical trial to test prism adaptation

found no advantage compared to a sham treatment (Halicka et al., 2020b). Mixed findings have also been reported regarding shifts of the visual subjective body-midline of people with CRPS, which has been found in some (Reinersmann et al., 2012; Sumitani et al., 2014; Sumitani, Shibata, et al., 2007; Uematsu et al., 2009), but not all studies (Christophe, Chabanat, et al., 2016; Kolb et al., 2012; Wittayer et al., 2018). The direction of this shift of the subjective body-midline varied between studies in which a bias was seen.

The fact that some studies have found significant visuospatial attention biases, but our and other studies have not convincingly shown this, could be due to high individual variability in CRPS-related visuospatial attention bias. Some suggest there is variation within CRPS, in that only some show a visuospatial attention bias away from their affected side whereas others show no bias at all, or a visuospatial attention bias towards their affected side (Christophe, Delporte, et al., 2016). However, subgroups of visuospatial attention bias could not be disentangled in a previous large study (Halicka et al., 2020a). Similarly, we found no evidence for individuals with CRPS showing a consistent visuospatial attention bias across tasks in the present study (see appendix E). Even so, there are cases of individuals presenting with unusual neuropsychological profiles (including visuospatial deficits; Christophe, Delporte, et al., 2016; Robinson et al., 2011), and our results suggest that visuospatial attention bias is a rare manifestation in CRPS.

A finding that is robust across CRPS studies is the presence of body representation disturbances. We found body representation disturbances in people with CRPS as measured with the Bath CRPS Body Perception Disturbance scale. Previous studies report similar subjective complaints (Galer et al., 1995; Galer & Jensen, 1999; Lewis et al., 2007). Moreover, people with CRPS are slower in perceiving touch on their affected versus unaffected limb, and show a bias in tactile processing and motor performance towards the unaffected side of space (Juottonen et al., 2002; Moseley et al., 2009, 2012; Reid et al., 2016, 2018; although not always replicated, De Paepe et al., 2020; Filbrich et al., 2017). In the current study, we only used tasks that measured visuospatial attention bias. It is yet possible that consistent, significant biases would have been found if we would have used somatosensory or motor tasks, and that these might have been greater under circumstances that recruited body representation to a great extent.

#### 4.1. Strengths and limitations

Our study has some limitations. Although we designed our tasks to involve body representation based on existing cognitive and neurological evidence, we had no way of confirming that body representation was recruited. Related to this, it is possible that the distance at which we presented stimuli in our ‘near’ conditions (at 60 cm), was nonetheless too far away from the affected limb to recruit body representation. Possibly, a visuospatial attention bias is only present for stimuli in the space immediately surrounding the affected limb instead of the space within reaching distance. There is evidence for the existence of, for example, a hand-based reference frame occupying a limited amount of space immediately surrounding the hand, in which multisensory information is integrated differently than outside this space

(Costantini & Haggard, 2007; Tsakiris, 2010). We did not present stimuli on the affected limb itself, as in the line bisection task of Reid et al. (2016), or immediately next to the affected limb, as in the temporal order judgement task of Filbrich et al. (2017). A visuospatial attention bias could have been observed in these tasks because stimuli were presented within the space directly surrounding the affected limb.

Another reason to question whether our procedure recruited body representation concerns the ongoing debate over whether a mental rotation task relies on motor imagery and thereby recruits body representation, as it has been shown in pain-free participants and people with CRPS that alternative strategies (i.e., visual imagery) can be used to perform such tasks (King et al., 2015; Mibu, Kan, Nishigami, Fujino, & Shibata, 2020). Therefore, it is not certain that the mental rotation conditions recruited body representation. In addition, with the exception of the free-viewing task, we did not present bodily postures but instead presented limbs in isolation (i.e., hands, arms, feet, and legs). Bodily expressions appear to have a special status in visual perception similar to the special status of faces, as shown for example in patients who can still process bodily expressions in their cortically blind hemifield, as opposed to other stimuli (de Gelder et al., 2010). There is evidence that people with chronic pain attend differently to painful facial expressions, although with a visuospatial attention bias towards these stimuli rather than away from them (Khatibi, Dehghani, Sharpe, Asmundson, & Pouretmad, 2009; Lee, Kim, Shin, Wachholtz, & Lee, 2018, although not always found, e.g.,; Lee, Beom, Choi, Lee, & Lee, 2019). Therefore, the use of limbs compared to whole body postures might explain the finding that there was no enhanced visuospatial attention bias induced by these body parts compared to neutral images. Finally, we used pictures of healthy limbs, whereas limbs affected by CRPS can look different regarding colour, shape, and size and could have recruited the representation of the affected limb more strongly. It is possible that experiments using such stimuli would indeed elicit visuospatial attention biases in people with CRPS, although the direction of such a bias is uncertain.

There were other potential methodological limitations aside from concerns about whether body representation was recruited for our tasks. The extended duration of the research session (2–3.5 h), means that despite the provision of several breaks, fatigue could have played a role and affected overall performance. However, it is not expected that a visuospatial attention bias would have been caused or overshadowed by fatigue. Furthermore, people always used their dominant hand, which could be at the affected side or unaffected side. Possibly, there was a response bias towards the side of the hand that was used, which was or was not the same side as the affected side. However, as the pain-free control participants used the same hand as the patient whom they were matched with; and the side that was treated as the affected side was also the same side as the affected side in the patient; any response bias towards the hand that was used should have been controlled for in this way. A related issue is that potentially, a visuospatial attention bias relates to whether the hand at the affected side or the hand at the unaffected side was used. Since people in the pain-free control group do not have an affected side, this was not controlled for. We explored

this hypothesis by evaluating how many people with CRPS who showed a visuospatial attention bias at an individual level had used the hand of their affected or unaffected side (appendix E). There was, however, no clear relationship between which hand was used and the presence or direction of a visuospatial attention bias. It should be stressed that this is exploratory, and no firm conclusions can be drawn based upon this. Future research could investigate whether using the hand of the affected versus unaffected side when responding in visuospatial tasks has an effect on performance. Another limitation regards the response modality in the temporal order judgement task: participants either had to indicate which image came first, or which image came second. Ideally, the same participant should perform the task with both response modalities to reduce the effect of any response bias. This would have, however, increased the total testing time too much. Therefore, potential response biases have not been controlled for at an individual level, but only at a group level.

Regardless, we think it is unlikely that our findings are due to these limitations in our tasks. We designed our tasks based on existing measures known to be sensitive to visuospatial attention bias in people with brain injuries and healthy controls. We selected a range of tasks so that we could test different types of visuospatial mechanisms: visual exploration of a scene, visual search, covert attention, and visual exploration of specific stimuli. To further increase the sensitivity to visuospatial attention bias, aside from our manual outcome measures, we measured eye movements, which are closely linked to visuospatial attention and could reveal subtle biases. Nevertheless, none of our eye movement measures (i.e., number of fixations, viewing time, direction of the first fixation, and latency of fixations towards the affected vs unaffected side) revealed any differences between people with CRPS compared to our control groups, nor any differences depending on the extent to which the tasks encouraged the use of body representation. Furthermore, we used Bayesian statistics as this allows to provide evidence in favour of or against the null hypothesis. Indeed, for several comparisons, we found evidence against a visuospatial attention bias. Altogether, we are confident that our results provide evidence against a visuospatial attention bias in CRPS.

## 5. Conclusions

Across four tasks, we found no evidence for a body-related, or general visuospatial attention bias in people with upper limb CRPS compared to people with other types of limb pain and pain-free controls. For the lower limb group, the evidence was less consistent across tasks, and in our secondary analyses we found indications that a body-related visuospatial attention bias might be present in some people with lower limb CRPS, and might be related to pain and/or body perception disturbances. Based on the existing literature and our own results, it is at least likely that there is no general, or body-related visuospatial attention bias away from the affected side in CRPS. Therefore, the previously reported neglect-like symptoms in CRPS most likely reflect disturbances in body representations rather than changes in visuospatial attention.

## CRedit author statement

**Antonia Ten Brink:** Conceptualization, Methodology, Software, Investigation, Formal analysis, Writing – Original Draft, Project administration, Funding acquisition. **Monika Halicka:** Resources, Writing – Review & Editing. **Axel Vittersø:** Resources, Investigation, Writing – Review & Editing. **Edmund Keogh:** Conceptualization, Methodology, Writing – Review & Editing. **Janet Bultitude:** Conceptualization, Methodology, Resources, Writing – Review & Editing, Supervision, Funding acquisition.

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## Declaration of competing interest

The authors declare that they have no conflict of interest.

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## Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.cortex.2020.12.007>.

## Open practices

The study in this article earned Open Materials, Open Data and Preregistered badges for transparent practices. Materials and data for the study are available at [https://osf.io/5dqjk/?view\\_only=d74b8a209fcf427b8e2c8484180829e3](https://osf.io/5dqjk/?view_only=d74b8a209fcf427b8e2c8484180829e3).

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