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Mechanism-specific rehabilitation management of complex regional pain syndrome: Proposed recommendations from evidence synthesis

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ABSTRACT

Study Design: Narrative review.*Introduction:* There are a variety of treatments with demonstrated effectiveness for the management of complex regional pain syndrome (CRPS). However given the variability in symptom presentation in this population, therapists may be unsure what treatments would be most effective for individual clients.*Purpose of the study:* To present a brief synthesis of the literature and propose a rehabilitation version of a mechanism-specific management algorithm to guide personalized treatment of CRPS.*Methods:* A systematic search of the literature was conducted to identify all randomized controlled trials, systematic reviews, and clinical practice guidelines addressing rehabilitation of CRPS. Results were reviewed independently by 2 reviewers and final selection of articles was reached by consensus. Data was extracted using standardized forms, and a single rater gave quality ratings. Both reviewers then used the extracted data to present a synthesis of the evidence categorized by the proposed mechanisms of effect.*Results:* A total of 111 articles were retrieved and reviewed for inclusion; 49 were selected for data extraction. A synthesis of the key recommendations was compiled into a rehabilitation-specific version of the mechanism-based management algorithm proposed by Gierthmühlen et al (2014).*Conclusions:* Consideration of mechanism-appropriate rehabilitation interventions may assist therapists to select the most appropriate and effective treatments from the body of evidence supporting rehabilitation of CRPS.

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Introduction

Complex regional pain syndrome (CRPS) is the current diagnostic label for a constellation of symptoms characterized by pain, sensory alterations, autonomic and trophic changes, and motor sequelae which may occur after trauma.¹ One of the hallmarks of this syndrome is the variability of presentation between individuals and the variability of signs and symptoms experienced by the individual.^{2,3} This condition was previously known as reflex sympathetic dystrophy, as the underlying mechanism was thought to be dysfunction of the sympathetic nervous system; or causalgia, reflecting the mechanism of altered sympathetic response to nerve

injury.^{4,5} While the exact etiology still eludes us, CRPS is now thought to be the result of multiple mechanisms driving both peripheral and central changes in the nervous system.^{6–8}

Despite the challenges of nomenclature and identification, progress continues in the creation and synthesis of evidence to guide individual management.^{1,9,10} However, despite both physical and psychological rehabilitation holding central places in clinical guidelines and care pathways,^{10–15} many such articles nonetheless focus on medical management and give little detailed guidance for the occupational and physical therapists likely to encounter these clients upon referral to rehabilitation. In the past several years, evidence syntheses (both narrative and systematic reviews) addressing CRPS rehabilitation have been published,^{16–19} but therapists may find these lacking in (1) the specific detail to make a clinical judgment on whether their individual client is likely to benefit from these interventions and (2)

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practical instructions on how to operationalize the treatment and tailor it to the needs of the individual. Indeed, one review openly asked if CRPS rehabilitation was evidence based or merely trial and error.²⁰

We were inspired by the thoughtful review presented by Gierthmühlen et al⁷ which outlined a model for mechanism-informed management of CPRS (see Fig. 1 for an adapted version). Without denoting causation, they proposed 8 key mechanisms for the signs and symptoms of CRPS: (1) inflammatory responses, (2) neurogenic inflammation, (3) increased catecholamine circulation, (4) peripheral sensitization, (5) sympatho-afferent coupling, (6) central sensitization, (7) maladaptive plasticity, and (8) psychological symptoms.⁷ However, only the last 3 domains were illustrated as having the potential to be addressed by multidisciplinary rehabilitation. In contrast, clinical practice recommendations support early rehabilitation intervention to reduce inflammation and sensitization.^{10,13} We hypothesized that a synthesis of the rehabilitation literature linked to mechanism-guided management could help therapists select treatments most likely to be effective for the unique individual client presentation of CRPS signs and symptoms. Thus, the guiding question of this literature review is: what is the extent and level of evidence for rehabilitation interventions linking to the proposed mechanisms of CPRS?

Methods

We conducted a systematic search of the literature using the MEDLINE, Embase, CINAHL, and AMED databases in June 2016 and updated it in September 2017. We limited the search to English text available and only searched the literature from 1996 onward to reflect the current nomenclature for CRPS (see Fig. 2 for list of search terms). After deduplication, 2 reviewers independently reviewed the abstracts for inclusion and conducted hand searches of reference lists, adding references from personal files (see Fig. 3 for flow diagram). Our search included terms for randomized controlled trials, systematic reviews, and clinical practice guidelines in preference for higher levels of evidence; however, we recognized some reviews and guidelines incorporated lower levels of evidence such as cohort and case studies, and we included these lower levels of evidence when they contributed to higher levels of evidence synthesis or appeared in clinical practice

Literature search terms	
1.	{complex regional pain syndrome.mp. AND rehabilitation.mp. OR physical therapy.mp. OR occupational therapy.mp.} limit to humans
2.	{randomized control\$ trial.mp. OR systematic review.mp. OR practice guideline.mp.}
3.	1 AND 2
4.	remove duplicates from 3

Fig. 2. Literature search terms.

guidelines. All selected articles were sorted by levels of evidence and critically reviewed using Critical Appraisal Skills Program checklists (available from <http://www.casp-uk.net/casp-tools-checklists>) to guide study design-specific appraisal and clinical relevance without assigning quality ratings. A single reviewer also completed PEDro ratings^{21,22} to consider risk of bias in rehabilitation trial reporting.

To be included, articles had to present original research describing a rehabilitation intervention for adults with CRPS and had to propose a theoretical mechanism for action or response. Papers were excluded if they were single case studies or did not include rehabilitation as a substantive focus. Papers addressing only persons with CRPS poststroke were also excluded, as the pathophysiological mechanisms involved are likely to be different.^{23,24} In studies of heterogeneous populations of persons with pain, the study was excluded if the sample described did not contain at least 10 persons with CRPS, as it would be too challenging to extract meaningful conclusions. Interventions described were further sorted by the proposed disease mechanism addressed, using the diagram from Gierthmühlen et al⁷ as a template.

Results

Eighty papers were identified for abstract review by the initial search; this increased to 126 after the addition of papers from reference lists and personal files, as well as updating the search during final manuscript preparation. After abstract review, 74 full-text papers were assessed for eligibility (see Fig. 3 for the study flow diagram). Any disagreement between raters was resolved by discussion. This yielded a total of 49 papers to include in the review. Each paper was examined to identify: (1) study type and level of

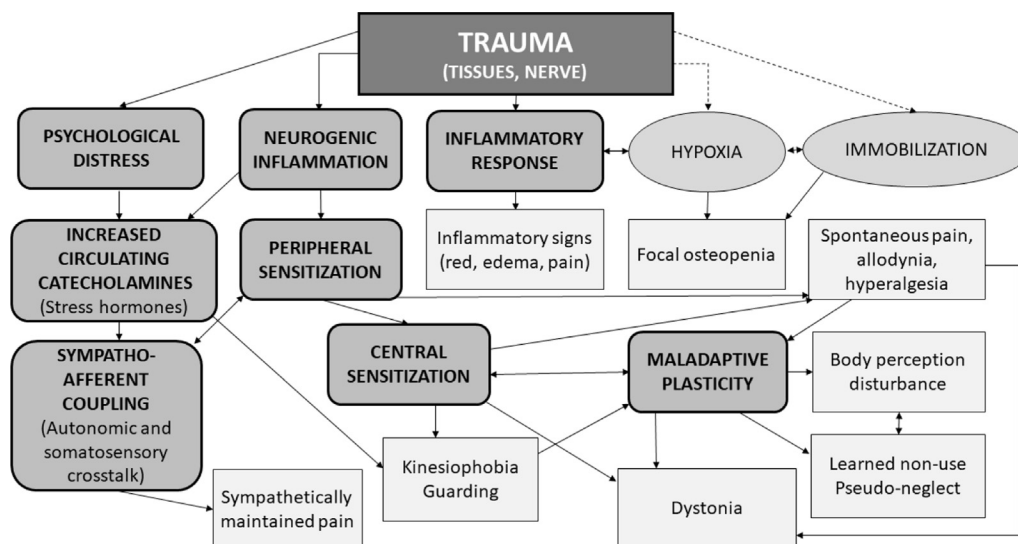


Fig. 1. Proposed mechanisms of CRPS. Primary mechanisms are in bolded capitals; secondary mechanisms are in sentence case type, with arrows denoting proposed relationships. Additional contributing factors are noted in circles. CRPS = complex regional pain syndrome. (adapted from the study by Gierthmühlen et al⁷)

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