

1 General introduction

1.1 Introduction

Studies that describe the disorder presently known as Complex Regional Pain Syndrome type I (CRPSI) have been published since the second half of the nineteenth century¹⁻⁵. Since then, a large number of names have been introduced for this disorder, until it was renamed CRPSI: the name the International Association for the Study of Pain (IASP) agreed upon in 1994^{6,7}. CRPSI is a symptom complex that may have several consequences on everyday life for the person concerned. Such consequences can be classified according to the International Classification of Functioning (ICF, defined by the World Health Organisation) at the three following levels; impaired body function or structure at the level of the body, activity limitations at the level of the person, and participation restrictions at the level of the society⁸⁻¹⁰. As for the consequences of CRPSI on everyday life, CRPSI may comprise a combination of sensory impairments (e.g. neuropathic pain, allodynia, hyperalgesia, hyperaesthesia, anaesthesia), autonomic impairments (e.g. oedema, hyperhydrosis, skin colour change, change of temperature), trophic impairments (e.g. atrophy of skin, nails, muscles and bone), and motor impairments (e.g. dystonia, muscle weakness, spasms, tremor, difficulty initiating movement, and increase of complaints after exercise). In addition to impairments, activity limitations during everyday life (including occupation) and participation problems such as social functioning and role fulfilment have also been described as possible consequences of CRPSI. When CRPSI occurs, it usually follows surgery or trauma and it is generally expressed in the extremities. Its course shows large variability, which makes interpretation of clinical findings and research data difficult.

The controversial syndrome of CRPSI has been increasingly investigated from various perspectives all over the world, and it may be said that health care professionals and researchers become more and more intrigued by this complicated syndrome. This growing interest and curiosity can, for example, be illustrated by the substantial number of theses that has been written about CRPSI during the last ten years in the Netherlands with only one thesis before this period of time, namely in 1972¹¹. In 1995, Veldman¹² provided a comprehensive overview of clinical aspects of CRPSI and analysed some treatment problems from the perspective of general surgery. After that, Kurvers¹³ performed a clinical and experimental study on the effects of partial nerve injury on activity and sensitivity of the sympathetic nervous system from the perspective of neurology. Geertzen¹⁴ studied CRPSI from the perspective of rehabilitation medicine; treatment effectiveness in early CRPSI, the role of social life events and psychological aspects, measurement error for range of motion and muscle strength instruments, and long term outcome of CRPSI in terms of impairments, disability, general health and vocational outcome. Oerlemans'¹⁵ thesis described the development of measurement instruments and the outcome of a randomised controlled clinical study on physiotherapy and occupational therapy. This thesis originated from the department of allied health services. Another thesis from

the perspective of surgery by vanderLaan¹⁶ was a clinical and experimental study on the pathophysiological mechanisms of CRPSI. Moesker¹⁷ studied the relationship between plasma carnitine levels and age, and the effects of treatment with ketanserin (relieving vasoconstriction) and carnitine (correcting metabolic changes) from the viewpoint of anesthesiology. Kemler¹⁸ performed a study on the effectiveness of spinal cord stimulation on the intensity of pain, function, depression, sensory characteristics and health-related quality of life in chronic CRPSI, also from the perspective of surgery. A second thesis originating with rehabilitation medicine was the thesis on pain and motor impairments by Ribbers¹⁹. Ribbers performed clinical studies on pain management, as well as experimental studies on motor impairments and immunology. Once more from the perspective of neurology, vandeBeek²⁰ described clinical, pathophysiological and etiological aspects of CRPSI with a special focus on mechanisms of development of dystonia and dryness of the eyes.

Even though CRPSI has often been investigated, its etiology and pathophysiology are not yet fully understood. Several theories with respect to the pathogenesis of CRPSI have been proposed throughout the years. Currently, the main theories that are still standing are hyperactivity of the sympathetic nervous system accompanied with peripheral and central sensitisation, an exaggerated inflammatory response with the production of toxic free oxygen radicals and accompanying ischemia, although both theories have been topic of discussion and neither has been irrefragably confirmed. This lack of consensus regarding pathogenesis does not affect the research that is described in the present thesis, however. This thesis is written from the perspective of Rehabilitation medicine, which focuses on the consequences that disorders, such as CRPSI, may have on everyday life and functioning as described in the ICF rather than pathophysiological mechanisms. Since extensive overviews of the different definitions of CRPSI, the heterogeneity with respect to diagnostic criteria for CRPSI, the as yet poorly understood pathogenesis of CRPSI plus the large number of treatment modalities for CRPSI have already provided by others in their theses¹²⁻²⁰, and such overviews can also be found in scientific medical literature, it was considered superfluous to repeat these in this introduction.

The aim of this introduction is to explain what another thesis on CRPSI from the perspective of rehabilitation medicine has to add to the understanding of the complicated entity CRPSI. Since the goal of rehabilitation medicine is regaining and/or maintaining of functionality by decreasing the consequences of a disease or disorder, measurement instruments that focus on everyday life are of fundamental importance. Feasible, reliable and valid instruments that objectively measure during everyday life are essential to provide insight into activity limitations of patient groups. For this reason, a research line on ambulatory monitoring of daily functioning was set up at the Institute of Rehabilitation Medicine in the early nineteen-nineties by Henk Stam and Hans Bussmann. Ambulatory monitoring means continuous observation of free-moving subjects in real-life situations and enables non space-bound data

gathering on postures, transitions between postures, and movements of the human body. Due to technological developments in ambulatory accelerometry at that time it was possible to develop and validate the Activity Monitor (AM)²¹⁻²⁶. The AM consists of acceleration sensors attached on thighs and trunk, connected to a small recorder worn around the waist. The AM is aimed at the measurement of quantity, quality and physical strain of exclusively mobility-related activities and could not be used for patient groups with an upper limb disorder. Since CRPSI affects the upper limb(s) in approximately half of the patient population, and because an upper limb problem such as CRPSI is thought to negatively affect performance of activities during everyday life with several possible consequences with that respect, it was decided to extend the technique and possibilities of the AM. Moreover, more commonly used techniques of actometers / actigraphy to measure activity of upper limbs (or other body parts)²⁷⁻³⁴ were, in our opinion, not specific enough to determine limitations of everyday activity in an upper limb CRPSI population sufficiently. Therefore, a novel Upper Limb-Activity Monitor (ULAM) with two additional acceleration sensors on both forearms was developed. Based on our definition of upper limb usage (i.e. active movement of (parts of) the upper limb(s) in relation to proximal parts, holding and leaning), a framework was compiled to classify several forms of upper limb usage and upper limb non-usage. The development and validation of this ULAM and its application in research with subjects with upper limb CRPSI will be described in the present thesis. In this way, the ULAM will add to the understanding of CRPSI because its consequences on everyday activity can now be determined and quantified objectively. Which, in turn, enables objective determination of treatment effect on everyday activity in future studies which is extremely important for CRPSI patients, research and clinic.

1.2 Outline of this thesis

First, in **chapter 2**, a large number of outcome measures that have been used in CRPSI research was classified according to the International Classification of Functioning (ICF), which describes the consequences of a disease. For each outcome measure a description of concept, operationalisation into variables and instrument was given to determine the availability of preferably objective outcome measures that are relevant for rehabilitation medicine. The lack of relevant outcome measures to determine presence or absence of activity limitations in subjects with CRPSI was the rationale for and starting point of the development of the ULAM, which is described in **chapter 3**. In this chapter, the feasibility of the ULAM to discriminate between upper limb usage and non-usage during performance of mobility-related activities in healthy and disabled subjects was investigated with video recordings as a reference method. **Chapter 4** provides a more extensive technical description of the ULAM. In **chapter 5**, the long-term impact of upper limb CRPSI on general mobility and upper limb usage during everyday life was determined. Several ULAM outcome measures were compared between ten female patients with chronic CRPSI and ten control subjects. The primary aim of **chapter 6** was to determine the

relationship between impairments and activity limitations in a group of thirty chronic CRPSI subjects. To measure the degree of impairment, we used a validated set of five items (temperature, pain 2x, active range of motion, volume) that has been previously developed especially for subjects with upper limb CRPSI and described by Oerlemans^{15, 35}. The ULAM outcome measures to determine activity limitations were the mean intensity of upper limb activity of the involved side, the percentage of upper limb activity of the involved side, the proportion of activity between both upper limbs and the percentage of dynamic mobility-related activities. Because the measurement technique of the ULAM clearly differs from what is commonly used in research and clinic with respect to methodological and practical criteria, in **chapter 7**, it is described how several questionnaires that also aim to measure activity limitations (and participation problems) are related to each other and the ULAM. Emphasis was placed on the ULAM because it is important to know its place in the field of outcome assessment. In contrast to the chronic CRPSI patients that were studied in all other chapters, in **chapter 8**, four patients with acute CRPSI are studied, who each wore the ULAM four times for 24 hours. This was done in order to explore upper limb activity over time as measured with the ULAM, and to compare the time course of the ULAM outcome measures to the time course of other outcome measures at the impairment and activity levels. Finally, in the general discussion in **chapter 9**, some of the issues already discussed will be brought together to discuss them from a more general viewpoint and some new issues will be introduced.

1.3 References

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