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Motor Dysfunction of Complex Regional Pain Syndrome Is Related to Impaired Central Processing of Proprioceptive Information

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Abstract: Our understanding of proprioceptive deficits in complex regional pain syndrome (CRPS) and its potential contribution to impaired motor function is still limited. To gain more insight into these issues, we evaluated accuracy and precision of joint position sense over a range of flexion-extension angles of the wrist of the affected and unaffected sides in 25 chronic CRPS patients and in 50 healthy controls. The results revealed proprioceptive impairment at both the patients' affected and unaffected sides, characterized predominantly by overestimation of wrist extension angles. Precision of the position estimates was more prominently reduced at the affected side. Importantly, group differences in proprioceptive performance were observed not only for tests at identical percentages of each individual's range of wrist motion but also when controls were tested at wrist angles that corresponded to those of the patient's affected side. More severe motor impairment of the affected side was associated with poorer proprioceptive performance. Based on additional sensory tests, variations in proprioceptive performance over the range of wrist angles, and comparisons between active and passive displacements, the disturbances of proprioceptive performance most likely resulted from altered processing of afferent (and not efferent) information and its subsequent interpretation in the context of a distorted "body schema."

***Perspective:** The present results point at a significant role for impaired central processing of proprioceptive information in the motor dysfunction of CRPS and suggest that therapeutic strategies aimed at identification of proprioceptive impairments and their restoration may promote the recovery of motor function in CRPS patients.*

***Key words:** Complex regional pain syndrome, pain, motor dysfunction, proprioception, body schema.*

Complex regional pain syndrome (CRPS) is characterized by chronic pain, in combination with sensory, autonomic, trophic, and motor abnormalities.[46] Reported motor impairments may include weakness, restricted range of motion (ROM), problems with the initiation and execution of movements, and abnormal posturing.[8,27,30,64,65,73] The pathophysiology of CRPS-related motor impairment, however, is still poorly understood.[14] Several pathophysiological mechanisms have been postulated, ranging from structural and functional alterations in skeletal muscle tissue[34,68,69,72] to maladaptive neuronal plasticity at various levels of the central nervous system.[45,46,67,70] The latter may have profound consequences for motor control, presumably through impaired processing of peripheral afferent input and abnormal integration of sensory signals during motor control.[1]

Adequate motor control requires intact proprioception (ie, the sense of position and movement) to facilitate planning and execution of movement.[32,57] To this end, information from various peripheral and central sources (ie, muscle spindles, joint receptors, skin stretch receptors, and centrally generated motor commands; for a review see[60]) has to be integrated within the context of a mental representation of the limb or "body schema."[42] The relative contribution of the various signals may vary across joints[12] and within their movement range[10] and depend on whether a position

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was achieved by passive displacement or voluntary movement.[13,16,29,43,56]

Given that pain may interfere with the processing of afferent signals contributing to position sense[53,62,63] and that the mental image of the affected limb is often distorted in CRPS patients,[21,22,40,41,51,58] a significant role of proprioceptive impairment in CRPS-related motor dysfunction seems plausible. The clinical observation that some CRPS patients need to closely watch their affected limb in order to control movements[24] may implicate an increased reliance on the visual system to compensate for disturbed proprioception. Unfortunately, little is known about proprioception in CRPS. Only recently, reported difficulties in limb position sense were supported by experimental data showing a reduced accuracy of upper limb positioning in CRPS patients.[41]

The aim of this study was to further our understanding of proprioceptive deficits in CRPS and its potential contribution to impaired motor function. To this end, we assessed accuracy and precision of joint position sense over a range of wrist positions using *passive* as well as *active* displacements. The purpose of including both types of displacement was to gain insight into the extent to which peripheral afferent signals and centrally generated efferent signals contribute to (deficits in) position sense. We also investigated whether proprioceptive performance was related to clinical characteristics and/or the sensory function of the affected limb.

Methods

Part of the experimental setup and a specific aspect of the data collected during this experiment have been described in a previous report,[4] in which we evaluated the electromyographic (EMG) data obtained during active maintenance of various wrist positions in 15 CRPS patients and 15 healthy controls.

Subjects

In the present study, joint position sense was evaluated in 25 patients diagnosed with CRPS type 1 of one or both upper extremities (see Table 1 for patient characteristics). All patients fulfilled the International Association for the Study of Pain criteria for CRPS[50] and had some degree of impaired motor function, evidenced predominantly by limitations in the ROM of fingers and/or wrist, and muscle weakness. In more severely affected patients, the affected body part preferably adopted an abnormal posture, impeding the ability to align the hand dorsum with the forearm. Abnormal postures were mainly characterized by flexion of the fingers and wrist and were typically more pronounced for the fingers than for the wrist (cf.[52,71]). Subjects were excluded if they 1) had a known genetic form of dystonia (eg, DYT1-DYT11 or Wilson disease), mobile dystonia, or lesions or diseases of the central nervous system; 2) had an implanted drug-delivery pump for intrathecal baclofen, or 3) had an active wrist ROM smaller than 30°. Healthy control subjects, who had normal function of both arms and suffered no known diseases of the central nervous system, were matched individually with respect to age (within 5 years) and gender to the CRPS patients in a 2-to-1 ratio (40 women, 10 men; mean ± standard deviation age = 50.1 ± 13.4 years). Informed consent was obtained according to the Declaration of Helsinki. The ethical committee of the Leiden University Medical Center approved the study's protocol before the study was conducted.

Table 1. Patient Characteristics

Variable	*Value*
Number of patients	25
Sex (male/female)	5/20
Age, mean (SD) in years	50.6 (13.7)
Disease duration, mean (SD) in years	9.0 (8.3)
Medication score,[31] median (IQR)	7.8 (1.1–18.7)
$Pain_{week}$, mean (SD)	6.4 (1.8)
Pain Rating Index of the McGill Pain Questionnaire,[49] mean (SD)	28.2 (11.6)
Radboud Skills Questionnaire,[54] mean (SD)	3.1 (.7)

Abbreviations: SD, standard deviation; IQR, interquartile range; $Pain_{week}$, average pain experienced during the week prior to the experiment as scored on a numeric rating scale (NRS, 0–10).

Measurement Instruments

In patients, pain and disability were evaluated using a numeric rating scale (NRS, 0 = no pain, 10 = unbearable pain) for average pain experienced during the week preceding the experiment ($Pain_{week}$), the Pain Rating Index of the McGill Pain Questionnaire (MPQ-PRI; maximum score = 63),[49] and the Radboud Skills Questionnaire (RSQ; range = 0–5).[54] Medication was quantified according to the Medication Quantification Scale Version III.[31] In controls, hand dominance was assessed using a Dutch version of the Edinburgh Handedness Questionnaire.[55]

ROM and proprioception were tested while participants sat comfortably in a chair with their elbows slightly flexed and their feet supported. On 2 stands, positioned on both sides of the chair, vertically oriented manipulanda were mounted that only permitted flexion-extension movements of the wrist in the horizontal plane (Fig 1). One hand (left, right) was measured at a time. The forearm of the tested side was placed in the apparatus in a neutral position (thumbs up and palms facing inward) and its position was restrained by foam-padded supports to prevent movements about the elbow. The distance of the handgrip (diameter 32 mm) on the manipulandum was adjusted such that the handgrip fell in the crease between thumb and index finger and the rotation axis of the wrist was aligned with that of the manipulandum. In *active conditions*, the manipulandum moved with negligible friction as it was mounted on a nearly frictionless potentiometer (FCP40 A, tolerance ±.1%; Sakae Tsushin Kogyo Co, Ltd, Nakahara-ku, Kawasaki City, Japan) to record wrist joint angles during active movement. In *passive conditions*, the manipulandum was connected to a servo-controlled motor that moved the hand passively toward the target positions along a bell-shaped velocity profile with a maximum speed of