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Attention upturned: Bias toward and away from the affected side of the body and near space in a case of complex regional pain syndrome

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ABSTRACT

People with Complex Regional Pain Syndrome (CRPS) following limb injury can show neuropsychological symptoms in the absence of observable brain pathologies. These can include sensory changes, distorted body representation, and inattention to their affected limb and its surrounding space, resembling post-stroke hemispatial neglect. The precise nature and mechanisms of these neuropsychological symptoms are unclear, however insights could be gained by testing for dissociations and associations that have been observed in stroke patients. Drawing from clinical and experimental methods for investigating spatial attention bias and related symptoms in stroke patients, we conducted a detailed investigation of neuropsychological symptoms in a woman with CRPS of her left arm who initially presented to us with pronounced inattention to her affected side. The patient showed visual and tactile neglect and extinction on her affected side on confrontation tests, but no attention deficits on "bedside" tests of neglect. On sensitive computer-based measures, attention biases were found in the patient's body and near space (in Temporal Order Judgements), but not far or imagined space (on the Greyscales task and Mental Number Line Bisection). Unique to the current literature, the patient showed a reversal in her Temporal Order Judgement bias across time, from inattention (first and second session) to hyperattention (third session) to her affected side. In contrast, pain and self-reported body representation distortion were similar across the three sessions. The patient had reduced central and peripheral visual acuity, however these deficits were near symmetrical and therefore could not explain her performance on the visual attention tasks. Given that spatial attention bias has been linked to imbalance in relative activation of the two cerebral hemispheres, we administered a Global-Local processing task to test for hemispheric asymmetry. This revealed no difference in global compared to local interference refuting any hemispheric imbalance. Instead, the patient showed impaired performance (compared to controls) on incongruent trials regardless of trial type, consistent with executive impairment. We conclude that spatial attention bias in CRPS can generalize across different sensory modalities and extend beyond the affected limb to the external space around it, independent of any low-level sensory disturbances. This bias is not necessarily directed away from the affected side or stable over time. People with CRPS can also demonstrate more generalized neuropsychological changes in sensory and executive functions. Our observations refute several existing theories about the mechanisms of attention bias in CRPS, and their relationship to pain, and have potential implications for treatment.

1. Introduction

Complex Regional Pain Syndrome (CRPS) is a condition that can arise following trauma to a limb, and is characterized by pain, sensory disturbances, motor abnormalities, and autonomic and trophic symptoms. Sensory disturbances have been observed in people with CRPS

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that suggest changes in the central nervous system, including somatosensory impairments on the entire affected side of the body (Drummond et al., 2018), and heightened sensitivity to sound and light (de Klaver et al., 2007; Drummond and Finch, 2021; Ten Brink et al., 2020, 2021b). People with CRPS can also present with distorted body representation (Lewis and McCabe, 2010; Lewis and Schweinhardt, 2012), and attention bias *away* from their affected limb and its surrounding space, resembling hemispatial neglect ("neglect") following a brain lesion (Legrain et al., 2012; Punt et al., 2013; Torta et al., 2016). Although people with CRPS often report "neglect-like" symptoms regarding the affected limb (Frettlöh et al., 2006; Galer et al., 1995), they usually do not show attention deficits on classic "bedside" tests of neglect (Christophe et al., 2016a; Förderreuther et al., 2004; Kolb et al., 2012; Reid et al., 2016; Reinersmann et al., 2012), although case studies provide rare possible exceptions (Cohen et al., 2013; Robinson et al., 2011). At a group level, subtle attention biases away from the affected side have been reported when more sensitive measures of attention are used (Bultitude et al., 2017; Filbrich et al., 2017; Moseley et al., 2009), but not in all studies (Halicka et al., 2020a; Ten Brink et al., 2021a). In contrast to these attention deficits for the affected limb and its surrounding space, when people with CRPS verbally indicate the visual point of far space that is straight ahead of their body midline (in the dark, i.e. without allocentric reference), their judgements err *towards* their affected side, suggesting an over-representation of that side of far space (Christophe et al., 2016a; Jacquin-Courtois et al., 2017; Sumitani et al., 2007a, 2014; Uematsu et al., 2009). The distorted representations of body and space could be interrelated with pain in CRPS. For example, placing the affected limb in the unaffected side of space reduced pain and increased subjective limb ownership (Moseley et al., 2012). Pain intensity also predicted the magnitude of spatial bias in processing body relevant information in the affected side of space (Reid et al., 2016). It has been proposed that these changes in bodily and spatial representations might contribute to the development and maintenance of CRPS (Bultitude and Rafal, 2010; Marinus et al., 2011; McCabe and Blake, 2008; Sumitani et al., 2007a). Therefore, there is a need to gain a better understanding of the circumstances under which such changes can arise and the extent to which they resemble known conditions such as neglect.

To this end, we conducted a case study of a woman with CRPS who presented with body representation distortion and inattention to her affected left limb in our previous study (Bultitude et al., 2017), here described as the first testing session. Her attention bias was more pronounced than for any other patient tested and, unusually for CRPS, manifested in confrontation testing, reminiscent of post-stroke neglect. This patient's particularly strong attention bias presented an opportunity to test specific predictions about attention bias in CRPS, since any differences between tested conditions would be more apparent. Therefore, we evaluated this patient's spatial attention deficits with respect to different regions of space and sensory modalities over two further testing sessions. Although it was not our objective to demonstrate what is typical of general CRPS population, a case study of a patient with strong signs of neglect could guide further research.

Subsequent to our first observing the patient's attention bias, we developed several hypotheses based on previous observations of CRPS and brain-lesioned patients. Because the patient showed attention deficits on confrontation testing in the first session, we predicted that she would also show biased performance on subsequently administered "bedside" tests of neglect and confrontation tests, in addition to sensitive computer-based measures of attention. Research on stroke patients with hemispatial neglect (often single cases) has established that neglect can manifest in specific regions of space, demonstrating that the processes governing attention to these regions are distinct (Aimola et al., 2012; Committeri et al., 2007; Guariglia and Antonucci, 1992; Halligan and Marshall, 1991; Keller et al., 2005; Vuilleumier et al., 1998). Drawing from this research, we hypothesized that the patient would show inattention to her affected side in different regions of space (body-, near-, and imagined space, but not far space; Bultitude et al., 2017; Filbrich et al., 2017; Moseley et al., 2009; Sumitani et al., 2014). Specifically, due to the particularly corporeal nature of CRPS, we predicted that attention bias would be stronger in body (i.e. personal) space compared to near space, and stronger in near hands working space at table level (i.e. where hands are more often positioned) compared to near space on eye level (Punt et al., 2013; Reid et al., 2016). Considering previous evidence of *over*-representations of the affected side of far space (Christophe et al., 2016a; Jacquin-Courtois et al., 2017; Sumitani et al., 2007a, 2014; Uematsu et al., 2009), we also expected that the attention bias will be absent or reversed in far space compared to near space. Inattention to both visual and tactile stimuli have been reported previously in CRPS, but few studies have assessed both in the same patients (Filbrich et al., 2017). We hypothesized that visual neglect would generalize to touch in this patient, in line with known supramodal mechanisms of spatial attention and post-stroke neglect (Bisiach et al., 2004; Kinsbourne, 1970; Weintraub and Mesulam, 1987).

Aside from spatial attention, we examined several hypotheses about related cognitive functions. Considering that body representation distortion in CRPS can involve misoplegia-like symptoms, such as aversion, disgust, and hostility towards the affected limb and concepts related to that limb (Bartolomeo et al., 2017; Critchley, 1974; Lewis et al., 2007), it is likely that verbal spatial judgements could introduce a response bias in the estimates of any spatial deficits. Thus we expected that the patient would show a response bias in spatial judgements (i.e. reluctance to give the verbal response "left", which refers to her affected side), but that attention bias would be seen even when response bias was accounted for (Filbrich et al., 2016). Importantly for research on spatial attention, we also examined potential hemisensory deficits (Drummond et al., 2018) to rule them out as alternative explanations for the spatial biases. Finally, we considered that the patient's inattention to the left side of space could reflect impaired function or reduced activity of the right hemisphere relative to the left hemisphere (Reuter-Lorenz et al., 1990). Based on this, we hypothesized that she would also present with a local processing bias, often observed in patients with right hemisphere damage (Robertson et al., 1988).

2. Materials and methods

2.1. Design

With a view to understand the mechanisms through which attention can come to be altered in CRPS, we tested the patient's spatial biases in different modalities and regions of her body and space across three sessions spanning three years. The first session (T1) was part of our previously published group study of 24 people with CRPS that provided evidence for a visual attention bias away from the affected side of space (Bultitude et al., 2017). Although results from this session have been reported previously, relevant information from T1 is included in this article so that we can provide a complete overview of the development of the patient's performance over time. The second session (T2; pre-registered at https://osf.io/zx8ad) took place 27 months after T1, and the third session (T3; pre-registered at https://osf.io/n6qgv) was conducted 10 months after T2 to address outstanding questions. The spacings of the research sessions were determined pragmatically, dependent on the timeline of finalizing the design and pre-registrations of T2 and T3, and the patient's availability.

On each occasion, the patient completed self-report questionnaires regarding pain, body representation, fear of movement, and handedness. Across the three sessions, we also tested her attention to different regions of her body and space using three groups of measures: (1) confrontation tests of visual, tactile, and motor neglect and extinction; (2) neuropsychological "bedside" tests of neglect, including the conventional Behavioral Inattention Test battery; and (3) sensitive computer-based measures of attention. The computer-based tasks controlled for potential response biases, and the patient also underwent tests of her sensory functions, including central and peripheral visual field acuity, and tactile detection and discrimination thresholds. Specific tests and the timing of their administration are presented in Table 1. Note that examining any changes in the neuropsychological functions over time was not an *a priori* objective of this study. The consecutive sessions rather aimed to test distinct hypotheses and address the new research questions arising from the preceding assessments. Therefore, not all tests were administered across all three sessions. Groups of control participants also completed questionnaires about body representation and handedness, computer-based measures of attention, and sensory tests. Written informed consent was obtained from all participants and the study was approved by Oxford A Research Ethics Committee (12/SC/0557).

2.2. Participants

2.2.1. Case summary

The patient was a right-handed woman, who at T1 was aged 63 years with CRPS affecting her left arm for eight years. Due to a fall, she suffered multiple fractures and dislocations to her left wrist, arm, and shoulder, requiring surgery and seven weeks of cast immobilization. She reported experiencing "excruciating burning pain" and sensory disturbances in her left arm during postoperative recovery (e.g., feeling and hearing the fingers of her injured hand scratching a pillow, although they were not touching it), as well as tightness of the cast in the weeks that followed. Her description of the period following the injury suggests distorted body representation, that is, her left arm felt bigger, heavier, and misshapen, she had difficulty recognizing her arm, and found mirror visual feedback therapy (McCabe, 2002) very confusing. The patient described the inciting injury as a traumatic experience and presented with aversion to certain words referring to her affected limb (e.g., "left" and "wrist", preferring to use the term "the base of the forearm"). In T1 and T2, we observed that she was reluctant to look at her affected limb, in particular when it was uncovered (the patient kept her left wrist in a bandage, but agreed to remove it for the time of the assessments). She expressed a desire to amputate the left arm, accompanied by feelings of disgust, and at the same time described and exhibited strong guarding and protective behaviors towards that arm. For instance, she reported wearing a makeshift sling and intentionally walking with her left side next to buildings or walls to avoid anyone touching her affected arm. In T2, we also observed that the patient kept her left arm close to her chest while walking. However, in T3, this guarding was no longer apparent and she did not wear a sling. Self-report measures across three sessions indicate that her body representation was severely distorted, relative to that of healthy controls (Table 2). For instance, in T2 she described the mental image of her affected hand as "a grotesque blob that has got not necessarily edges to it (…), does not seem to have a definition like the other hand, it is very big in comparison to the unaffected side", and the rest of her arm as "a stick that connects to the blob, just holding it there, but it has a problem supporting itself (…), it is not connected at the top, it is too high up". The patient provided a similar description in T3, which is illustrated in Fig. 1. Moreover, her pain-related fear of movement across three sessions was stronger than is usually found in chronic pain patients (Roelofs et al., 2004) (Table 2).

In addition to her recounted sensory disturbances in her affected arm, the patient reported double vision and loss of peripheral vision. She reported visiting the optometrist every six months to update her prescription and was using custom-made corrective lenses during each research session. The patient described having problems with balance for several years since her injury, up to and including the research sessions. Until inpatient rehabilitation 6 months prior to T2 she had relied on a crutch to help her walk straight, as she tended to "veer off to the left". At the time of T3, the patient reported that her balance was still impaired and she experienced falls, yet with no need for a crutch. Magnetic Resonance Imaging scans performed two and five years prior to T1 to investigate her problems with vision and balance ruled out any observable lesions or other brain pathologies. Other neurological disorders were also ruled out by a neurologist. Her performance on the Montreal Cognitive Assessment (Nasreddine et al., 2005), Animal Fluency Test (Goodglass and Kaplan, 1983), and a Calculation test in T2 did not indicate any cognitive impairment (Table 2).

The patient reported a history of post-traumatic stress disorder and depression following the inciting injury. No psychiatric evaluation for mood disorders was conducted during the research sessions. However, according to the Profile of Mood States (McNair et al., 1971) and Revised Life Orientation Test (Scheier et al., 1994) completed in T1, the patient's depression and anxiety scores were above, and optimism below, normative values for her age range (Table 2). The patient reported no other neurological or psychological comorbidities.

Pain medications taken at the time of the assessments were tramadol (400 mg/day) at T1; gabapentin (2100 mg/day), tapentadol (300 mg/day), and amitriptyline (75 mg/day) at T2 and T3; and aspirin (75 mg/day) at T2. The patient had stellate ganglion blocks for left shoulder pain approximately once per year (the last one 3 months before T3). She also attended three two-week inpatient multidisciplinary pain management programs for CRPS (twice between T1 and T2, and once between T2 and T3). The pain management programs involved physiotherapy, hydrotherapy, occupational therapy, psychological support, patient-centered goal-setting, education about CRPS, and consultation about pain medication.

The patient's CRPS symptoms were consistent over time and fulfilled

Table 1
Test administration across three sessions.

Measure	T1	T2	T3
Self-report questionnaires			
Brief Pain Inventory, BPI (Cleeland, 1996)	●	●	●
Pain Detect Questionnaire, PDQ (Freynhagen et al., 2006)	●	●	●
Edinburgh Handedness Inventory, EHI (Oldfield, 1971)	●	●	●
Tampa Scale for Kinesiophobia, TSK (Miller et al., 1991)	●	●	●
Profile of Mood States, POMS (McNair et al., 1971)	●		
Revised Life Orientation Test, LOTR (Scheier et al., 1994)	●		
Bath CRPS Body Perception Disturbance Scale, BPDS (Lewis and McCabe, 2010)	●	●	●
General cognitive assessments			
Montreal Cognitive Assessment, MoCA (Nasreddine et al., 2005)		●	
Animal semantic fluency (Goodglass and Kaplan, 1983)		●	
Calculation		●	
Sensory tests			
Mechanical Detection Thresholds, MDT (Rolke et al., 2006)			●
Two-Point Discrimination, TPD			●
Freiburg visual acuity test, FrACT (Bach, 1996)		●	
RareBit Perimetry (Frisén, 2002)			●
Landolt C test			●
Confrontation tests			
Visual neglect/extinction	●	●	●
Tactile neglect/extinction		●	●
Motor neglect/extinction		●	
Neuropsychological "bedside" tests of neglect			
Behavioral Inattention Test battery (Wilson et al., 1987)		●	
Bells cancellation (Gauthier et al., 1989)		●	
Fluff test (Cocchini et al., 2001)		●	
Room description (Zoccolotti and Judica, 1991)		●	
Computer-based measures of attention			
Visual Temporal Order Judgement, TOJ (Bultitude et al., 2017) – Uncrossed Hands	●	●	
Visual TOJ – Crossed Hands	●	●	
Visual TOJ – Board	●	●	●
Visual TOJ – Wall			●
Tactile TOJ – Knees			●
Greyscales task (Nicholls et al., 1999) – Near		●	●
Greyscales task – Far		●	
Mental Number Line Bisection (Sumitani et al., 2014; Zorzi et al., 2002)		●	
Global-Local Processing task (Bultitude et al., 2009; Navon, 1977)		●	●

Note. T1 = Session 1; T2 = Session 2; T3 = Session 3.

Table 2
The patient's scores on self-report questionnaires of pain, body representation, and limb use; tests of cognitive functions; and sensory testing.

Clinical/Sensory/ Cognitive tests	Measure	Patient's score		
		T1	T2	T3
Pain severity	BPI (Cleeland, 1996) – severity (/10)	7.75	8.25	7.00
Pain interference with daily life	BPI – interference (/10)	8.28	7.00	7.86
Neuropathic pain component	PDQ (Freynhagen et al., 2006) (/38)	29[a]	35[a]	27[a]
Recalled handedness before CRPS	EHI (Oldfield, 1971) (−100 to +100)	100	73	-[b]
Current handedness	EHI (−100 to +100)	100	100	100
Pain-related fear of movement and re-injury	TSK (Miller et al., 1991) (/68)	45[a]	42[a]	46[a]
Mood disturbance	POMS (McNair et al., 1971) (/200)	104[a]	–	–
Depression	POMS - Depression (/60)	34[a]	–	–
Anxiety	POMS - Anxiety (/30)	26[a]	–	–
Optimism	LOTR (Scheier et al., 1994) (/24)	6[a]	–	–
Body representation	BPDS (Lewis and McCabe, 2010) (/57)	55[c]	55[c]	52[c]
General cognitive functions	MoCA (Nasreddine et al., 2005) (/30)	–	29	–
Semantic verbal fluency	Animal fluency (Goodglass and Kaplan, 1983)	–	22	–
Arithmetic abilities/ numerical processing	Calculation[d] (/12)	–	12	–
Tactile detection threshold	MDT (Rolke et al., 2006) – hands[e]	–	–	−6.09[c]
	MDT – knees[e]	–	–	0.50
Tactile discrimination threshold	TPD – hands[e]	–	–	−1.17[c]
	TPD – knees[e]	–	–	−0.98

Note. T1 = Session 1; T2 = Session 2; T3 = Session 3; BPI = Brief Pain Inventory; PDQ = Pain Detect Questionnaire; EHI = Edinburgh Handedness Inventory, scored from −100 (extreme left-handedness) to +100 (extreme right-handedness); BPDS = Bath CRPS Body Perception Disturbance Scale; TSK = Tampa Scale for Kinesiophobia (compared to mean scores of chronic lower back pain and fibromyalgia patients; Roelofs et al., 2004); POMS = Profile of Mood States (compared to mean scores of healthy 60–69 years old adults; Gibson, 1997); LOTR = Revised Life Orientation Test (compared to normative values for healthy 61–70 years old females; Glaesmer et al., 2012); MoCA = Montreal Cognitive Assessment; MDT = Mechanical Detection Threshold; TPD = Two--Point Discrimination.

[a] Significantly different to normative cut-off score, indicating pathology.
[b] Not tested.
[c] Significantly different from control participants.
[d] Non-standardized measure with arbitrary cut-off score of <9 correctly resolved mathematic equations indicating arithmetic skills impairment.
[e] Calculated as side ratio: [(left-right)/left], where a negative number indicates higher sensitivity (MDT) or better precision (TPD) on the left (affected) side.

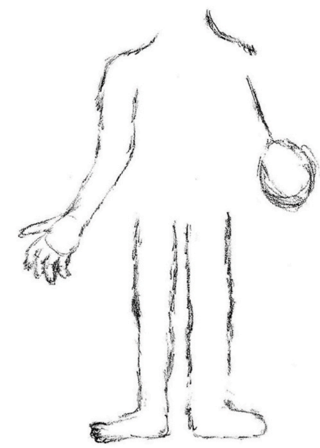

Fig. 1. Self-reported body representation distortion. A sketch of the patient's cognitive representation of her limbs as she described them during a mental imagery task from BPDS in T3.

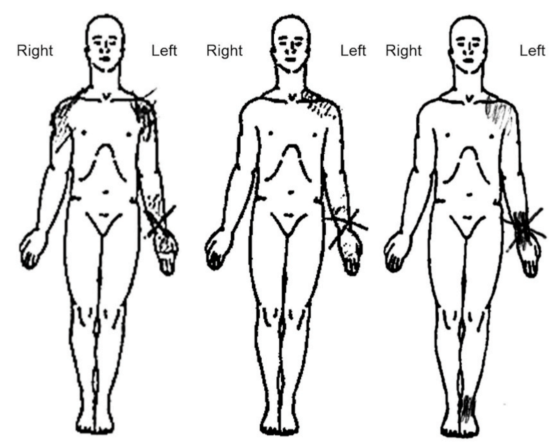

Fig. 2. Areas of pain shaded on the body diagrams. Images were taken from the Brief Pain Inventory in T1, T2, and T3 (from left to right, respectively). A cross represents the region of worst pain.

the Budapest research diagnostic criteria (Harden et al., 2010) in each session of the study. She reported severe, persistent pain (Numerical Rating Scale [NRS] T1 = 8; T2 = 8; T3 = 7/10) in her left wrist that radiated up to the shoulder (Fig. 2). According to the patient's description, the left shoulder also felt heavy, like it was being pulled down. In T2, the patient was not willing to allow the researchers to touch her left wrist and hand due to severe allodynia, however, in T3 she was able to undergo sensory assessments on the affected hand. The only other changes in her physical pain symptoms across the three sessions were that she had pain in her right shoulder in T1 that was not present in T2 or T3, and that she injured her left foot (trip and fall) five months before T3. According to the patient's description, her leg was badly bruised below the knee down to the foot and swollen for several weeks. In T3 the patient reported – in addition to the symptoms in her left arm – discontinuous pain in her left leg (NRS = 5/10 at the time of assessment), tingling in the toes of her left foot, difficulty distinguishing between the toes of her left foot, and altered cognitive representation of that limb (Fig. 1). The patient also described the left ankle turning inwards and that she used the outside part of her foot while walking. She disclosed that her General Practitioner attributed these symptoms to peripheral neuropathy. As the pain in her foot was not continuous, it would not meet the Budapest diagnostic criteria for CRPS.

We tested for hemisensory changes on the patient's upper and lower limbs in T3. We used Von Frey filaments to establish mechanical detection thresholds on the hands and knees according to a standardized protocol from Quantitative Sensory Testing (Rolke et al., 2006). The patient had lower detection threshold, i.e., increased sensitivity to touch on the left hand (0.079 g) than the right one (0.557 g). A staircase assessment of tactile discrimination thresholds on her index fingers and knees was conducted using a Two-Point Discrimination disk (see Supplemental Material). The patient had a lower threshold, i.e., more precise tactile discrimination on the left hand (3.86 mm) than the right one (8.38 mm). Side ratios [(left-right)/left] of the patient's sensory thresholds were significantly different from control participants on the hands, but not on the knees (Table 2), suggesting that hemisensory changes were restricted to the upper (CRPS-affected) limb.

2.2.2. *Control participants*

Healthy, pain-free participants with normal or corrected-to-normal vision and no history of neurological disorders were recruited to provide control data for computer-based and non-standardized measures. The control samples were in T1: 19 females, 5 males, mean age 46.21 years, $SD = 14.96$, 2 left-handed, 22 right-handed (age- and sex-matched to the group of CRPS patients in the original study; Bultitude et al., 2017); in T2: 12 females, mean age 62.42 years, $SD = 3.23$, all right-handed; in T3: 11 females, 1 male, mean age 50.50 years, $SD = 13.09$, all right-handed. The size of control groups for T2 and T3 was determined to statistically compare data from a single case to a control sample using the Revised Standardized Difference Tests (RSDT). According to Crawford and Garthwaite (2005), control samples of $n = 10$ are necessary to limit Type I error rates to 5% or lower. We used samples of $n = 12$ in case any control participants would need to be excluded from individual analyses due to incomplete data. The mean age of control participants was not significantly different from the patient's age across the three sessions ($p = .26$; $p = .46$; $p = .28$, respectively). Despite modest effect of sex differences on visuospatial attention (Jewell and McCourt, 2000), it is unlikely that the inconsiderable number of male participants in the control samples in T1 (5/24) and T3 (1/12) would bias the results of this study.

2.3. Procedures

2.3.1. Confrontation tests

We tested for visual and tactile neglect and extinction using confrontation testing. Unilateral or bilateral finger movements were presented in the patient's peripheral visual field on eye level within arm's reach, and light taps were delivered to the knees while the patient was sitting in a chair and had her eyes open or closed. During eyes open conditions, the patient fixated on the experimenter's nose. Due to the patient's severe allodynia, it was not feasible to perform tactile tests on her hands. In T1 the experimenter presented six left, five right, and six bilateral stimuli. In T2 and T3 the experimenter presented five right, five left, and five bilateral stimuli in a pre-defined pseudorandom order for all tests. The presence of motor neglect and extinction was assessed by asking the patient to lift five times her left arm, right arm, or both arms, with her eyes open or closed (T2). These tests were performed according to the standard procedures for neurological assessment (Bender, 1952; Karnath et al., 1993) by trained psychologists. Any number of unilateral and bilateral omissions in the patient's performance on the confrontation tests was considered abnormal and indicated neglect (failing to report a singly presented unilateral stimulus) and extinction (failing to report one of the two bilateral stimuli). We hypothesized that the patient would omit particularly left-sided stimuli, consistent with inattention to her affected side.

2.3.2. Neuropsychological tests

Classic "bedside" tests of neglect, including the conventional Behavioral Inattention Test battery (Wilson et al., 1987), were administered by trained psychologists. This set of measures comprised tests of visual-motor neglect in near space (e.g., line bisection, bell cancellation; Gauthier et al., 1989), representational and visual-motor neglect in near space (representational drawing; Wilson et al., 1987), visual neglect in near (article reading; Wilson et al., 1987) and far space (room description; Zoccolotti and Judica, 1991), and neglect in body space (fluff test; Cocchini et al., 2001). The results obtained in neuropsychological tests by the patient were compared against available cut-off scores for neglect. Rightward biases and omissions of more left-sided relative to right-sided stimuli would be consistent with the hypothesized inattention to the patient's affected side.

2.3.3. Computer-based measures of attention

The type and purpose of all computer-based measures of spatial attention, mental representation of space, and global and local processing are summarized in Table 3.

Table 3
Summary of the computer-based tasks and conditions with operationalization of measured constructs and time points of assessments.

Condition	Time point	Measured construct	Operationalization
Visual Temporal Order Judgement task (Bultitude et al., 2017)			
Uncrossed Hands	T1, T2	Visual spatial attention to body (personal) space and near space (in hands working space). Body and near space are congruent.	Point of Subjective Simultaneity (amount of time by which stimulus on the left side must precede or follow the stimulus on the right side for the two stimuli to be perceived as simultaneous), averaged across two response conditions ("which side occurred first" and "which side occurred second").
Crossed Hands	T1, T2	Visual spatial attention to body (personal) space and near space (in hands working space). Body and near space are incongruent.	
Board	T1, T2, T3	Visual spatial attention to near space (in hands working space).	
Wall	T3	Visual spatial attention to near space (on eye level).	
Tactile Temporal Order Judgement task			
Knees	T3	Tactile spatial attention to body (personal) space.	
Greyscales task (Nicholls et al., 1999)			
Near	T2, T3	Visual spatial attention in near space (on eye level).	Bias index = (Number of responses where the participant chose the stimulus that is darker on the right side as being darker overall – number of responses where the participant chose the stimulus that is darker on the left side as being darker overall)/Total number of responses.
Far	T2	Visual spatial attention in far space (on eye level).	
Mental Number Line Bisection task (Sumitani et al., 2014; Zorzi et al., 2002)			
	T2	Mental representation of space.	Mean deviation of subjective midpoint of mental number line from the actual midpoint.
Global-Local Processing task (Bultitude et al., 2009; Navon, 1977)			
Global Local	T2, T3 T2, T3	Processing bias towards global/local information; local interference.	Mean reaction times and accuracy rates for congruent and incongruent trials.

2.3.3.1. Temporal order judgment (TOJ).

The TOJ task is a sensitive psychophysical measure of spatial attention (Spence and Parise, 2010). In brief, two identical stimuli are presented, one on each side of the body or external space with different temporal onsets, and participants report their order. We conducted this task in several different conditions across the three sessions, the rationale for which are outlined below.

Visual TOJs in T1 and T2 were conducted in three Presentation conditions (Uncrossed Hands, Crossed Hands, and Board), designed to test if any bias was restricted to the patient's body; extended to near external space; or if it was near space- or body-specific. In the Uncrossed Hands condition, the visual stimuli were presented on the participants' hands (body space), which they placed on the left and right side of their body midline on a table. In that condition, both spatial and body coordinates were available and congruent. In the Crossed Hands condition, the visual stimuli appeared on the participants' hands, which were crossed over their body midline, thus spatial and body coordinates were incongruent (e.g., the left hand was in the right side of space). In the Board condition, the stimuli were presented on the left and right side of a blank board (near/hands working space), thus only spatial coordinates were available. In T3, visual TOJs were conducted in two Presentation conditions to test whether the patient's attention bias is stronger in inferior hands working space (Board), compared to superior near space on eye level (Wall). The Board condition was identical to that described for T2. In the Wall condition, the visual stimuli were projected onto a wall in front of the participants (near space on eye-level). In addition to visual TOJ tasks, we also administered tactile TOJ tasks on the participants' knees in T3 to provide a measure of tactile spatial attention to suprathreshold tactile stimulation in body space that would be more sensitive than the tactile confrontation tests conducted in the same location. We expected tactile stimulation on patient's hands (analogically to the visual Uncrossed Hands condition) to be problematic due to her severe allodynia in T2.

The TOJ tasks in the three sessions followed the same general method of constant stimuli. In the visual TOJ tasks, participants were seated at a table with their head stabilized by a chinrest. Pairs of brief (10 ms), identical red point-light stimuli (3 mm diameter) were projected 9 cm to the left and to the right of the central fixation point on a white background. In the Board condition, the stimuli were projected onto the surface of a 46.5 × 35.5 cm board that lay on the table in landscape orientation such that the fixation point was approximately 28 cm from the torso. In the Uncrossed/Crossed Hands conditions, the participants placed their hands on top of this board such that the lights projected to the same spatial locations but were seen on the dorsal surface of the participants' hands (uncrossed or crossed over the body midline). In the Wall condition (T3), the fixation point and lights were presented at eye level on a white wall at a 50 cm viewing distance. In all visual TOJ tasks, the pairs of lights, one on each side, were presented with different Stimulus Onset Asynchronies (SOAs) in pseudo-random order using custom-built laser pointers that were triggered by Eprime 2.0 software running on Windows 7 operating system (T1 and T2); or via an Arduino platform that was integrated with PsychoPy version 1.85.1 software (Peirce, 2007), running on Windows 10 operating system (T3). In the tactile TOJ tasks, pairs of brief tactile stimuli were delivered as static indentations ("single taps") using miniature electromagnetic solenoid-type stimulators (© Dancer Design) attached to each of participants' knees (center of kneecaps; 1.8 diameter contact surface) with adhesive rings. The stimulators were controlled via Tactamp amplifier (© Dancer Design) integrated with MATLAB R2013b software (MathWorks Inc., Natick, MA, USA), running on Windows 7 operating system. The participants were seated at the table with their head supported by a chinrest, eyes closed, and arms hanging loosely next to the torso such that the arms were straight and the fingers pointed to the floor. During each tactile TOJ block, they listened to white noise via headphones to prevent their decisions from being influenced by auditory information. The SOAs were ±5, 15, 30, 60 and 120 ms in T1; and ±10, 30, 60, 120, and 240 ms for both the visual TOJ tasks in T2 and T3 and the tactile TOJ task in T3. Negative values represent the trials in which the stimulus was presented on the left side first. The SOAs in T2 and T3 were doubled compared to T1 because the patient's responses in the Board condition of T1 suggested that the range of SOAs was insufficient for quantifying her attention bias (see Results section). In each session, each SOA was presented 15 times in pseudorandom order, giving 150 trials per block. Each trial began with a pause that varied in length randomly between 500 ms and 1000 ms. Then the two stimuli were presented with SOAs as detailed above. Participants gave a verbal response to indicate the perceived temporal order of the stimuli. In T1, participants reported "which side occurred first". To separately account for attentional and response biases (Filbrich et al., 2016; Shore et al., 2001), two Response blocks per Presentation condition were added in T2 and T3, that is, participants reported "which side occurred first" in one block, and "which side occurred second" in another block. They had unlimited time to give their response and were instructed to guess if they were unsure. The researcher keyed the responses into the computer, initiating the next trial. Every block (except for the tactile TOJs) was preceded by a training session with six trials using the maximum SOA to ensure that participants understood the instructions and could perceive the stimuli. If necessary, the training session was repeated until 100% accuracy was achieved. Each block of the task lasted approximately 7 min, and their order was counterbalanced across participants in all sessions.

For every "which side occurred first" block, the proportion of "right occurred first" responses to each SOA was fitted with a cumulative Gaussian using the criterion of maximum likelihood to derive the Point of Subjective Simultaneity (PSS). PSS represents the temporal offset between the two stimuli at which "right" and "left" responses would be equally probable (i.e., at which the psychometric function crosses the proportion of .5). Thus, PSS indicates the amount of time by which the stimulation on the left side should precede (negative PSS) or follow (positive PSS) the stimulation on the right side for the two stimuli to be perceived as simultaneous. For every "which side occurred second" block, the proportion of "left occurred second" responses to each SOA was used to calculate the PSS. A negative PSS value indicates inattention to the left side, i.e., relative slowing in noticing the stimulation on the left side, regardless of the Response condition. For the primary analysis, the PSS values for each Presentation condition were averaged across the two Response conditions. Additional analyses of the Just Noticeable Difference index, which provides a measure of temporal acuity, are presented in the Supplemental Material.

Overall, negative PSS values in any Presentation condition would indicate the patient's hypothesized reduced attention to her affected side if their magnitude was greater than in the control groups. Consistent directional deviations and magnitude of the PSS in visual and tactile TOJs would suggest generalized supramodal attention bias. We further expected that the magnitude of the patient's PSS would be greater (more negative) in the Uncrossed Hands compared to the Board condition, indicating stronger attention bias in the body space compared to near external space. If the PSS in the Crossed Hands condition was similar to that in the Uncrossed Hands condition, this would suggest a body-specific bias, whereas if it was similar to that in the Board condition, it would suggest a space-specific bias. The patient's PSS was expected to be greater in the Board compared to the Wall condition, indicating stronger attention bias in the hands working space compared to near space on eye level. We predicted that these differences between the conditions would be greater than between the same conditions in the control participants.

2.3.3.2. Greyscales. We administered a Greyscales task (Nicholls et al., 1999) to measure visual spatial attention in near and far space. Pairs of identical, vertically aligned, short (9.95° × 1.95°) or long (12.00° × 1.95°) horizontal bars with brightness gradients changing gradually from white to black across their horizontal length were presented simultaneously such that one was the mirror-reverse of the other. One bar was darker on its left side, and the other bar, positioned immediately above or below, was darker on its right side. The bars were on constant display until the participants indicated which bar appeared darker overall. In T2 they gave verbal responses ("top bar was darker" or "bottom bar was darker") that were keyed into the computer by the researcher, and in T3 the participants pressed "up" or "down" arrow keys with their right hand. Following the response, an 18° × 8° random dot pixel mask was displayed for 150 ms, and then the next trial began. There were 40 trials per condition, preceded by five demonstration trials. Bias scores were calculated for each participant by subtracting the number of times the participants chose the bar that was darker on the left (the patient's affected) side from the number of times they chose the bar that was darker on the right side, and dividing the difference by the total number of trials. A positive score would indicate a bias for making the darkness judgements based on the right side of the stimuli, consistent with the hypothesized inattention to the left side for the patient (while controls' score should be closer to zero). In T2, the Greyscales task was conducted with the participants standing Near (50 cm) and Far (150 cm) from the wall-mounted screen. The absolute size of the stimuli was scaled according to the distance, allowing to use equivalent stimuli to compare these two regions of space within the same task. Such manipulation would not be possible for the visual TOJ set-up using the available equipment. We predicted that the patient's bias score would be less positive, or reversed, in the Far relative to Near condition, indicating inattention in near, but no bias or hyperattention to the affected side in far space, and that this difference would be greater than among the control participants. In T3, the Greyscales task was repeated in Near space, with the participants seated at the table with their head stabilized by a chinrest. This was to provide comparative testing conditions to the TOJ tasks from within the same session (T3), and to determine whether the patient's performance on the Greyscales task was stable over time. In all conditions the stimuli were displayed at participants' eye-level.

2.3.3.3. Mental Number Line Bisection. To measure mental representation of space, a Mental Number Line Bisection task (Sumitani et al., 2014; Zorzi et al., 2002) was used. This task takes advantage of evidence that people implicitly represent numbers in a linear arrangement, with smaller numbers on the left, and larger numbers on the right side of space (Cutini et al., 2014). The participants had to indicate the midpoint numbers between given number intervals (e.g., the midpoint between 11 and 19 is 15), without making any calculations. Our procedure followed those described in previous papers (Rossetti et al., 2004; Zorzi et al., 2002). There were 40 number pairs separated by different intervals (3, 5, 7, and 9) selected from the 1–49 number range. The same pairs were presented once in ascending, and once in descending order, giving 80 trials in total. The mean deviation of the perceived midpoint from the actual midpoint between pairs of numbers was calculated. Analogously to the classic line bisection task, a positive score would indicate a rightward bias, consistent with hypothesized under-representation of the affected side of imagined space for the patient, whereas controls' scores would be unbiased.

2.3.3.4. Global-Local Processing. To test whether the CRPS patient showed neuropsychological deficits typical of right-hemisphere lesions other than inattention to the left side of space, we administered a Global-Local Processing task (Bultitude et al., 2009; Navon, 1977). Participants were asked to identify the global or local levels of hierarchical stimuli (Navon letters; Navon, 1977) presented in the left and right visual fields. The stimuli in T3 were small letters (0.92° × 1.26°) that formed the shape of the same (Congruent) or a different (Incongruent) larger letter (5.13° × 7.10°). Four types of Navon letters (Navon, 1977) were used in each block (two Congruent: small A's forming a large A; small S's forming a large S; and two Incongruent: small A's forming a large S; and small S's forming a large A). The task was conducted in two Target Level conditions over separate blocks: in the Local condition, the participants identified the local level of the stimuli (small letters); in the Global condition, they identified the global level of the stimuli (large letters). The combination of Target level and Stimulus types constituted four conditions: Global Congruent, Global Incongruent, Local Congruent, and Local Incongruent.

Each trial started with a black fixation cross (0.57° × 0.57°) displayed in the center of a white screen. After 1000 ms one of the hierarchical stimuli was presented with its center located 3.38° to the left (left visual field, LVF) or right (right visual field, RVF) of the fixation cross. The stimulus was presented for 200 ms. If the participants identified the local/global stimulus as A, they pressed the "up" arrow key, and if they identified it as S, they pressed the "down" arrow key. The response keys were aligned with the participant's body midline. Reaction time and accuracy were recorded. Each trial ended with the participant's response without time limit (see Fig. 3). Each of the four types of stimuli (two Congruent and two Incongruent) was presented 16 times in each visual field (LVF, RVF) in pseudorandom order, giving 128 trials per Target Level condition. There were 16 training trails before each Target Level condition, with a requirement to achieve at least 75% accuracy level before proceeding to the task.

The patient had low accuracy in the Local Incongruent condition in T2 (<20%) suggesting that she was not able to perform the task as instructed (see Supplemental Material). We inferred that poor peripheral visual acuity could have diminished the patient's ability to perceive

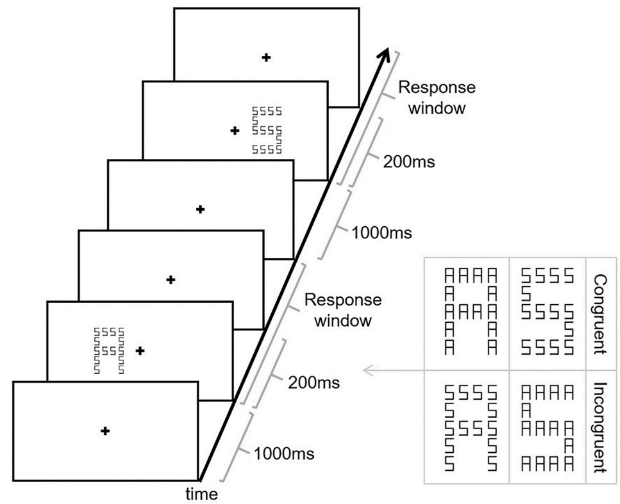

Fig. 3. Global-Local Processing task. The time course of two example trials is presented. The right inset panel illustrates four types of stimuli used.

the local level (small letters) of the hierarchical stimuli. Therefore, in T3 we measured the patient's peripheral vision, adjusted the size of the visual stimuli (see Supplemental Material), and confirmed that the patient was able to discriminate its local features before administering the main Global-Local Processing task. Thus, only the final procedure of the Global-Local Processing task in T3 is presented in the main text, whereas the procedures used in T2 and to determine the size of the stimuli in T3 can be found in the Supplemental Material.

We hypothesized that, compared to controls, the patient would be less accurate and slower in the Global Congruent than the Local Congruent condition (consistent with a local processing bias), in the Global Incongruent than the Global Congruent condition (indicating greater local interference), in the Local Incongruent than the Local Congruent (indicating smaller global interference), and have a local to global interference ratio >1, suggesting stronger local processing bias.

2.3.4. Visual acuity and peripheral vision

We conducted a set of vision tests, prompted by the patient's self-reported problems with visual acuity and loss of peripheral vision, and her difficulty completing the Global-Local task in T2. The Freiburg visual acuity test (FrACT) was administered in T2 to assess participants' central visual acuity, according to the original procedure (Bach, 1996). The participants were required to recognize Sloan letters presented in the center of the screen, in varying size, and at a viewing distance of 50 cm. Participants gave verbal free-choice responses that were keyed into the computer by the researcher. The results were expressed as decimal visual acuity (decVA) and Snellen fraction (normal decVA = 1, equivalent to 20/20 Snellen fraction).

In T3, RareBit Perimetry was used (following the original procedure; Frisén, 2002) to test participants' monocular peripheral vision in each eye in two separate conditions (see Supplemental Material). The results were expressed in percentages as hit rates in each quadrant of the visual field. The upper and lower quadrants of each visual field were averaged for analysis.

Participants' binocular peripheral visual acuity was also tested in T3. With a key press response, they indicated the orientation (left, right, up, or down) of Landolt C optotypes that were presented at 6 different horizontal distances from a central fixation cross from 3° to 23° eccentricity in both visual fields (12 stimuli per location). The accuracy (%) of responses was calculated for each visual field and position relative to central fixation. Detailed description of the stimuli and procedure is included in Supplemental Material.

2.4. Analyses

The patient's performance was compared to either pre-existing normative data or clinical cut-offs where available; or to data sets from the control participants for each session using Crawford t-tests (Crawford and Howell, 1998) or RSDTs (Crawford and Garthwaite, 2005). These methods enable the comparison of single case data with a control sample while controlling for Type I error rate. The Crawford *t*-test provides a point estimate of the deviation of the patient's score relative to the control sample mean, equivalent to the *p* value for the significance test. Crawford t-tests were used to compare the patient's scores to those of the controls on the following measures: Bath CRPS Body Perception Disturbance scale, TOJ tasks, Greyscales tasks, Mental Number Line Bisection task, Global-Local Processing tasks, Freiburg visual acuity test, and Landolt C task. The RSDT compares the differences between patient's scores in two different conditions of a task to the distribution of these differences in the control sample data. The RSDTs were performed for the following measures: TOJ tasks (for comparing results for different Presentation conditions and Response conditions), Greyscales task in T2 (Near vs Far), Global-Local Processing tasks (Global vs Local, Global Congruent vs Global Incongruent, and Local Congruent vs Local Incongruent in each Visual Field; LVF vs RVF for global precedence, local interference, and global interference), and RareBit Perimetry (LVF vs RVF). Following the recommendations for reporting statistical results involving comparisons of a single case to controls (Crawford et al., 2010), the raw scores of the patient, and the means and SDs of the control samples and associated effect sizes are reported. Detailed statistical analysis plans with specified comparisons were pre-registered at https://osf.io/zx8ad (T2) and https://osf.io/n6qgv (T3), and the data underlying the presented results are available at https://osf.io/5dy3y/.

3. Results

3.1. Confrontation tests

The results of the confrontation tests for visual and tactile neglect and extinction are presented in Table 4. In line with our hypothesis, when the patient was presented with unilateral visual stimulation in T2, she omitted (failed to detect) twice as many stimuli on her left (affected) side than on the right, suggesting neglect of the left side. However, she omitted no (left or right) unilateral stimuli in T3. Omissions of some left-sided visual stimuli during bilateral presentation in T2 and T3 are indicative of extinction. In T3, there were also signs of extinction of right-sided visual stimuli. A pattern of neglect and extinction similar to that in visual tests was also found for tactile stimulation in T2, however, there were only signs of tactile extinction on the left side in T3. The patient also reported some referred sensations (unilateral touch was concurrently perceived bilaterally) and allochiria (unilateral stimulation to the left side was only perceived on the right side of the body). There were no other visual or tactile false detections. Contrary to our predictions, the patient showed no signs of motor neglect or motor extinction when they were assessed in T2.

Table 4
Percentage of omissions, referred sensations, and allochiria on the confrontation tests.

Time point	Left extinction	Left neglect	Right extinction	Right neglect	Referred	Allochiria
Visual						
T1	17%	50%	0%	0%	0%	0%
T2	40%	80%	0%	40%	0%	0%
T3	40%	0%	20%	0%	10%	0%
Tactile (knees) eyes closed						
T2	40%	20%	0%	0%	10%	10%
T3	60%	0%	0%	0%	20%	0%
Tactile (knees) eyes open						
T2	80%	20%	0%	0%	10%	10%

Note. T1, = Session 1; T2 = Session 2; T3 = Session 3.

3.2. Neuropsychological tests

As presented in Table 5, no systematic lateralized attention bias was found on standard neuropsychological assessments of neglect in T2.

3.3. Computer-based measures of attention

3.3.1. Temporal Order Judgements

For the Crossed Hands condition of the visual TOJ tasks (T1 and T2), the lack of systematic pattern of the patient's responses across different temporal offsets prevented fitting the cumulative Gaussian to determine the PSS. Thus, the hypotheses regarding the Crossed Hands condition could not be addressed and no results are presented for this. In T1, the patient responded "right" on 95% of trials (to the question "which side occurred first?") in the Uncrossed Hands condition and thus there was insufficient variability in the responses to fit the cumulative Gaussian and determine the PSS. For this condition, the patient's visual attention bias was conservatively estimated using nearest neighbor replacement with the PSS value of the patient with the most extreme fittable data in the same group study (Bultitude et al., 2017). Her pattern of responses suggests marked inattention to the left side of her body, but could also be attributed to response bias, which was not controlled for in T1. The cumulative Gaussian was successfully fitted for all the remaining TOJ tasks administered across the three research sessions, indicating that the patient and control participants were able to complete these tasks as instructed.

The analyses confirmed a significant response bias, that is, differences between Response conditions ("which side occurred first?" and "which side occurred second?") on visual TOJs in hands working space in T2, $t(11) = 2.64$, $p = .011$, $z_{cc} = -2.939$, 95% CI [−4.502, −1.617], and on tactile TOJs in T3, $t(11) = 2.54$, $p = .027$, $z_{cc} = -2.802$, 95% CI [−5.217, −0.841]. The direction of the differences between PSS values from the two Response conditions suggests that the patient was less likely to give "left" responses regardless of the Response condition. No

Table 5
The patient's scores on the subtests the Behavioral Inattention Test battery and other "bedside" tests of neglect administered in T2.

Measure (region tested)	Patient's scores	Cut-off scores
Behavioral Inattention Test battery – conventional (near space)	144	<129
Line crossing	0%	>70% omissions
Letter cancellation	2	>4 omissions
Star cancellation	0.5	<0.46 or >0.54 side-to-side ratio
Figure copying	0	Any major lateral omissions or distortions
Shape copying	0	
Line bisection	5.6% left, 0.2% left, 5.1% right	>14% deviation from the center
Man, clock, and butterfly drawing	0	Any lateral omissions or distortions
Behavioral Inattention Test battery – behavioral: Article reading (near space)	<1%	>42% omitted words
Bells cancellation (near space)	1	Side-to-side difference of 3 omissions
Fluff test (body space)		
Left side	14 (eyes closed); 15 (eyes open)	<13 detached targets
Right side	7 (eyes closed); 9 (eyes open)	<9 detached targets
Room description (far space)		
Left side	2	>2 omitted items
Right side	2	>2 omitted items

significant response bias was found in other TOJ task conditions in T2 and T3. The patient's and controls' mean PSS values in each Response condition, and PSS values averaged across two Response conditions in each Presentation condition, are reported in Supplemental Material (Table S1). The effects of response bias on all attained responses in T2 and T3 were removed through averaging PSS values across two Response conditions. The PSS results are illustrated in Fig. 4.

In T2, we used a larger range of SOAs than in T1 to increase the likelihood of being able to quantify the patient's attention bias, and we controlled for response bias. The results for the Uncrossed hands condition in T2 were broadly consistent with inattention to the left side in T1, and were significantly different to controls' mean score, $t(11) = -2.96$, $p = .006$, $z_{cc} = -3.083$, 95% CI [−4.463, −1.682]. The patient showed significant inattention to the left side of hands working space (Board) in T1 and T2 compared to controls, $t(11) = -2.00$, $p = .038$, $z_{cc} = -2.045$, 95% CI [−3.048, −1.017], but hyperattention to that side in T3, $t(11) = 3.04$, $p = .011$, $z_{cc} = 3.160$, 95% CI [1.730, 4.568], demonstrating a reversal in the direction of the spatial attention bias between T2 and T3. In T3, the patient also showed significant hyperattention to the left side of near space on eye level (Wall), $t(11) = 2.83$, $p = .016$, $z_{cc} = 2.943$, 95% CI [1.594, 4.270], and hyperattention to touch delivered to the knees on the left side of the body, $t(11) = 4.41$, $p = .001$, $z_{cc} = 4.594$, 95% CI [2.613, 6.561]. In summary, the patient's PSS scores were significantly different to control participants in all TOJ conditions across all sessions. We found inattention to the affected side in T1 and T2 and hyperattention to the affected side in T3.

Contrary to our hypotheses, the magnitude of the patient's visual spatial attention bias was not larger in body space (Uncrossed Hands) compared to hands working space (Board) in T2, $t(11) = 0.94$, $p = .188$, $z_{cc} = 1.058$, 95% CI [−0.361, 2.618]. There was also no significant difference in the magnitude of attention bias between hands working space (Board) and near space on eye level (Wall) in T3, $t(11) = 0.17$, $p = .435$, $z_{cc} = 0.186$, 95% CI [−1.363, 1.756]. Thus, within these sessions, the *magnitude* of the attention bias shown by the patient was similar regardless of which modality/spatial domain was tested, although the *direction* of attention bias for T3 was different to T1 and T2.

3.3.2. Greyscales

Counter to our hypotheses, the patient's attention bias scores in the Near condition of the Greyscales task (T2 = −0.30; T3 = −0.45) were not significantly different from the mean (±*SD*) scores of the healthy controls (T2 = −0.23 ± 0.41; T3 = −0.06 ± 0.39), neither in T2, $t(11) = -0.18$, $p = .432$, $z_{cc} = -0.182$, 95% CI [−0.749, 0.393], nor in T3, $t(11) = -0.96$, $p = .360$, $z_{cc} = -0.995$, 95% CI [−1.679, 0.281]. This was also

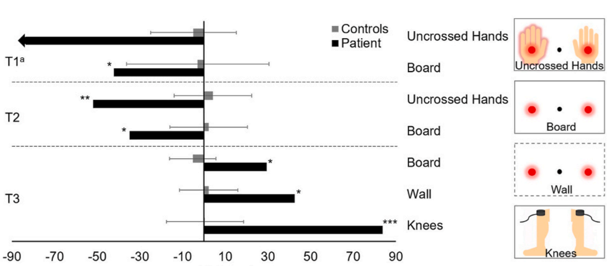

Fig. 4. Temporal Order Judgement task (TOJ) - Point of Subjective Simultaneity (PSS). The patient's and controls' mean PSS values for each Presentation condition (right inset panel) across the three sessions. A negative PSS value indicates inattention to the left (affected) side, and a positive PSS value – hyperattention to the left side. Error bars represent standard deviations of the controls' mean PSSs and are not presented for the patient's single PSS values. An arrow in the Uncrossed Hands condition in T1 represents nearest neighbor replacement and indicates that the bias could be more extreme. *p < .05; **p < .01; ***p < .001. T1 = Session 1; T2 = Session 2; T3 = Session 3. [a]The TOJ tasks in T1 were conducted using a smaller range of stimulus onset asynchronies compared to T2 and T3, and without controlling for response bias.

the case for the Far condition of the Greyscales task (patient T2 = −0.40; controls T2 = −0.25 ± 0.36), $t(11) = -0.39$, $p = .350$, $z_{cc} = -0.41$, 95% CI [−0.993, 0.189]. The difference between bias scores for Near vs Far condition for the patient was not significantly different from that for the controls in T2, $t(11) = 0.26$, $p = .801$, $z_{cc} = 0.291$, 95% CI [−0.302, 0.898].

3.3.3. Mental Number Line Bisection

Contrary to what we predicted, the patient did not demonstrate spatial bias in the bisections of mental number line (bias score = 0.13) compared to healthy controls (mean bias score = 0.10 ± 0.09), $t(11) = 0.31$, $p = .764$, $z_{cc} = 0.321$, 95% CI [−0.268, 0.894].

3.3.4. Global-Local Processing

Since the patient's results from T2 suggest the stimuli were too small for her to be able to perform the task as instructed (see Supplemental Material), only the results from T3 are reported in the main text (see Fig. 5 for accuracy and Fig. 6 for reaction times).

To test whether the patient showed a local processing bias, we first compared her performance in Global Congruent vs Local Congruent conditions to the control sample performance in these conditions. Contrary to our predictions, the patient's reactions times were significantly faster for the Global vs Local levels compared to controls in the LVF, $t(11) = 9.94$, $p < .001$, $z_{cc} = -14.291$, 95% CI [−28.550, −1.198] and the RVF, $t(11) = 20.19$, $p < .001$, $z_{cc} = -43.099$, 95% CI [−68.051, −21.745]. The differences in the patient's accuracy rates for Global vs Local levels compared to controls were not significant in either visual field (*ps* > .05).

Expecting that the patient would show greater interference from irrelevant local level information, we used RSDTs to determine if the difference in performance for Global Congruent vs Global Incongruent conditions was greater for the patient compared to the controls. The patient had larger local interference relative to the controls, both in accuracy rates for the LVF, $t(11) = 13.61$, $p < .001$, $z_{cc} = 14.447$, 95% CI [9.100, 25.624], and the RVF, $t(11) = 7.34$, $p < .001$, $z_{cc} = 9.344$, 95% CI [5.565, 13.961], and reaction times in the LVF, $t(11) = 27.38$, $p < .001$, $z_{cc} = -75.574$, 95% CI [−114.677, −42.652], and the RVF, $t(11) = 17.81$, $p < .001$, $z_{cc} = -34.616$, 95% CI [−56.115, −16.074]. This suggests that, in line with our hypothesis, the patient was significantly less accurate and slower in Global Incongruent than Global Congruent trials relative to controls.

To evaluate whether the patient would show smaller interference from irrelevant global level information (consistent with a local processing bias), we used RSDTs to determine if the difference in performance for Local Congruent vs Local Incongruent conditions was smaller for the patient compared to the controls. Contrary to this prediction, the patient showed greater global interference compared to controls. This is evidenced by significant results of RSDTs for accuracy rates in the LVF, $t(11) = 15.26$, $p < .001$, $z_{cc} = 20.878$, 95% CI [11.741, 32.300], and the RVF, $t(11) = 9.90$, $p < .001$, $z_{cc} = 13.005$, 95% CI [7.329, 20.013], and reaction times in the LVF, $t(11) = 33.19$, $p < .001$, $z_{cc} = -106.477$, 95% CI [−162.723, −59.128], and the RVF, $t(11) = 25.38$, $p < .001$, $z_{cc} = -65.559$, 95% CI [−107.019, −29.188]. That is, the patient was less accurate and slower in Local Incongruent than Local Congruent trials, and these differences were larger than in the control sample.

Finally, we derived the local/global interference ratios from the reaction time data. The patient's ratios were 0.88 (LVF) and 0.86 (RVF), consistent with a global processing bias (greater global than local interference) and contradicting our predictions. However, this was not significantly different to the ratios of the controls (LVF = −1.97; RVF = −0.46). Overall, the patient showed larger local *and* global interference than controls in both visual fields. Statistical comparisons between LVF and RVF are reported in the Supplemental Material.

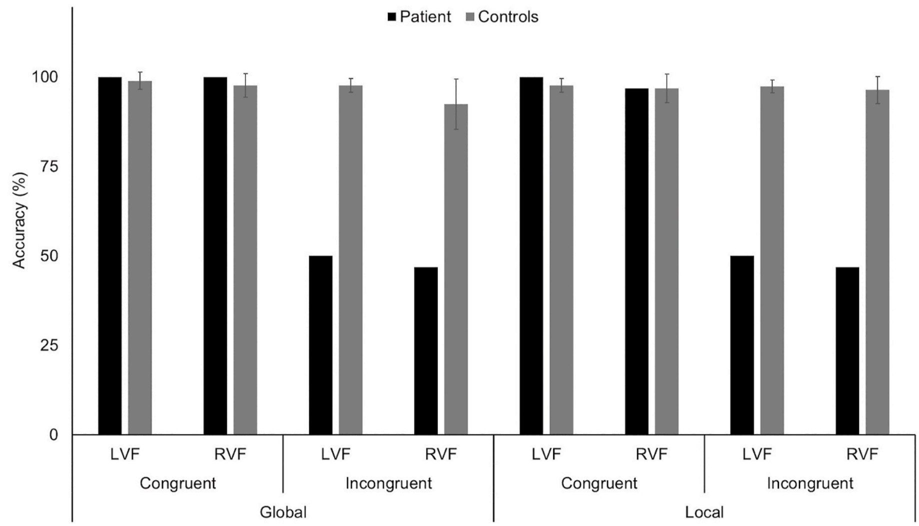

Fig. 5. Global-Local Processing task (T3) – accuracy. The patient's and controls' mean accuracy rates (%) for congruent and incongruent stimuli in left and right visual field (LVF and RVF, respectively) in T3. Error bars represent standard deviations of the controls' means and are not presented for the patient's single accuracy rates.

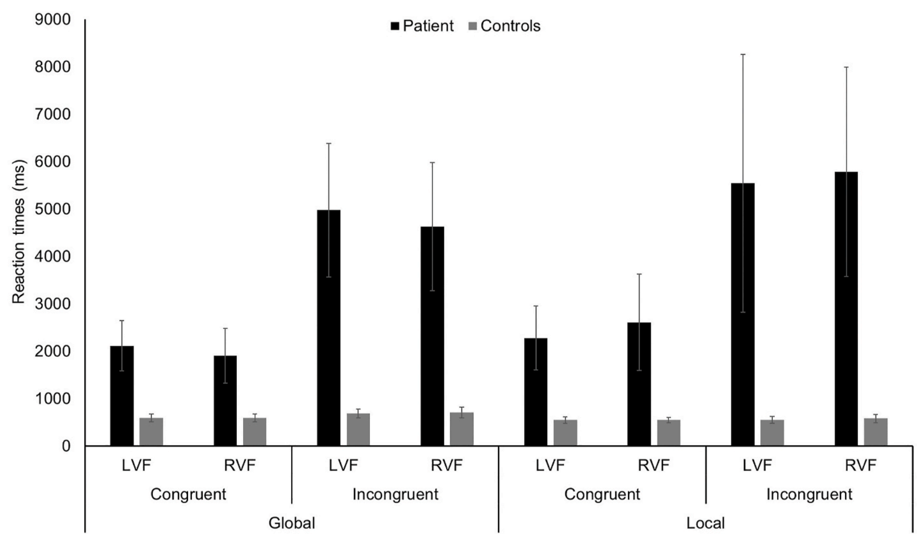

Fig. 6. Global-Local Processing task (T3) – reaction times. The patient's and controls' mean reaction times (ms) for congruent and incongruent stimuli in left and right visual field (LVF and RVF, respectively) in T3. Error bars represent between-subjects standard deviations of the controls' means and within-subject standard deviations for the patient.

Table 6
The patient's results for visual acuity test in T2 and perimetry in T3 compared to healthy controls.

				Significance test			Estimated effect size	
Measure	Time point	Patient's score	Control sample score ($M \pm SD$)	t	df	p	z_{cc}	95% CI
FrACT (decVA; Snellen fraction)[1]	T2	.38; 20/50	.52 ± .03; 20/40	−3.89[a]	11	.003	−4.046	−5.797, −2.279
RareBit Perimetry (hit rate, %)								
Left eye	T3			3.88[b]	8[2]	.005	−4.928	−10.867, 0.360
LVF		46.85	93.72 ± 5.01					
RVF		44.17	95.74 ± 8.29					
Right eye	T3			6.05[b]	8[2]	<.001	−8.473	−16.593, −1.358
LVF		45.00	96.20 ± 4.25					
RVF		42.84	93.28 ± 6.81					

Note. FrACT = Freiburg visual acuity test; LVF = left visual field; RVF = right visual field. [1] Normal decimal visual acuity (decVA) equals 1 (equivalent of 20/20 Snellen fraction), with lower scores indicating impaired visual acuity. [2] Due to results saving error, only 9 out of 12 complete data sets from control participants were obtained for this test. [a] Crawford *t*-test. [b] Revised Standardized Difference Test.

3.4. Visual acuity and peripheral vision

The results of the FrACT and the Rarebit perimetry tests showed that the patient had significantly impaired monocular and binocular visual acuity compared to the control groups (Table 6). Perimetry also showed that in both eyes, the patient had significantly greater asymmetry between her LVF and RVF acuity compared to controls, with better peripheral vision in the left (affected) visual field.

Fig. 7 illustrates the percentage accuracy of the patient's and controls' responses on the test of binocular peripheral vision over different eccentricities, as tested in T3. The patient had worse than normal performance for eccentricities of 12° or greater, and there was little difference between her performance for the LVF and RVF.

4. Discussion

In this case study of a patient with CRPS of the left arm we observed several sensory, attentional, and cognitive changes that provide insights into the potential characteristics and mechanisms of neuropsychological changes in CRPS. The most striking result of our study is that the patient presented with a dramatic change in TOJs from inattention to the affected side in T1 and T2, to hyperattention in T3, despite no change in pain or self-reported body representation distortion. This refutes the proposal that attention bias might be related to these symptoms. We also found that, like many post-stroke neglect patients (Bisiach et al., 2004; Weintraub and Mesulam, 1987), the patient showed both visual and tactile attention biases on confrontation tests and TOJ tasks. However, neurological examination revealed no neglect-like motor bias, indicating that perceptual and motor/intentional biases can be dissociated in CRPS, just as in post-stroke neglect (Bisiach et al., 1990; Buxbaum et al., 2004; Liu et al., 1992). The patient did not show attention bias on classic "bedside" visuospatial tests. This is in contradiction to our prediction that a strong bias would also be apparent on less sensitive tests, but it is consistent with previous studies on CRPS (Christophe et al., 2016a; Förderreuther et al., 2004; Kolb et al., 2012; Reid et al., 2016) and the conclusion that any attention bias shown by people with CRPS is likely to be subtle and only detected using sensitive tasks (Bultitude et al., 2017; Filbrich et al., 2017; Moseley et al., 2009, 2012; Reid et al., 2016). Also contrary to our hypotheses, the TOJ attention biases were not stronger in body space compared to near space, or in near hands working space compared to near space on eye level, refuting the proposal that attention biases are linked to the body or the space it normally occupies (Moseley et al., 2009; Punt et al., 2013; Reid et al., 2016). We found no evidence of attention bias in near, far, or imagined space on two other computer-based measures of spatial cognition (the Greyscales task and Mental Number Line Bisection). However, as predicted the patient showed a significant response bias consistent with a misoplegia-like aversion to verbalizing words associated with her affected side. Finally, rather than observing the hypothesized local processing bias in the Global-Local task that would be consistent with relatively impaired right-hemisphere function (Bultitude et al., 2009; Navon, 1977), the patient had non-lateralized cognitive difficulties in processing incongruent hierarchical visual information.

It is important to rule out alternative explanations for apparent neuropsychological deficits. The patient's TOJ biases cannot be explained by sensory deficits. Although she had impaired central and peripheral visual acuity, her peripheral vision was better in the affected hemifield. Her tactile sensitivity was equal on both lower limbs (where we tested tactile spatial attention), and slightly better in the left side on some measures. Furthermore, attention biases were present even when we controlled for response bias.

The curious shift of TOJ bias from inattention to the affected side in T1 and T2 to hyperattention in T3 was an incidental finding and it should be noted that only one presentation condition (visual stimuli appearing on a blank board in near space) was consistent across all three sessions. The procedural choices for each session were driven by specific hypotheses which did not include directly investigating the stability of spatial attention. While our confidence in this finding is strengthened by the fact that the direction of any biases was consistent *within* each session across different TOJ conditions, this topic should be further addressed by confirmatory studies. Nonetheless, the reported attention shift is a relatively rare neuropsychological finding and has implications for understanding the role of attention bias in CRPS. There are only a handful of cases of brain-lesioned patients showing opposite directions of attention bias (on different assessments: Beschin et al., 2000; Costello and Warrington, 1987; Dove et al., 2007; Van der Stoep et al., 2013; or over time: Kim et al., 1999; Kwon and Heilman, 1991). To the best of our knowledge, the only studies that involved repeated testing of spatial cognition in CRPS patients were those of Christophe et al. (2016a) and Halicka et al. (2021), who did not find any deficits in spatial attention in groups of patients with CRPS at any time point. Where significant spatial attention biases have been observed in CRPS (Bultitude et al., 2017; Filbrich et al., 2017; Moseley et al., 2009, 2012; Reid et al., 2016), none of these studies investigated whether the bias was stable over time.

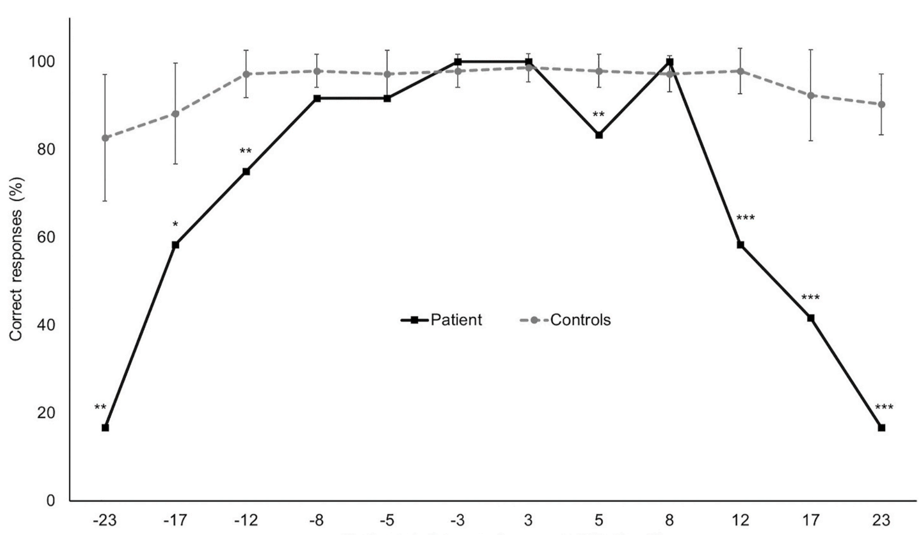

Fig. 7. Landolt C test. The patient's and controls' mean accuracy rates for different positions of Landolt C optotypes. Negative distance indicates positions in the left (affected) visual field. Error bars represent standard deviation of the controls' means. *p < .05; **p < .01; ***p < .001.

Therefore, our findings provide the novel insight that the direction of attention bias in CRPS can be independent of pain and body representation distortion, and it may not be stable over time despite sustained pathology. In conjunction with reports of pain intensity being unrelated to spatial attention bias (Bultitude et al., 2017; Halicka et al., 2020a; Reinersmann et al., 2012), it appears that the emergence of these biases in CRPS does not simply depend on sensory information from the affected limb (or vice versa). While our conclusions regarding stable body representation may be limited by the self-reported nature of the data, as we did not assess this construct experimentally (e.g. using limb laterality recognition or tactile distance judgements; Halicka et al., 2021; Vittersø et al., 2020), there is further emerging evidence that spatial attention is unrelated to body perception in CRPS (Ten Brink et al., 2021a), in contrast to the previously hypothesized presence of such relationship (Reid et al., 2016).

The reversal of attention bias despite unchanged pain and self-reported body representation distortion also has implications for CRPS rehabilitation using prism adaptation. Prism adaptation is a sensory-motor rehabilitation method that is commonly used to normalize spatial attention in post-stroke neglect patients (Rossetti et al., 1998), where adaptation is induced by laterally shifting patients' visual field during pointing to visual targets. Building on the "neglect-like" hypothesis of spatial attention deficits for the affected side in CRPS, three small, uncontrolled, studies reported pain reduction following prism adaptation conducted in such a way as to increase attention to the affected side (Bultitude and Rafal, 2010; Christophe et al., 2016a; Sumitani et al., 2007a). However, we recently reported a double-blind randomized controlled trial involving 49 patients and found no benefit of prism adaptation beyond sham treatment for pain or symptom severity outcomes (Halicka et al., 2021). The current case study provides a possible explanation for the ineffectiveness of prism adaptation, by refuting the connection between inattention to the affected limb and pain. It is possible that its previously reported effects on pain were due to a placebo response.

We propose two speculative explanations of the "reversal" of attention bias observed in our study. First, the patient injured her left leg five months prior to T3, and at that time reported discontinuous pain and other symptoms. Since people with CRPS can be hypervigilant to potential spreading of CRPS symptoms to other limbs (Rijn et al., 2011), the new pain could have led to increased top-down monitoring of sensations and other information on the affected side of the body, and therefore attracted her attention back to the left side. Alternatively, our patient's attention towards the affected side could have been directly driven by increased somatosensory input from the lower limb on that side of the body in a bottom-up fashion (Sumitani et al., 2007b). Christophe et al. (2016b) and Jacquin-Courtois et al. (2017) attributed the hyperattention of their CRPS patient to avoidance of external (hyperalgesia, allodynia) or movement induced painful stimulation (kinesiophobia). Such an interpretation, however, could not explain the hyperattention shown by our patient in T3, since her kinesiophobia was comparable in all three sessions, including T1 and T2 in which she showed inattention to the affected side. Furthermore, the patient was able to tolerate touch to the painful site in T3, but not T1 or T2, indicating that allodynia *decreased* while attention to the affected side increased.

The second possible explanation is that by T3 the patient might have been undergoing adaptive reengagement with the affected limb, thanks to comprehensive pain management programs she attended throughout the entire three-year period of this study. During these programs, patients are encouraged to actively focus on their affected limb, work towards reconditioning normal movement, learn strategies aimed at restoring function, and cope with emotional disturbances. A limitation of this study is that mood could potentially exert effects on attention (Tucker et al., 1999) but no data on the patient's emotional state was collected during T2 and T3. Therefore we cannot evaluate the direct role of depression or anxiety in the change in spatial attention, although it seems unlikely considering comparable spatial biases in people with and without affective disorders (Ribolsi et al., 2015). During the months following the final research session we learned that thanks to her involvement in pain management program, the patient had begun to take part in leisure and sporting activities that involved her affected arm and whole body, despite having experienced no reduction in pain and other CRPS symptoms. Thus, the "reversal" of attention bias that we observed on the TOJ tasks could have been an effect of increasing attention to and functional use of the affected limb. Development of compensatory strategies to endogenously orient attention towards the affected side (Dove et al., 2007) could help to explain why we observed a degree of *right* extinction in T3, which was not present in the previous sessions (although left extinction in T3 was still twice as frequent as right extinction). People who had a stroke can develop ipsilesional neglect over time, which is thought to arise due to compensatory left-sided scanning strategies and non-lateralized attention deficits (Robertson et al., 1994; Williamson et al., 2018). One could speculate that similar compensatory strategies were effective on TOJs in T3, but less so on confrontation tests, potentially due to the chronicity of her inattention or task specificity.

In addition to the reversal of attention bias over time, another novel observation of this study is that of both visual and tactile attention bias in the same patient with CRPS. Previous studies have separately reported attention bias in vision and touch in CRPS (Bultitude et al., 2017; Moseley et al., 2009). There is also evidence that attention bias can dissociate in CRPS, being evident only for visual, but not tactile information (Filbrich et al., 2017). However, this is the first study to report attention bias on confrontation tests and sensitive computer-based measures in both vision and touch in the same person. This suggests that attention bias in CRPS can develop through supramodal mechanisms (Kinsbourne, 1970). The patient also showed attention bias in multiple regions of space, as has been reported in brain-lesioned neglect patients (Kerkhoff, 2001; Pizzamiglio et al., 1989). Specifically, she showed bias in body (hand) space and near hands working space in visual TOJ tasks, and in body (knee) space in the tactile TOJ task. However, the bias was not significantly stronger when the TOJs involved the patient's hands compared to other conditions, nor for hands working space compared to near space on eye level. This refutes existing proposals that spatial cognition deficits in CRPS are strongly linked to the body, either because they are driven by distorted body perception ("somatospatial inattention" hypothesis; Bultitude et al., 2017; Reid et al., 2016), or because they are due to limited amount of action in the affected side of space ("selective disuse" hypothesis; Punt et al., 2013). The patient showed severe distortions in body representation reminiscent of misoplegia, as evidenced by high BPDS scores, her own descriptions of her affected hand (see Fig. 1), aversion to the words "wrist" and "left", preference for keeping her arm out of sight, and a significant response bias in some TOJ tasks. She also reported high pain-related fear of movement. Given these deficits, her generalized TOJ biases suggest that attention bias in CRPS is not driven by body representation or limb disuse. Finally, we found no signs of motor neglect, consistent with the evidence of dissociations between perceptual and motor neglect that been shown in brain lesioned patients (Bisiach et al., 1990; Buxbaum et al., 2004; Liu et al., 1992). It is possible that motor neglect would become evident if a more sensitive test was used (Reid et al., 2018), although other studies using sensitive motor tests found no spatially-defined motor deficits in CRPS on a group level (Christophe et al., 2016a; Halicka et al., 2020). The presence of perceptual bias in the absence of motor bias is further evidence against the proposal that attention bias in CRPS is driven by disuse of the affected limb (Punt et al., 2013). In sum, the performance of the patient in this study indicates that attention bias can develop in CRPS supramodally and affecting multiple regions of space, without necessarily being selective to regions that are more closely linked to the body.

When we formally tested the patient's attention in far space using the Greyscales task, she showed no attention bias. However, she also showed no bias when tested on the same task in near space, despite evidence of attention biases on TOJ tasks in near space. For this reason, we are unwilling to conclude that this patient showed a dissociation between attention to near and far space. Instead, this difference in the results could be because the Greyscales task was performed under free viewing conditions, thus employing overt attention, whereas TOJs of brief stimuli employ covert attention (Wright and Ward, 2008). The same explanation would apply to the discrepancy between normal performance on "bedside" tests of neglect, and evidence of neglect and extinction on confrontation tests. In our study, the attention bias appeared to be present only when the patient had to quickly, covertly attend to visual or tactile information, but not when she had the opportunity to explore the visual display freely over longer periods. Further research to examine attention in far space could use a TOJ task, which was not possible using the available equipment in the current study. In contrast to previous findings in patients with CRPS (Christophe et al., 2016b; Jacquin-Courtois et al., 2017; Sumitani et al., 2014) and post-stroke neglect (Priftis et al., 2006; Rossetti et al., 2004; Zorzi et al., 2002, 2006), we found no evidence of a bias in the mental representation of space assessed using Mental Number Line Bisection. Thus, her bias appears limited to situations that require processing of external sensory information, and not internal representations.

Although hemisensory impairments have been reported in patients with CRPS (Drummond et al., 2018), we are able to rule these out as reasons for the biases that the patient showed in confrontation testing and TOJ tasks. Nonetheless, the visual acuity deficits shown by the patient are themselves potentially relevant for understanding CRPS. Co-morbid eye conditions have been scarcely reported in CRPS, despite their prevalence in clinical anecdotes (Hall et al., 2011). Viewing ambiguous images has been found to exacerbate pain and other CRPS symptoms (Hall et al., 2011), including asymmetric vasomotor response (Cohen et al., 2012), possibly through supraspinal interactions between pain networks and somatomotor and autonomic pathways. Patients report greater visual discomfort from stimuli and situations that normally cause discomfort (Ten Brink et al., 2021b), and this discomfort can be greater on the affected than unaffected side (Drummond and Finch, 2021). These previous and present findings advocate the idea that centrally modulated visual symptoms might be associated with pain and other diagnostic signs of CRPS. In a study of 40 people with CRPS, we recently found impaired visual acuity in 10 individuals, and no impairments in peripheral vision (Ten Brink et al., 2021a). Thus, it appears that visual acuity impairments might only be seen relatively infrequently in CRPS, and might reflect an as-yet uncharacterized subgroup. The etiology of the patient's visual impairment is unknown and it is not possible to differentiate between central and peripheral mechanisms based on the available data; yet the similar patterns in both eyes and visual fields suggest that central mechanisms cannot be ruled out.

Behavioral evidence for changes in spatial attention imply possible functional changes to the posterior parietal cortex (PPC; in particular the supramarginal gyrus at the temporal-parietal junction), which has been implicated as a crucial lesion site for neglect (Halligan et al., 2003). Neuroimaging studies in CRPS predominantly considered primary sensory and motor cortices as regions of interest (Di Pietro et al., 2013a, 2013b, 2013b). However, one magnetoencephalography study showed weaker PPC activation in CRPS patients compared to healthy controls in response to tactile and nociceptive stimulation to the fingers and hand. Functional magnetic resonance imaging studies of people with CRPS (as compared to healthy controls) demonstrated abnormal activation of PPC and supplementary motor cortices related to action observation (Hotta et al., 2017) and impaired reach to grasp movements (Maihofner et al., 2007). Parietal dysfunction in CRPS has also been implied from behavioral research in which patients showed impairments on a test battery of cognitive functions known to be related to parietal lobe function (Joseph, 1990), such as spatial orientation, constructional abilities, object recognition, numerical and language processing, and imitating complex movements (Cohen et al., 2013; Maihofner and Peltz, 2011; Robinson et al., 2011). Our observation of "reversal" of the direction of the attention bias suggests the role of plastic functional changes in parietal attentional networks that are not necessarily lateralized, in contrast to primarily structural deficits in post-stroke neglect. This is further suggested by the absence of a predicted local processing bias, which would have indicated relative impairment of the hemisphere contralateral to the affected limb (i.e., the right hemisphere). Instead, difficulties with processing incongruent information generally in the Global-Local Processing task suggest possible executive dysfunction - also found in other chronic pain conditions (Berryman et al., 2014) - that could reflect more widespread cortical reorganization in the frontal areas.

In sum, the current case study provides evidence refuting several possible explanations for attention bias in CRPS and its relationship to pain. Our observations suggest there is no link between attention bias and pain, that attention bias cannot be explained by self-reported body representation disturbance or limb disuse, and that there is no evidence of broad dysfunction of the cerebral hemisphere contralateral to the affected limb. They further show that attention bias in CRPS can affect multiple sensory modalities and regions of space, indicating involvement of higher-level supramodal mechanisms. In our case study, attention bias appeared limited to covert perception of brief stimuli, with motor intention unaffected. The patient showed no bias when she was able to direct attention overtly and endogenously. Aside from spatial attention deficits, we observed evidence of visual and executive deficits, which support the idea that "neglect-like" framework may be insufficient to fully characterize neuropsychological changes in CRPS (Halicka et al., 2020b), and highlight the importance of assessing broader neuropsychological function. Most striking, this study suggests that spatial attention bias in CRPS is not necessarily stable over time, prompting further longitudinal research on cognitive changes in CRPS and how they might be relevant for treatments. There is insufficient evidence to determine whether changes to spatial attention and body representation are primary or secondary to the clinical signs of CRPS, but the disorder itself likely emerges for more physiological reasons following a physical trauma, such as exaggerated inflammatory response and peripheral and central sensitization; these persistent processes are thought to be associated with brain changes, giving rise to cognitive symptoms (Birklein et al., 2018). It is possible that concomitant functional reorganization in the parietal and frontal areas, also implied by the behavioral findings from the current case study, play a role both in the maintenance of the clinical signs and neuropsychological changes in CRPS.

Credit author statement

Monika Halicka: conceptualization, data curation, formal analysis, investigation, methodology, resources, software, visualization, writing - original draft, writing - review and editing, project administration; Axel D Vittersø: conceptualization, methodology, resources, writing - review and editing; Michael J Proulx: conceptualization, funding acquisition, methodology, supervision, writing - review and editing; Janet H Bultitude: conceptualization, formal analysis, funding acquisition, investigation, methodology, resources, software, supervision, writing - original draft, writing - review and editing, project administration.

Declaration of competing interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at doi: https://doi.org/10.1016/j.neuropsychologia.2021.108079

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