

The rubber hand illusion in complex regional pain syndrome: Preserved ability to integrate a rubber hand indicates intact multisensory integration[☆]

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ABSTRACT

In patients with complex regional pain syndrome (CRPS) type 1, processing of static tactile stimuli is impaired, whereas more complex sensory integration functions appear preserved. This study investigated higher order multisensory integration of body-relevant stimuli using the rubber hand illusion in CRPS patients. Subjective self-reports and skin conductance responses to watching the rubber hand being harmed were compared among CRPS patients (N = 24), patients with upper limb pain of other origin (N = 21, clinical control group), and healthy subjects (N = 24). Additionally, the influence of body representation (body plasticity [Trinity Assessment of Body Plasticity], neglect-like severity symptoms), and clinical signs of illusion strength were investigated. For statistical analysis, 1-way analysis of variance, *t* test, Pearson correlation, with $\alpha = 0.05$ were used. CRPS patients did not differ from healthy subjects and the control group with regard to their illusion strength as assessed by subjective reports or skin conductance response values. Stronger left-sided rubber hand illusions were reported by healthy subjects and left-side-affected CRPS patients. Moreover, for this subgroup, illness duration and illusion strength were negatively correlated. Overall, severity of neglect-like symptoms and clinical signs were not related to illusion strength. However, patients with CRPS of the right hand reported significantly stronger neglect-like symptoms and significantly lower illusion strength of the affected hand than patients with CRPS of the left hand. The weaker illusion of CRPS patients with strong neglect-like symptoms on the affected hand supports the role of top-down processes modulating body ownership. Moreover, the intact ability to perceive illusory ownership confirms the notion that, despite impaired processing of proprioceptive or tactile input, higher order multisensory integration is unaffected in CRPS.

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1. Introduction

In patients with complex regional pain syndrome (CRPS) type 1, there is a well-known relationship between sensory disturbances and cortical reorganization phenomena associated with this syndrome [46,47,53,54]. Several studies linked decreased tactile acuity with the reduced size of cortical hand representation and altered

excitability in the somatosensory cortex of CRPS patients [27,34,46,47]. At the same time, recent findings indicate that despite dysfunctional sensory processing, integration of body-related multisensory perceptions is intact in CRPS [40,51,64]. For example, despite decreased tactile spatial acuity, CRPS patients present intact 2-dimensional form-recognition abilities, provided that the form is above the spatial resolution performance [51]. Moreover, visuotactile integration was shown to be unaffected when CRPS patients underwent tactile training while simultaneously watching their healthy hand [40]. These findings imply that brain regions associated with multisensory integration may be preserved in CRPS. Multisensory integration of body signals underlies coherent body representation, which can be distorted in CRPS patients [15–17,28,29,38,39,45,49,50]. Unfortunately, there are no studies that directly investigate multisensory integration related to body representation in CRPS. However, a better understanding of

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body-related sensory integration could provide information on the precise localization of those somatosensory functions that are impaired and add to the understanding of distorted body representations in CRPS.

A useful paradigm to investigate multisensory integration related to body representation is the rubber hand illusion (RHI) in which covert stroking of a participant's hand, synchronous with overt stroking of a rubber hand, elicits a sense of body ownership (the perception that bodily sensations arise from oneself) is argued to arise in a process in which congruent visuotactile stimulation is integrated in prefrontal and parietocerebellar regions and matched with preexisting mental body representations [1,4,7,10,12,48,60–63]. Various studies have used the RHI to explore the sense of body ownership showing that compared with healthy subjects, patients with fragile body representation (eg, patients with eating disorders) are more susceptible to the illusion [4,10–12,14,25,32,41,48,60,67]. In contrast, amputees with centrally disrupted sensory processing experience a reduced RHI, whereas poststroke patients may even fail to experience it at all [10–12,25,41,48,60,67]. In the current study, the RHI was used for the first time in CRPS patients to explore body ownership and the underlying multisensory integration in CRPS for which (bilateral) cortical reorganization phenomena, sensory disturbances, and distorted body representations are reported [33,34,46,47,53]. The illusion strengths in CRPS patients were compared with healthy subjects and patients with upper limb pain of other origin (clinical control group), for whom cortical reorganization is confined to the unaffected hemisphere and body representation is presumed to be unimpaired [27,55–57]. Additionally, the influence of pain intensity, motor impairment, body plasticity, and neglect-like severity symptoms on illusion strength was investigated [15,16,18,32]. Based on previous RHI findings in patients with centrally disrupted sensory processing, chronic pain, or distorted body representation [11,41,48,67], we hypothesized that CRPS patients with chronic pain, dysfunctional sensory processing, and disrupted body repre-

sentations would experience reduced illusion strengths compared with a clinical control group and healthy subjects.

2. Methods

2.1. Participants

This study included 24 patients (12 women) with CRPS type 1 of the upper extremity (mean age, 53.4 years; range, 34–78 years), 21 patients (12 women) with pain of the upper extremity of other origin (clinical control group) (mean age, 51.8 years; range, 32–71 years), and 24 healthy subjects (mean age, 52.8 years; range, 29–76 years), age and sex matched to CRPS patients. Except for 2 patients in the clinical control group, all participants were right-handed. Details on recruitment of all participants and detailed clinical characteristics of both patient groups were previously reported [50] and can in part be found in Table 1. Note that the experiment conducted in this study was independent of the previously published study [50] and that the testing was performed by a different investigator. The study was approved by the Ethics Committee of the Ruhr-University Bochum, Germany (no. 3412-09, July 2010; Clinical Trials: NCT01618578), and all subjects gave written informed consent before participation. CRPS type 1 was diagnosed based on the recently modified diagnostic research criteria [22] and additionally confirmed by typical enhancement in the late phase of the 99m-technetium triple-phase bone skeleton scintigraphy [66].

2.2. Questionnaires

Before testing, patients rated their average and current pain intensity during the past 7 days on an 11-point numerical rating scale, ranging from 0 (= no pain) to 10 (= worst pain imaginable).

The severity of neglect-like symptoms, indicating body image distortion in CRPS, was assessed in both patient groups using a standardized questionnaire by Frettlöh et al. [15]. This is a German

Table 1
Summary of patient characteristics and frequency of sensory, sudomotor, vasomotor, trophic, and motor signs in CRPS patients and patients with upper limb pain of other origin (clinical control group).

	CRPS type 1			Clinical control group		
	Left affected (n = 12)	Right affected (n = 12)	Total (N = 24)	Left affected (n = 9)	Right affected (n = 12)	Total (N = 21)
Initiating event						
Fracture	6	7	13	6	2	8
After surgery	2	1	3	—	2	2
Other kind of surgery	4	4	8	3	8	11
Illness duration, mo (mean ± SD)	23.6 ± 2.7	14.1 ± 3.4	18.9 ± 8.8 ^a	51.8 ± 0.3	53.5 ± 4.9	52.8 ± 50.1 ^a
Current medications						
NSAIDs	2	3	5	3	3	6
Antidepressants	2	4	6	3	3	6
Anticonvulsants	2	2	4	2	1	3
Opioids	1	2	3	2	4	6
Other	3	7	10	4	1	5
Sensory abnormalities						
Tactile hypesthesia	7	11	18 ^a	6	2	8
Sudomotor dysregulation						
Edema/sweetening	6	6	12 ^a	1	1	2
Vasomotor dysregulation						
Skin changes and/or temperature difference	5	5	10 ^a	0	0	0
Trophic dysregulation						
Impaired hair and/or nail growth	9	8	17 ^a	1	0	1
Motor impairment						
ROM wrist (quotient of affected side to nonaffected side)	0.6 ± 0.3	0.3 ± 0.3	0.5 ± 0.3 ^a	0.8 ± 0.3	0.7 ± 0.3	0.8 ± 0.3
Finger to palm distance, cm (mean ± SD)	4.2 ± 3.1	4.2 ± 4.0	4.2 ± 3.5 ^a	1.6 ± 3.7	0.6 ± 1.3	1.0 ± 2.4

CRPS, complex regional pain syndrome; NSAIDs, nonsteroidal anti-inflammatory drugs; ROM, range of motion.

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