Development and evaluation of an integrated multidisciplinary rehabilitation program for patients with neuralgic amyotrophy

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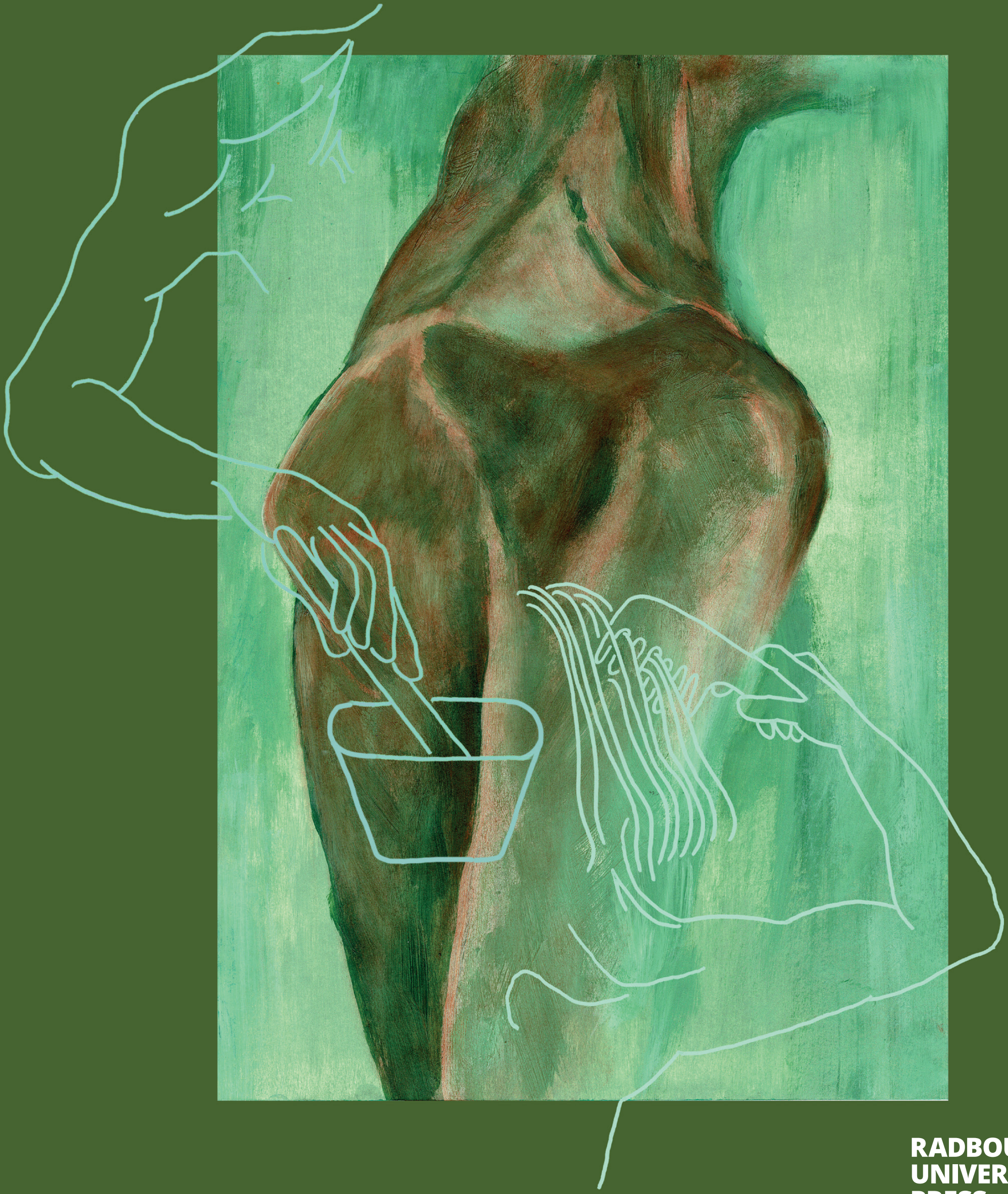

Renske Janssen

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Development and evaluation of an integrated multidisciplinary rehabilitation program for patients with neuralgic amyotrophy

Renske Maria Johanna Janssen

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Development and evaluation of an integrated multidisciplinary rehabilitation program for patients with neuralgic amyotrophy

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Chapter 1

General introduction

Early in the morning, miss B wakes up with a horrific pain in her right shoulder. It is an overwhelming sensation with no possibility to reduce the pain intensity. Regular pain killers do not provide relief and she has no idea how to sit, lie down, or how to place her arm to handle the pain effectively. This situation continues for a period of 4 weeks. When the worst pain decreases, she experiences muscle weakness in her right arm and difficulty reaching, lifting and making repetitive movements with her arm. In addition, she suffers from general fatigue and muscle fatigability during the entire day.It takes several months to get the correct diagnosis. She recalls: "My doctor told me I have neuralgic amyotrophy and need to learn to live with it. He only forgot to tell me how…".

After another 12 weeks, miss B still experiences many difficulties in performing her daily activities. She is not able to do her work as a management assistant and taking care of her three young kids costs a lot of energy as it increases the pain. Her condition is hard to understand for the people around her. They see her as a healthy person, because she does not suffer from visible impairments. They do not see that she has to lie down frequently to cope with the fatigue and pain. She regularly moves from the couch, to the bed, to the chair and back again trying to find a position in which she suffers the least amount of symptoms. She visits a physical therapist, but unfortunately her pain increases after the strength training she performs with her affected right arm. She becomes desperate and does not know what to do with her complaints and impairments and how to regain control over her life again.

The case history above illustrates a common situation for patients[1] with neuralgic amyotrophy (NA). It often takes a considerable time before the correct diagnosis is made. Subsequently, it is regularly unclear for patients how to cope with the complaints of this condition, which is often a combination of chronic pain, fatigue, muscle weakness, and activity limitations. Because the literature on NA does not report effective interventions for this disabling condition, the overall objective of this thesis is to describe the development and evaluation of an outpatient multidisciplinary rehabilitation program, combining occupational and physical therapy, for patients with NA.

Neuralgic amyotrophy

NA is an acute autoimmune inflammation of, most often, the proximal nerves in the brachial plexus distribution. It is a distinct peripheral nervous system disorder characterized by one or more episode(s) of acute severe pain, leading to multifocal

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[1] With the term 'patient' we refer to a person who actually suffers from a specific condition (here: neuralgic amyotrophy). Although we regard our patients as 'clients' from a person-oriented perspective, we chose to use the term 'patient' for consistency throughout this thesis.

paresis and atrophy of the upper extremity muscles [1, 2]. In the acute phase, which may involve the first 3 months after onset [3], the neuropathic pain is predominant and often accompanied by loss of neurological function of the upper extremity and shoulder girdle. After the acute neuropathic pain, there is a chronic phase with partial recovery [2, 3].

Previously, NA was known to be a rare disease with an incidence of 2 to 3 per 100,000 persons per year [4, 5]. However, research from our group has shown that NA is much more common showing an incidence of 1 in 1000 persons per year [6]. NA can be either idiopathic (INA) or hereditary (HNA) [7, 8] with INA being most prevalent. A broad phenotypic spectrum of NA exists [3, 9], whereby the 'classic' presentation with involvement of the nerves in the brachial plexus territory is found in approximately 70% of the patients. Other presentations include involvement of the nerves in the lumbosacral plexus territory [10], phrenic nerve involvement leading to diaphragm dysfunction [11], and a so called 'distal form' leading to paresis and/or sensory dysfunction in the hand [12]. A painless onset occurs in approximately 4% of the cases [3].

What is the impact of NA on daily functioning and participation?

Originally, it was thought that – after 2 to 3 years – 80-90% of the patients fully recovered from an acute episode of NA [13]. However, currently, there are several studies that report substantial long-term residual complaints and activity limitations after NA with a continuous impact on daily life [3, 14-16]. Most common residual complaints are severe pain (> 50%), general fatigue (> 60%), and muscle atrophy and/or residual paresis (about 60%). These symptoms and signs cause activity limitations, increased muscle fatigability, and altered (often compensatory) movement patterns. Impaired humero-scapulo-thoracic coordination and winging of the shoulder blade (scapula alata) are frequently observed [3, 16].

Patients with NA experience many problems when performing daily activities in several domains of their lives, for which they need appropriate support and rehabilitation [16]. There is some evidence for the use of oral corticosteroid and intravenous immunoglobulin in the acute phase of NA; as soon as possible, but at least within 2 weeks [17-19]. No treatment has proven its effectiveness in the chronic phase of the disease [17]. Two studies have reported on the effect of physical therapy in patients with NA. While Tsairis et al. [13] found that physical therapy did not speed up recovery after NA, Cup et al. [16] reported that 'standard physical therapy' even aggravates symptoms in more than 50% of the cases.

Outpatient Plexus Clinic and rehabilitation

Since 2009, the departments of Neurology and Rehabilitation of the Radboud university medical center host an expertise center including an outpatient “Plexus Clinic” for patients with brachial plexus pathology, mainly due to NA. Patients are referred to this Plexus Clinic for diagnostic and treatment advice. A selected group of patients additionally receive an outpatient multidisciplinary rehabilitation program in our center. During their intake visit, patients are asked about their experiences, hopes, goals and needs, and about how they have managed so far. Nearly all patients report that they are limited in performing important daily life activities due to a combination of pain, muscle weakness, increased muscle fatigability and general fatigue. Moreover, patients experience limited to no control over their own complaints and activity limitations. They often state that they continuously feel pain and fatigue during activities, and at rest [15, 16]. Most patients also feel misunderstood by the people around them and often also by medical professionals, not in the last place because NA is often underrecognized and diagnosed quite late [6].

At the Plexus Clinic, patients expect to get a better understanding of their condition, to receive advice for reducing and managing their complaints and activity limitations, and to learn how to regain control over their life again. In order to meet these expectations, we started to develop a multidisciplinary rehabilitation program that we aimed to address two important clinical needs:

1) how to normalize altered, often maladaptive, movement patterns; and
2) how to self-manage and control pain and fatigue in daily life.

Rehabilitation of a disturbed movement pattern

Clinical experience shows that many patients with NA have a winging scapula and/or scapular dyskinesia during abduction and anteflexion movements of the arm. How can these deviating movement patterns be explained? The long thoracic nerve innervates the serratus anterior muscle, which is the most important stabilizer of the scapula, keeping the scapula aligned with the thoracic wall during abduction and anteflexion movements. This nerve is affected in about 70% of the patients with NA [3]. In more than half of the patients, initial weakness of the serratus anterior muscle leads to compensatory, abnormal positioning and movements of the scapula in the post-acute and chronic phase, causing musculoskeletal pain in both the paretic and compensating muscles [16]. Over time, the strength of the serratus anterior muscle often returns, but this does not automatically lead to a reduction of scapular dyskinesia or related pain and activity limitations. Remarkably, in daily practice, we see many patients with good strength of the serratus anterior muscle in the chronic phase who still have residual scapular dyskinesia and related complaints.

As for scapular winging and dyskinesia, a crucial diagnostic finding has been reported by van Eijk et al. [2]. They found that – in patients with NA – functional and well-trained movements such as reaching are often affected, but functionally non-relevant and untrained movements, such as reaching or pushing forward with the elbow, may nevertheless be intact. This finding may explain why no correlation was found between the severity of chronic pain or fatigue and the degree of residual paresis [15]. For this reason, it was assumed that central neural adaptations may contribute to altered peripheral motor control in NA [2]. Recently, our group was the first to investigate this assumption and provided evidence that central neuroplasticity – leading to maladaptive motor patterns – may underlie lack of motor control and cause persistent pain in patients with NA [20, 21]. These results support the notion that rehabilitation should be directed at improvement of scapular coordination and stability rather than strength in order to reduce the dyskinetic movement pattern and reduce residual complaints.

Self-management of pain and fatigue

As many patients are left with residual complaints, NA can be considered a chronic condition. Living with a chronic condition inevitably implies the need for disease management. Lorig and Holman [22] emphasized that even if someone decides not to be active in managing a disease, this decision reflects a management style in itself. They argued that the patient is primarily responsible for his or her day-to-day care over the course of the illness, which is often a lifelong task. Regarding proper self-management, Corbin and Strauss [23] identified three sets of tasks: medical, behavioral and emotional management. According to them, self-management programs need to address all these three tasks. In addition, Lorig and Holman [22] distinguished six core self-management skills: problem solving, decision making, utilizing resources, partnering with healthcare providers, taking action, and improving self-efficacy. It is useful to support these skills during treatment to help patients better self-manage their residual complaints of NA.

Self-management is based on learning principles to achieve behavioral change and sufficient skills. To manage pain and fatigue, there often is a need for behavioral change. It is important for a therapist to understand in what stage of behavioral change a patient is to be able to choose an appropriate treatment strategy and technique. The stages of change theory states that behavioral change involves six stages: precontemplation, contemplation, preparation, action, maintenance and termination [24]. The distribution of persons over the different stages of change within an at-risk population is generally 40% in precontemplation, 40% in contemplation, and 20% in preparation. This indicates the importance of assessing the stage of behavioral change a patient is in and – if necessary – coach the patient into the next stage, in order for self-management interventions to be effective. To this end, motivational interviewing is an important diagnostic and prognostic tool [25].

Another important aspect of self-management and behavioral change is self-efficacy. Self-efficacy reflects the beliefs a person holds about his or her ability to succeed in particular situations [26]. Self-efficacy is a strong predictor of success: persons with strong self-efficacy are much more likely to change and maintain their behavior. Hence, effective self-management interventions support individuals to develop knowledge, skills and confidence (self-efficacy) to internalize all aspects of medical, behavioral and emotional management [27]. A critical review of Augustine et al. [28] showed that the content of most self-management interventions only focuses on medical management, but there are some exceptions. Particularly interventions developed and tested by occupational therapists (also) focus on behavioral and emotional management, such as reported by Ghahari and Packer [29]. Their research evaluated the effectiveness of a self-management program for persons with neurological conditions reporting severe fatigue. This "Managing Fatigue Program", originally developed by Packer [30], formed the basis for the (occupational therapy) intervention for patients with NA studied in this thesis. This Packer Managing Fatigue Program has recently been updated with manuals for individual and group interventions [31, 32]

Development of a multidisciplinary rehabilitation program for patients with NA

After the start of the Plexus Clinic in 2009, the population of patients with NA kept growing, as did our expertise regarding the disease and its optimal treatment. Hence, over the years, we developed our own rehabilitation approach that became more and more disease-specific, which process even continued during the creation of this thesis. In our approach, we developed a treatment model addressing all components of our multidisciplinary rehabilitation program (see figure 1).

The multidisciplinary Plexus Clinic team consists of a neurologist, rehabilitation physician, occupational therapist and physical therapist, collaborating closely together and providing rehabilitation as a team. As presented before, the two main goals of the rehabilitation program are:

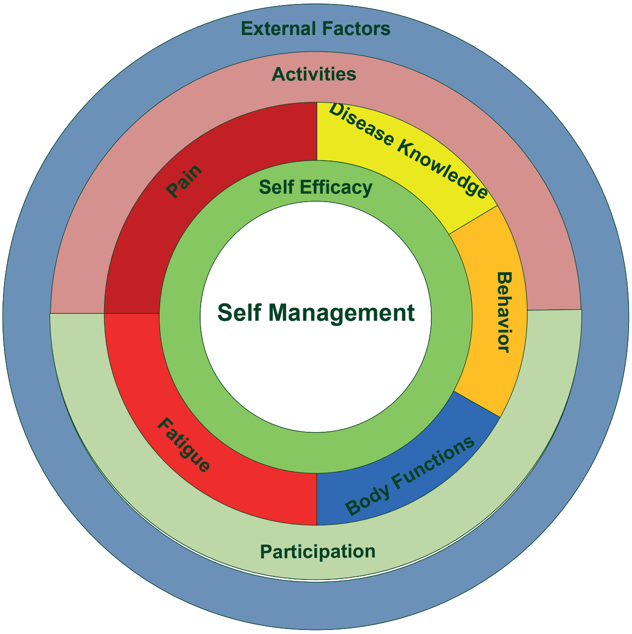

Figure 1: Treatment model which includes the components addressed during the multidisciplinary rehabilitation program for patients with neuralgic amyotrophy [33] – chapter 3.

1) improving upper extremity motor control, scapular stability and coordination, combined with
2) training of self-management strategies to reduce pain and fatigue.

To achieve these goals, all components mentioned in figure 1 are addressed and all team members work (to various degrees) on different components, making the treatment in many ways more interdisciplinary rather than multidisciplinary [34]. Here follows an elaboration on all components.

Optimizing *disease knowledge* is an important aspect of our rehabilitation program. This is addressed by all team members, as education is a prerequisite for our intervention to be successful. Patients need to understand the disease itself and what to expect from (nerve) recovery and the pain and fatigue they experience to be able to deal with their complaints. Education is also important for expectation management. It is essential to be clear in advance what a patient may expect from our rehabilitation program, but also to make clear what we expect from a patient. Furthermore, education increases awareness, which is a prerequisite for behavioral change. Overall, the literature strongly supports the importance of education. For instance, decision making (one of the six core self-management skills) is based on having enough and appropriate information [22], and activated patients have better health outcomes [35].

Overuse (or sometimes underuse) is a common aspect that contributes to the maintenance of *pain and fatigue*. Patients are asked to draw pain and fatigue graphs which gives them and the occupational therapist insight in the pattern of complaints and the possible relation between the complaints and daily activities. This allows the advice regarding the management of pain and fatigue to be tailored to an individual's situation. Finding a balanced distribution between activity and rest is important, which includes three essential aspects: 1) planning and scheduling of daily tasks, 2) implementation of frequent 'mini-breaks' to recuperate and prevent overburdening of muscles, and 3) achieving so called 'effective rest' during (mini)breaks. In addition, attention must be paid to the appropriate ergonomics (i.e. posture and support of the shoulder and arm).

Regarding *body functions*, the focus is on improving the shoulder movement pattern and reducing scapular dyskinesia. Patients recovering from NA usually have a tendency to move less selectively with their affected arm. This results in 'en bloc' movements of the shoulder girdle in a typical fashion (with the shoulder in protraction and elevation). Usually the scapula tends to show combined elevation, downward rotation, anterior tilt and internal rotation, see figure 2 [36]. Retraining scapular stability focuses on making selective movements of the affected arm while the scapula is kept in posterior tilt as much as possible, mainly activating scapular upward rotators and limiting muscle activity in scapular downward rotators. Multiple feedback methods are often needed to help patients alter their motor control. The physical therapist focuses on the precise and specific performance of the correct pattern. Both the physical and occupational therapist promote the implementation of the correct movement pattern into daily practice. The occupational therapist in particular also focuses on the outer two circles of the model in figure 1: analysing and adapting *activities* to enhance the implementation of the correct movement pattern in daily routines and improving *participation* of the patient, with consideration of *external factors,* such as social situation and life circumstances. To this end, the occupational therapist performs activity analyses with regard to shoulder posture and quality of movement to reduce the load of daily activities on the affected and compensating muscles, sometimes using assistive devices. Importantly, physical therapy does not focus on strength training. When dyskinesia is present, strength training would only increase the dyskinetic movement pattern, causing the already overburdened compensating muscles to become even more overloaded.

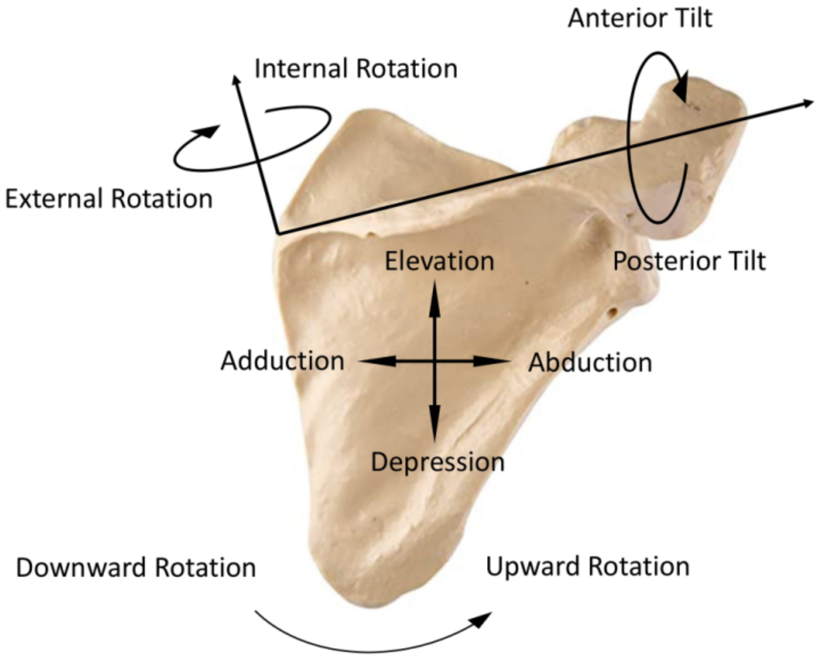

Figure 2: Motions of the scapula are defined as internal-external rotation, upward-downward rotation and anterior-posterior tilting [36].

All components mentioned above require a change in a patient's *behavior*. All members of the Plexus Clinic team support such behavioral change, while the overall goal of treatment is to optimize a patient's *self-efficacy and self-management.* Setting both short-term and long-term goals helps to enhance self-efficacy and self-management. Table 1 elaborates on the disease-specific components addressed during the multidisciplinary rehabilitation program.

We standardized our rehabilitation program to eight therapy sessions after the initial outpatient Plexus Clinic assessment. One session comprises one hour of physical therapy and one hour of occupational therapy. We start with a weekly frequency and end with a monthly frequency, so that patients are enabled to manage themselves over increasingly longer periods of time between treatment sessions.

Table 1: Disease specific components addressed during the multidisciplinary rehabilitation program for patients with neuralgic amyotrophy.

Topic	Approach
Education about NA	• Occurrence of nerve damage and what (not) to expect from nerve recovery • How the brain can adapt or maladapt to peripheral nerve damage • Muscle strength will only recover with nerve regeneration, not through strength training • How residual complaints correlate with the observed scapulothoracic and humeral movements • How to differentiate between different types of pain (tendogenic, myogenic, neurogenic).
Pain education	Use pain neuroscience education to help patients understand pain modulation and adaptation of the nervous system.
Treatment goal setting	Use shared goal setting to manage pre-treatment expectations and align treatment content with patient expectations.
Scapular movement control	• Start supine with manual or visual feedback on posture. • Choose arm movement that the patient can do selectively while stabilizing the scapula in posterior tilt. • In the early treatment phase, local mobilization techniques or local reduction of muscle tone can be used to allow more selective movement. • Progress exercise with increased movement (sitting or standing) and gradually increase range of motion of the arm. • Use mirror feedback, exteroceptive feedback by placing patients with their scapula against a wall, or palpation of the shoulder (coracoid process, or acromioclavicular joint) by the other hand. • Limit feedback when movement control increases. • Make patients responsible for the amount of repetitions and series during exercises. Guidelines: 1. The duration of symptom increase after exercise should not exceed the time of exercise. 2. Scapular posture should be maintained comfortably in a degree of posterior tilt. 3. The arm and hand are able to move selectively.
Ergonomics	Implementing the right ergonomics and posture to achieve 'effective rest' during mini-breaks, by 1. sufficient lumbar support to prevent protraction of the shoulder, 2. shoulder in 'neutral position' with the upper arm parallel to the upper body, 3. support the arm (at the elbow) at the right height. → A mini-break is effective when muscles are 'fully relaxed' so they can recuperate.

Table 1: Continued

Topic	Approach
Scapular movement control - implementation and activity analyses	• Implement exercises as described in "scapular movement control" into daily activities that are important or perceived problematic by a patient. • If needed use feedback as described in the section "scapular movement control". • Observe daily activities with respect to: 1. posture, 2. ergonomics, 3. shoulder position. • Adaptations and use of assistive devices can reduce the burden of an activity on the affected and compensating muscles.
Energy conservation	• Find a balanced distribution between activity and rest • Implement several mini-breaks during the day. • Use diaries to gain insight into the amount and weight of daily activities: 1. weight of activities, specific for the shoulder, 2. number of mini-breaks, 3. content of mini-breaks (is it effective resting?). • Communicate with family members, friends and colleagues about the consequences of NA and how to manage the complaints. • Evaluate norms, values, priorities and the need to do certain activities.

Aims and outline of this thesis

The aim of this thesis is to develop and evaluate a multidisciplinary rehabilitation program for patients with NA. The UK Medical Research Council (MRC) framework for the development and evaluation of complex interventions was used as a reference [37], see figure 3. According to the UK-MRC, an intervention is called complex, if there are several interacting components, if the intervention is dependent on the behaviors of those delivering and receiving the intervention, if there is a range of possible outcomes, and/or if there is a need to tailor the intervention to different contexts and settings [38]. Hence, our intervention can be considered a 'complex intervention', since all aspects mentioned by the UK-MRC framework are included.

The outline of this thesis reflects most of the phases as identified in the UK-MRC framework [37]. Within this thesis, the developmental, feasibility and evaluation phase are investigated. Core elements are revisited throughout the entire research process, see figure 3.

In this introduction **(chapter 1)**, the *development phase* of our intervention is addressed. **Chapter 2** describes a literature review providing an up-to-date overview of NA disease characteristics (clinical phenotype, pathophysiology, genetics, epidemiology, nerve imaging) and interventions in the acute and post-acute phases.

Chapters 3, 4 and 5 represent the *feasibility phase* of the MRC-framework. In **chapter 3**, we present the results of a pilot study that evaluated the effectiveness of a combined physical and occupational therapy intervention in patients with NA. Because we valued the perspectives of patients and therapists, the qualitative study described in **chapter 4** reports their views on the critical ingredients of the program. In **chapter 5** we report the results of a reliability and validity study investigating the usability of patient-generated graphs as outcome measures for pain and fatigue.

Chapter 6 reports a Randomized Controlled Trial (RCT), the NA-CONTROL trial, to investigate the effectiveness of a multidisciplinary rehabilitation program compared to usual care. This chapter represents the *evaluation phase* of the MRC-framework.

In **chapter 7,** we summarize and critically discuss all previous steps and chapters and provide recommendations for further *implementation* of our multidisciplinary rehabilitation program.

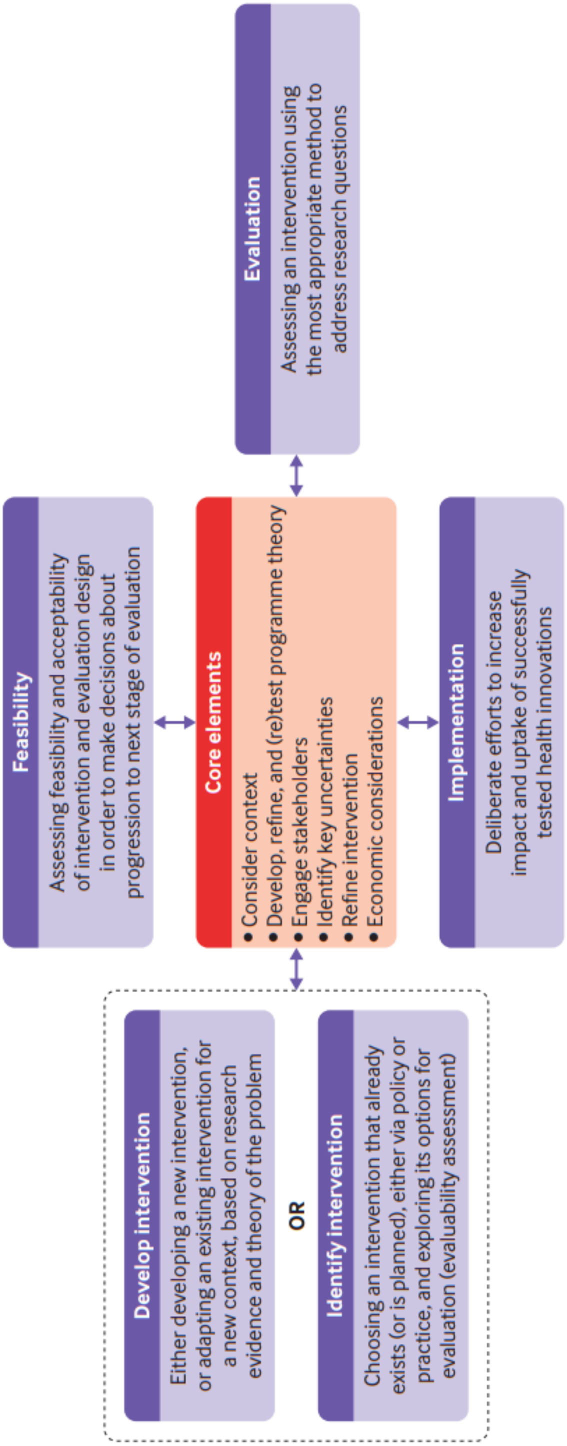

Figure 3: Medical Research Council (MRC) framework for the development and evaluation of complex interventions [37].

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Chapter 2

Neuralgic amyotrophy

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Abstract

Purpose of the review

This review focuses on the current insights and developments in neuralgic amyotrophy (NA), an auto- immune multifocal peripheral nervous system disorder that leaves many patients permanently impaired if not recognized and treated properly.

Recent findings

NA is not as rare as previously thought. The phenotype is broad, and recent nerve imaging developments suggest that NA is the most common cause of acute anterior or posterior interosseous nerve palsy. Phrenic nerve involvement occurs in 8% of all NA patients, often with debilitating consequences. Acute phase treatment of NA with steroids or i.v. immunoglobulin may benefit patients. Long term consequences are the rule, and persisting symptoms are mainly caused by a combination of decreased endurance in the affected nerves and an altered posture and movement pattern, not by the axonal damage itself. Patients benefit from specific rehabilitation treatment. For nerves that do not recover, surgery may be an option.

Summary

NA is not uncommon, and has a long term impact on patients' well-being. Early immunomodulating treatment, and identifying phrenic neuropathy or complete nerve paralysis is important for optimal recovery. For persistent symptoms a specific treatment strategy aiming at regaining an energy balance and well-coordinated scapular movement are paramount.

Key points

- Neuralgic amyotrophy is not rare, and residual deficits and impairment are common. Early immunomodulating treatment may improve recovery.
- New nerve imaging methods may facilitate the diagnosis and help select patients for surgical treatment.
- Persistent symptoms need a specific rehabilitation strategy, focused on energy conservation and regaining coordinated scapular movement

Introduction

Neuralgic amyotrophy (NA), also known as Parsonage Turner syndrome or idiopathic brachial plexopathy, is a multifocal inflammatory neuropathy that usually affects the upper limbs. The classic presentation is a patient with acute onset of asymmetric upper extremity symptoms, with unbearable pain in about 95% of the attacks, a swift onset of multifocal paresis that often includes a winging scapula, and a monophasic disease course [1]. NA was first described in 1879 [2], and gained its eponymous name following a detailed report by Parsonage and Turner in 1948 [3]. However, the phenotype is broader than this classic presentation [4]. NA is also not a rare disease [5], and recovery is often not satisfactory for patients [6]. This review provides an update on NA, highlighting recent development in the diagnosis, pathophysiology and treatment.

Clinical phenotypes

NA has a broad phenotypic spectrum [7,8] with the "classic" presentation found in about 70% of the patients. Classic NA most often involves the long thoracic, suprascapular, superficial radial and anterior interosseous nerves (figure 1). Other presentations include involvement of other brachial plexus nerves, a so-called "distal" variety with predominant lower trunk involvement [9], lumbosacral plexus affection in 10% [7, 10], phrenic nerve involvement leading to diaphragm dysfunction in 8% [11], a pure sensory form [12, 13*], and, infrequently, affection of the recurrent laryngeal nerve, a painless onset occurs in about 4% [7]. Of note, while lumbosacral radiculoplexoneuropathy is common in diabetics [14], there is no association at the group level of brachial plexopathy and diabetes in our cohort of 3000+ NA patients.

Recently, detailed nerve imaging studies showed that what was often thought to be "isolated" posterior or anterior interosseous nerve palsy, is actually almost always part of the NA spectrum [15, 16, 17**]. Another NA subtype, often found in middle-aged males with extensive, asymmetric affection of the extremities, phrenic neuropathy, and elevated liver enzymes [7], was recently found associated with a hepatitis E virus infection [18,19**]. A new phenotype is that of a patient with chronic progressive pain and axonal loss, that is steroid-responsive [20]. However, as the majority of NA patients will have persisting pain [6] [Cup 2013], it is crucial to objectify progressive axonal damage to diagnose this rare phenotype, to avoid overtreating the majority of NA patients.

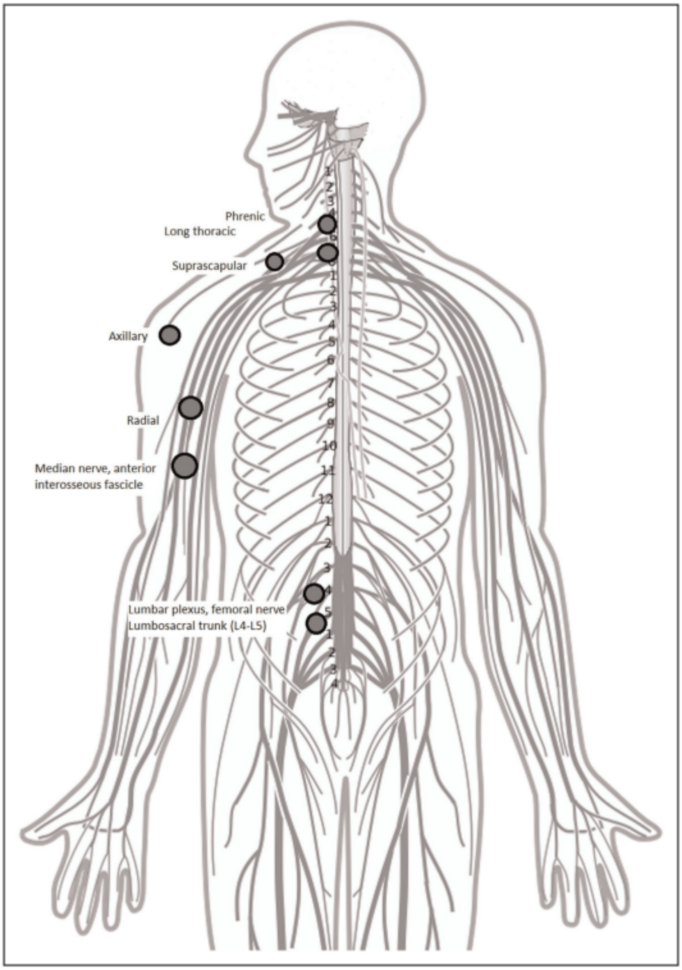

Figure 1: A graphic overview of the most commonly affected nerve sites in neuralgic amyotrophy.

Recurrences are not uncommon, and 25% experiences them the first 5-10 years after onset. Recurrences are more often seen in patients with a familial history of NA (hereditary neuralgic amyotrophy, HNA), that has a 75% recurrence rate [7]. At the individual level a recurrence does not discriminate between idiopathic and hereditary NA, as in both disorders individual patients can experience just a single attack or multiple episodes. However, the number of recurrences is limited across the lifespan, and any patient who thinks they have multiple recurrences each year should be considered to suffer from exacerbations in a relapsing-remitting pattern of pain and fatigue, caused by the typical combination of an altered movement pattern and decreased endurance in the affected muscles [21].

Epidemiology

The average onset age of idiopathic NA is around 40 years, while in HNA it is around 20 years [7]. The occurrence of NA across the lifespan follows a bell-shaped distribution, and it is seen in neonates and very elderly people too. Until the start of the 21st century it was generally assumed that NA was a rare disorder with an estimated incidence of 2-3 per 100,000 per year [22,23]. Subsequent work indicated the diagnosis was likely underrecognized and underreported [7]. A recent prospective study in the general population found a one-year incidence rate for the classic phenotype of 1 per 1000 [5], suggesting the disorder is not rare but actually 5 times more common than ulnar neuropathy at the elbow, and as frequent as cervical radiculopathies [24, 25, 26].

Pediatric NA

Pediatric NA is similar to the adult phenotype, but may be harder to recognize, especially in the very young who cannot verbally communicate their symptoms [27, 28, 29*]. Painless episodes seem more common in children, and a right-sided predominance of the attacks is not yet evident in preschoolers [27, 30]. A particular phenotype is NA in neonates < 6 weeks old, in whom a concomitant septic osteomyelitis of the humerus is almost always present [30], and should be actively sought in this group. Overall, the impression exists that NA has a more favorable long-term prognosis in children [27], which makes sense as peripheral nerve recovery and adaptive strategies are better when people are younger [31].

Clinical examination

NA is a clinical diagnosis first and foremost. Making the diagnosis requires a sufficiently high index of suspicion combined with specific physical exam skills [5,7]. To diagnose the classic phenotype, eliciting a typical history of acute onset severe, numerical rating scale (NRS) ≥7 upper extremity pain, combined with a focused exam that captures scapular movement during abduction – anteflexion and strength testing of the serratus anterior, shoulder exorotation and the long flexor of the thumb will usually suffice [5]. The key features of phrenic nerve involvement in NA are orthopnea, sleep disturbance and extreme fatigue [11]. A targeted workup for diaphragm dysfunction consists of a sitting versus supine vital capacity measurement, maximal inspiratory pressure measurement, and diaphragm ultrasound, which has a very high sensitivity and specificity for phrenic neuropathy [32]. Both unilateral and bilateral phrenic neuropathy are symptomatic, and recovery usually takes several years [11]. For the other phenotypical presentations a tailored neurologic exam is needed, and when there is a genuine differential diagnosis to be explored additional laboratory, electrodiagnostitesting and imaging studies are warranted [1].

Following the diagnosis, the history and exam should focus on further examination of secondary complaints caused by and persisting after an NA attack. The majority of patients in the chronic phase will have persisting upper extremity pain, paresthesia, fatigue and impairments [6]. This is the result of decreased muscle endurance following axonal injury, and an altered posture and scapular movement pattern, that leads to muscle strain, subacromial tendinopathy, and subpectoral impingement [1, 21].

Pathophysiology and immunological triggers

Because direct access to the plexus and nerves in acute NA is unavailable, the exact onset and pathophysiology are still obscure. Most evidence points to NA being an auto-immune disorder, in which several independent predisposing factors will lead to the occurrence of an actual episode [1]. With a presumed incidence rate of 1/1000/year but a recurrence in at least 1/4 with idiopathic NA, an intrinsic factor is presumed present that makes patients more vulnerable than the general population. Mechanical factors also seem to play a role as strenuous activity or local trauma can trigger an attack, and NA patients are more often physically active than the general population.

Mechanical strain is suspected to cause a focal disturbance of the fascicular perineural blood-nerve barrier [33], especially in nerve segments that routinely undergo large mechanical deformation, such as the brachial plexus and certain arm nerves. The final step leading to the onset of an attack seems to involve activation of the immune system, that in the context of a “leaky” blood-nerve barrier leads to an auto inflammatory response with subsequent damage of the nerve segments. Scant histologic evidence suggests that an attack is the result from an aspecific activation of the innate immune system at the level of the blood-nerve barrier, resulting in focal inflammatory infiltrates [4], severe pain caused by the release of inflammatory mediators and ischemia of the nervi nervorum, and acute damage to the paranodal regions of large nerve fibers, as an early conduction block has been described in proximal nerve segments in NA [34, 35]. If left untreated, this inflammatory response will progress into axonal loss and denervation, and perineurial and epineurial fibrosis with the formation of constrictive bands that constrict the nerve and hamper recovery [36**].

Any immune-related factor can trigger NA, including infection, vaccination, immunotherapy such as interferone or immune-checkpoint inhibitors [37,38], recovery from surgery, pregnancy or childbirth, trauma or psychological distress [7]. The list with micro-organisms reported to have triggered an attack keeps expanding [39], with s. aureus and SARS-CoV2 (COVID-19) being the most recent additions [40*, 41*]; see table. A prominent antecedent infection is hepatitis E virus (HEV), which acts as a potent trigger for various peripheral nervous system disorders [42], and may be responsible > 10% of the acute NA episodes [43]. HEV is commonly found in pork-derived food products, which suggests a potential role for increased vigilance from the authorities. It causes an extensive phenotype that may present with multiphasic symptoms [44**]. As HEV rarely causes hepatitis and no difference in outcome was found in HEV- positive NA patients that did or did not recieve ribavirine, no specific antiviral treatment seems needed in this group [18].

Table 1. Reported antecedent infections that triggered an NA episode

Viral	Bacterial	Other
Hepatitis E virus	Borrelia burgdorferi	Aspergillus species
Parvo virus B19	Escherichia coli	
SARS-CoV2	Staphylococcus aureus	
Human immunodeficiency virus	Neisseria gonorrhoe	
Herpes simplex virus	Salmonella panama	
Epstein--Barr virus	Yersinia enterocolica	
Cytomegalovirus	Streptococcus group A	
Varicella zoster virus	Brucella species	
Vaccinia virus	Coxiella burnetti	
Coxsackie B virus	Chlamydophila pneumoniae	
West Nile virus	Leptospira species	
Hepatitis B virus	Mycoplasma pneumoniae	

NA, neuralgic amyotrophy

Genetics

About 1 in 10 patients report a family history for the disorder (HNA), typically transmitted in an autosomal dominantly. HNA and INA are phenotypically identical, except that the underlying vulnerability to the disorder seems more pronounced in HNA, reflected by the earlier onset age, an increased affection of nerves outside the typical distribution, and the overall higher recurrence rate [4]. Only one gene, SEPT9, has been implied in the transmission of an increased vulnerability to NA [45]. Mutated septin-9 isoforms interfere with intracellular microtubule bundling and impair asymmetric neurite outgrowth in cell cultures [46]. How this leads to a predisposition for NA is unknown. Of note, the prevalence of a mutation or duplication in SEPT9 seems to be much lower in the Dutch population (< 5%) than in North America (around 50%), and HNA appears to be genetically heterogeneous in a significant proportion of the patients (personal communication, prof. van Engelen).

Role of EMG and imaging

With a typical history and the classic clinical phenotype, the a priori chance of having NA is so high that any further investigation will not increase the likelihood. In less typical cases, for example those without pain or with gradual progression, or when there is a genuine differential diagnosis to explore, nerve conduction studies, needle EMG and nerve imaging may help improve diagnostic certainty. Nerve conduction studies are often normal in NA [47], and paraspinal abnormalities can be found on needle EMG, making it difficult to use these tests to differentiate NA from a cervical radiculopathy. The clinical pattern will determine if weakness and sensory symptoms fit the distribution of a discrete nerve root or a multifocal mononeuropathy. Needle EMG carries a significant risk of sample error and misdiagnosis when only "routine" muscles are explored. It is therefore recommended not to rely on EMG for confirming the diagnosis [48]. Obviously, the electrodiagnostic exam can assess the extent of de- and reinnervation if clinically needed, and can help in selecting patients and nerves for surgical intervention if no recovery occurs.

Recent advances in nerve imaging show focal abnormalities in the nerve roots or proximal nerve segments in 75%-80% of NA patients [17, 49, 50, 51]. This makes nerve imaging a patient-friendly option to support the diagnosis. Remarkably, abnormalities are usually not found in the brachial plexus proper, suggesting the term "brachial plexopathy" as a synonym for NA should probably be abandoned [52]. Affected nerve segments in NA show focal enlargement indicating inflammation, and some nerves develop typical focal "hourglass" constrictions [53].

Acute phase treatment

Multiple case series and reports suggest that corticosteroids and intravenous immunoglobulin can be effective in the acute phase of NA [7, 18, 19, 28, 54, 55, 56, 57*, 58, 59], and the sooner the treatment can be started, the higher the chance of a positive response. In practice, a positive responder is a patient who is nearly pain-free within 24-48 hours after starting treatment. Treatment started beyond 2 weeks has no expected effect, and chronic treatment is not warranted.

Pain in acute NA can be managed as any other nociceptive pain, using the steps of the WHO modified analgesic ladder used in proportion as the NRS pain score increases. The large majority of acute NA patients will have an NRS score of ≥7, for which a combination of NSAIDs and opioids was found most effective. The acute phase pain is usually unresponsive to co-analgesics [7]. Clinically, very few NA patients will develop true chronic neuropathic pain, and in practice persistent pain is almost always caused by decreased endurance and an altered movement pattern indicated above [6].

Patients with phrenic neuropathy can benefit from non-invasive nighttime bilevel positive airway pressure ventilation and coordinative inspiratory muscle training, and may benefit from diaphragm plication when no spontaneous nerve recovery occurs [11, 60*].

Chronic phase treatment and rehabilitation

The majority of NA patients is left restricted in their daily activities because of residual pain and fatigue [6, 7, 61]. These symptoms are perpetuated by inefficient motor control of the affected shoulder/arm, loss of endurance in the affected muscles and strain of the compensating musculature. Specific outpatient rehabilitation treatment can help overcome this [21, 62*, 63**]; see figure 2. For NA patients, important topics are an interdisciplinary approach, shared goal setting and decision making, and honest explanation and education on how NA works in relation to their complaints, and how to self-manage these complaints [64*]. To support the rehabilitation process, behavioral change techniques such as motivational interviewing are recommended [65].

Physical therapy for NA focuses on regaining motor control. Patients are trained to maintain and automate scapular position in subtle posterior tilt while using the arm selectively, with supportive feedback on posture and movement control from their therapist. Initially this is practiced with relatively simple arm movements, with slow progression to more natural activity-like exercises, with supportive feedback gradually phased out. The focus is on movement technique, not on strength or endurance training [21, 62]. To enable muscle relaxation, manual myofascial treatment or costovertebral joint mobilization techniques can additionally be used [66, 67].

Occupational therapy for NA focuses on management of pain and fatigue with use of energy conservation strategies [68]. Key elements include ergonomics during activities such as self-care, household, work, education, sports and leisure and on an optimal arm and shoulder position at rest. Other strategies include activity adaptation, the use of assistive devices and planning and pacing of activities, including so-called “minibreaks” to find a balance during the day and week [69]. Specific coaching is provided to facilitate return to work.

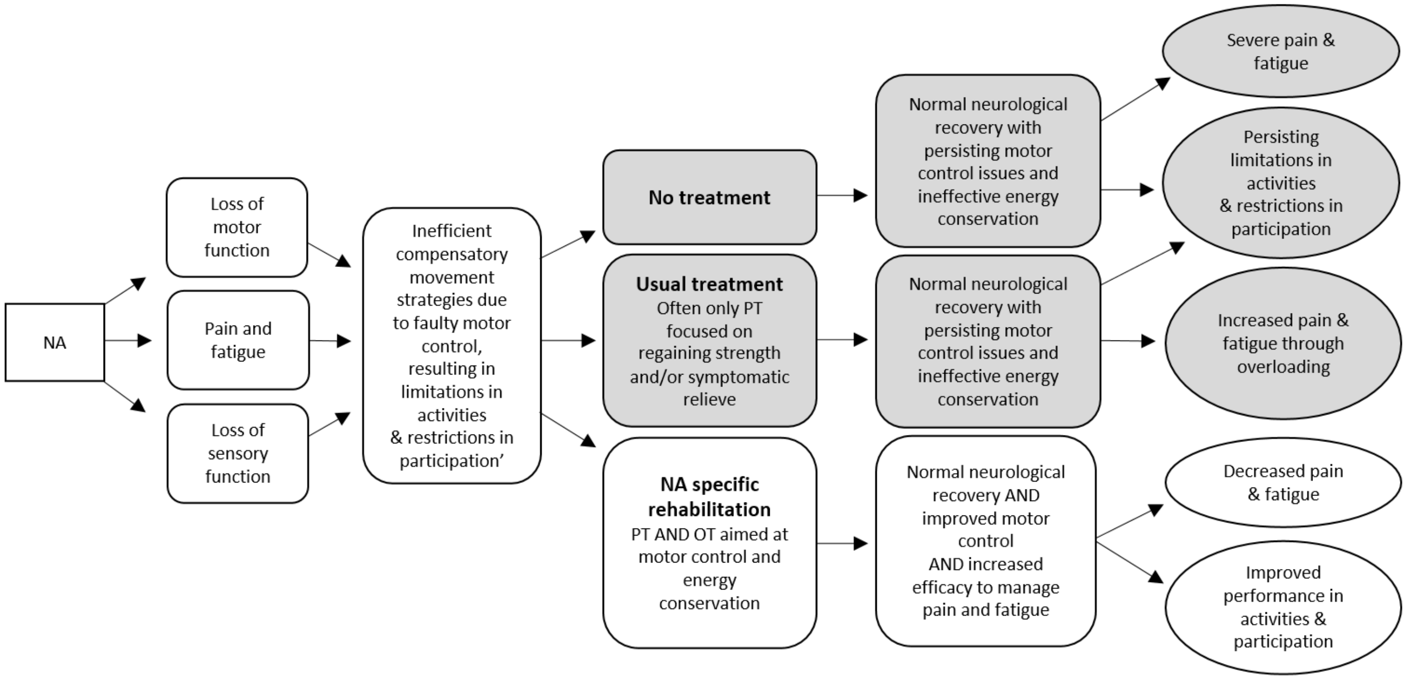

Figure 2: Persisting consequences following NA and the practice-based effect of different treatment approaches currently used for rehabilitation. NA, neuralgic amyotrophy

Surgical treatment

Up to 30% of NA patients has residual motor deficits [7] [Brain 2006]. Nerves that fail to recover usually exhibit focal hourglass constrictions that can lead to severe nerve narrowing [53, 69]. When there is a (near-)complete paralysis without recovery after 6 months, surgical neurolysis is indicated within 6-12 months to allow reinnervation [36**]. With this treatment, improvement was seen in 90% of the patients [70**]. In patients for whom neurolysis is not an option, but who have impairment from residual deficits, other surgical options such as nerve transfer or secondary surgery using tendon transfers should be considered [71, 72].

Conclusions

NA is not uncommon, and has a long term impact on patients' well-being. Early immunomodulating treatment, and identifying phrenic neuropathy or complete nerve paralysis is important for optimal recovery. For persistent symptoms, a specific rehabilitation strategy aimed at regaining energy balance and well-coordinated scapular movement, and identifying non-recovering nerves for surgical treatment are paramount.

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Chapter 3

Efficacy of a combined physical and occupational therapy intervention in patients with subacute neuralgic amyotrophy: a pilot study

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Abstract

Background

Neuralgic Amyotrophy (NA) is characterized by neuropathic pain, subsequent patchy paresis and possible sensory loss in the upper extremity. Many patients experience difficulties in performing activities of daily life and are unable to resume work. We developed a combined physical- and occupational therapy program for patients recovering from NA.

Objective

Evaluation of the effectiveness of a multidisciplinary intervention program for patients with subacute NA.

Methods

We performed a within subject proof-of-principle pilot study in eight patients with subacute NA. Patients followed 8 hours of physical and 8 hours of occupational therapy spread over a 16-week period. Primary outcome measures: The Canadian Occupational Performance Measure (COPM) and Shoulder Rating Questionnaire (SRQ). Secondary outcome measure: Disability of Arm Shoulder and Hand (DASH).

Results

Improvements (mean (95% CI)) were found in the performance and satisfaction scores of the COPM +2.3 (0.9–3.7) and +1.4 (0.4–2.4) points, respectively and the SRQ +14.8 (7.4–22.0) points. The majority of patients (6 out of 8) also demonstrated improvements in the DASH.

Conclusion

The proposed physical and occupational therapy program, may be effective for patients with subacute NA, as demonstrated by improvements in activity, performance and participation.

Introduction

Neuralgic Amyotrophy (NA; Parsonage Turner Syndrome, brachial plexus neuritis) is a peripheral nerve disorder which affects the brachial plexus [1]. In about 10% of cases the lumbar plexus is also affected, resulting in pain and loss of neurological function of the lower extremity [2]. The onset of NA is usually characterized by severe neuropathic pain (numeric rating scale (NRS) 8-10), which on average lasts three to four weeks. Generally it is accompanied by loss of neurological function of the upper extremities and shoulder girdle. This acute phase is followed by a chronic phase, in which the primary neuropathic pain is replaced by both neuropathic stretching pain of affected nerves and musculoskeletal pain localized to the origin and/or insertion of paretic and compensating muscles [3].

NA can be either idiopathic (INA) or hereditary (HNA) [4,5]. INA is the most common variant with a reported incidence of 2-3 per 100,000 per year and a median onset in the fourth decade. HNA is about 10 times less common and has a median onset in the second decade. In general NA is under-recognized [3]. The etiology of NA is still not fully understood, but the current assumption is that the disease is caused by a combination of genetic, mechanical, auto-immune and environmental factors [1].

The primary consequences of NA are paresis, muscle atrophy, movement restrictions, fatigue, impaired humero-scapulo-thoracic coordination and scapula alata (winging of the shoulder blade) [6,7]. These impairments lead to difficulties over time, when performing activities above shoulder height, reaching, lifting below shoulder height, maintaining body positions and, in the majority of patients, when performing sustained or repetitive movements [8]. In addition, shoulder exorotation, pinch grip and pronation strength are also often affected [3]. Eighty-two percent of patients become impaired in performing activities of daily living (ADL) such as self-care, household, work-related activities, hobbies and sport for years after onset of symptoms [8]. A correlation between coping strategies and persistent complaints has been suggested [8].

Although there are promising results on the use of prednisolone treatment in the acute phase of NA [9], there is insufficient evidence to support any medical intervention to restore impairments resulting from NA [10]. In addition, very little is known about rehabilitation interventions, including physical and occupational therapy, focusing on consequences of NA in terms of functional impairments or restrictions in activities and participation [10].

Since 2009 the departments of Rehabilitation and Neurology of the Radboud university medical centre host a multidisciplinary outpatient clinic, which serves as a national referral center for NA in the Netherlands. In this clinic, a neurologist, rehabilitation physician, physical therapist and occupational therapist examine NA patients. The clinic has developed a multidisciplinary outpatient rehabilitation intervention program for patients in the subacute phase of NA (>6 months after onset of disease). The aim of this combined allied health care intervention is to educate patients on how to regain control over their complaints and manage their lives with the residual symptoms after NA. Physical therapy (PT) focuses on educating and training movement and position sense, coordination of the affected shoulder girdle and improving functional endurance. Occupational therapy (OT) focuses on prevention and reduction of overuse of affected and compensating muscles, body ergonomics at rest and during activities and adaptation of activities and environmental changes. From our clinical experience this approach seems to be effective, but this has not yet been formally established. Therefore, this pilot study aims to evaluate the effectiveness of the proposed multidisciplinary intervention program in patients with subacute NA.

Methods

Design

A within subject proof-of-principle pilot study was performed. Measurements were carried out during a baseline period (three months prior to intervention), at start, and at completion of the multidisciplinary intervention program. Patients were recruited by the neurologist or rehabilitation physician from our outpatient clinic.

Participants

Ten patients were invited to participate in the study from November 2011 to February 2012. Eight patients were included and all completed the intervention program (figure 1). They all fulfilled the following inclusion criteria: 1) diagnosed with NA by an experienced neurologist (NvA); 2) uni- or bilateral complaints with a NRS pain score >5; 3) NA >6 months after onset; 4) aged >18 years; 5) understanding Dutch written and spoken language. Patients were excluded if they had: 1) previous surgery of the affected neck and or shoulder.; 2) history of other central neurological disease; 3) a Beck Depression Inventory (BDI) score >20 [11]. Two patients were excluded from the study for the following reasons; one patient had a recurrent attack of NA and was therefore no longer in de subacute phase of the disease, the second patient scored >20 points on the BDI. The study was approved by the medical ethics committee of the Radboud university medical centre and written informed consent was obtained from all patients.

Intervention

The aim of the multidisciplinary intervention program was to support patients in their self-management strategies to regain control over their complaints. The program teaches problem solving skills as described in the model of D'Zurilla [12], combined with role management skills [13]. We developed a model, shown in figure 1, that gains insight into different components that need to be addressed during the intervention program (figure 1).

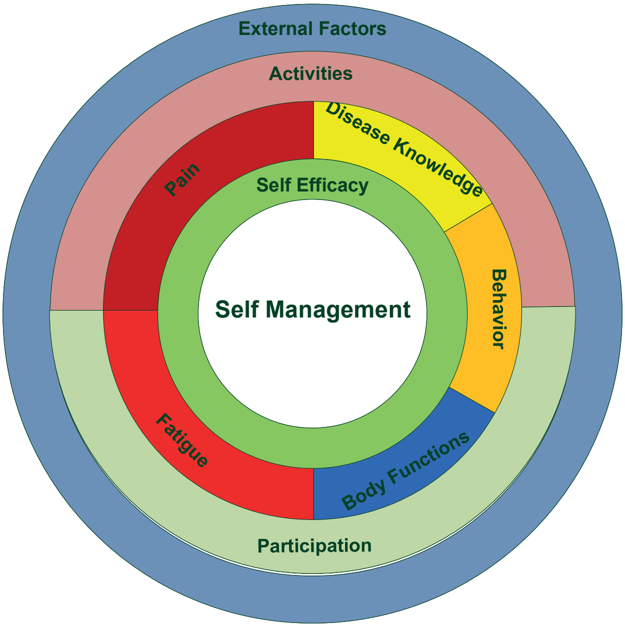

Figure 1: Model showing treatment components.

This model can be used as a checklist during treatment; it shows possible components that might be addressed and which may vary for each patient. For instance, in some patients improvement of body functions may be more important than adaptation of behavior. Optimally, the intervention focuses on all aspects of the model. Which results in a decrease in pain and fatigue, an improvement of body functions and activity levels, performance and participation. This may also lead to increased self-efficacy and ultimately self-management.

OT focuses mainly on issues in the outer two circles (activity, participation and external factors) and PT mainly addresses improvement of body functions. Both, PT and OT, address adaptation of behavior and the conveying of knowledge about NA related to functioning in daily life. Self-efficacy was improved by increasing self-control over complaints. Motivational interviewing techniques were used for behavioral changes and changes in coping style [14].

The program consisted of a 16-week treatment period during which patients were treated weekly in week 1-4, once every two weeks in week 5-8 and monthly in week 9-16. Each treatment session involved one hour PT and one hour OT.

Physical therapy interventions

PT included training to regain scapular muscular balance and progressive resistance training of rotator cuff muscles; the latter only after scapular muscular balance was achieved since scapular stability is essential for the function of arm muscles that control position [15-17]. All exercises were carried out without or only with minimal pain during and after exercises. If patients did experience (excessive) pain during or after the exercises, intensity of the program was adjusted accordingly.

If patients had difficulty in implementing the scapular control movements in daily life, scapular proprioceptive taping was used to increase awareness of their scapular position during posture and movement [18]. Some patients with NA experience neural stretching pains of the brachial plexus, which are likely caused by neural entrapment in case of a habitually protracted and adducted scapula because of serratus anterior weakness and compensatory activation of the pectoralis and trapezius muscles. When present, this complication was treated by increasing scapular control as described above and by using neural mobilisation techniques [19], using movements designed for the Upper Limb Tension Test [20]. These involved patients to grab hold of the doorframe and stretch out their arm until they experienced mild neurological sensations such as tingling or radiating pain. They were instructed to perform this stretching exercise three times a day in three repetitions, lasting 20 to 30 seconds. Patients who lacked control of their primary cervical stabilizing muscles, tested using the cranio-cervical flexion test with pressure biofeedback [21], received sensomotory cervical stability training [22]. When increased muscle tone and/or myofacial trigger points were found in the neck or shoulder region patients were treated with muscular relaxation exercises and trigger point releases as pre-conditioning for sensomotory scapular and cervical training [23].

Occupational therapy interventions

The focus of the OT intervention lied on enabling daily occupations. Patients gained insight into activities that provoked pain and into strategies focussed on preventing and reducing pain caused by overuse of affected and compensating muscles. To this end, energy conservation strategies were taught including taking mini-breaks, practicing optimal body ergonomics during rest and action, and analysing and adapting activities or the environment with or without use of aids and adaptations [24]. Patients learned self-management strategies to reduce stress and physical strain and to find a balanced distribution of activities during the day/week. As readiness and willingness to change are needed to implement these strategies in daily life, motivational interviewing techniques were used [14, 25].

Outcome measures

Several domains of the international classification of functioning (ICF) were assessed [26].Outcome parameters were used at the level of

1) *Body functions:* strength of rotator cuff musculature was evaluated by using Hand Held Dynamometry (HHD) (Microfet2®), handgrip was measured using handgrip dynamometry (Takei Grip dynamometer®) and pinch grip was measured using pinch grip dynamometry (B&L systems pinchgauge)

2) *Activities and function:* Shoulder Rating Questionnaire (SRQ) and Disabilities of Arm Shoulder and Hand (DASH) questionnaire, in the Dutch language version, were used to measure activity performance and to quantify disability. The SRQ is used in combination with the DASH because SRQ scores showed high correlation with functioning in patients with NA, although the DASH is reported more sensitive to change and has higher reliability and validity in general shoulder populations [8, 27].

3) *Participation:* the Canadian Occupational Performance Measure (COPM) was used to evaluate occupational performance and satisfaction with performance of the most important daily occupations identified as a problem by the patients [28].

4) *Quality of life:* The short form 36 questionnaire (SF-36) was used to measure health-related quality of life [29].

5) *Personal factors:* The Checklist Individual Strength 20 (CIS-20) was used to measure fatigue. The CIS-20 [30] was also used at the time the patient was referred to the outpatient clinic and was checked for changes in perceived fatigue before patients entered the program [31]. In addition, the Self Efficacy for Performing Energy

Conservation Strategies Assessment (SEPECSA) was used [30]. Primary outcome measures were the SRQ and the COPM with the DASH as a secondary outcome measure. All instruments used are reported sensitive to change, valid and reliable in various shoulder populations [8, 27]. An assessment schedule is presented in figure 2.

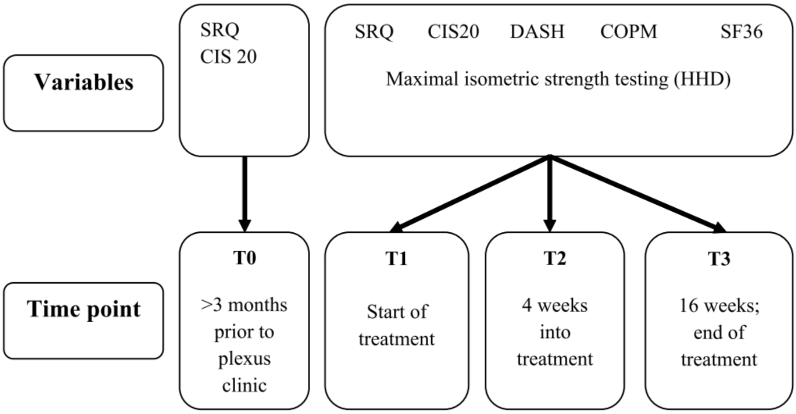

Figure 2: Study procedures timeline.

COPM: Canadian Occupational Performance Measure, DASH: Disabilities of the Arm, Shoulder and Hand, CIS: Checklist Individual Strength, SEPECSA: Self Efficacy for Performing Energy Conservation Strategies Assessment, SF-36: Short Form (36) health survey

Procedure

As standard screening procedure, patients received several questionnaires (including SRQ and CIS) at the moment they were referred to the outpatient clinic, on average three months prior to the outpatient clinic visit. Therefore the SRQ and the CIS were used to control for changes in functional ability during the waiting list period. Afterwards, questionnaires were completed by the patients at the start, during, and after the intervention program. The patients' therapist carried out COPM, and HHD measurements.

Statistical methods

Descriptive statistics were used; results were presented by use of mean, standard deviation (SD) and 95% confidence intervals. Pre- to post-treatment within subject difference scores were checked for normality by use of descriptive statistics (skewness and kurtosis) and quantile probability plots (QQ-plots). Pre and post measurements were compared and tested by use of the paired samples *t*-test and Wilcoxon signed-rank test. Significance level was set at 0.05. Statistical analyses were performed using SPSS 18 (IBM PASW Statistics, IBM Corporation, Somers).

Results

The mean ± SD age of the 8 patients (6 males) who completed the program was 46 ± 10 years (range 34-58). Mean duration of complaints until start of treatment was 35 ± 50 months (range 7-156). In 6 patients their dominant arm was affected. Pre- to post-treatment within subject difference scores were normally distributed.

During the program 2 patients developed therapy resistant glenohumeral capsular inflammation, which was treated with steroid infiltration. This decreased the symptoms, after which the intervention program was resumed. Another patient experienced prolonged nerve irritation of the middle plexus with radiating sensory symptoms in the distribution territory of the pectoral nerves, median and radial nerve. This was treated with a short course of oral prednisolone (60mg daily for one week, tapering over the next week), which decreased paresthesia and hypesthesia and reduced muscle tone in the pectoralis minor muscle. The outcome for these patients was not different from the other patients on outcome measures used. Figure 3 shows an overview of inclusion and interventions.

Two patients experienced neural stretching pains, that slowly diminished over the course of eight weeks using neural stretching exercises. All patients had myofacial triggerpoints in the neck extension muscles, trapezius descendens, levator scapulae, pectoralis minor or rhomboid muscles. Trigger point releases reduced muscle tone and increased of range of motion for up to three days. Four patients carried out cervical stabilizing exercises, which lead to a diminished muscle tone and increased activity in secondary cervical stabilizers. All eight patients received scapular sensomotory facilitation taping, which helped them to implement scapular positioning in ADL.

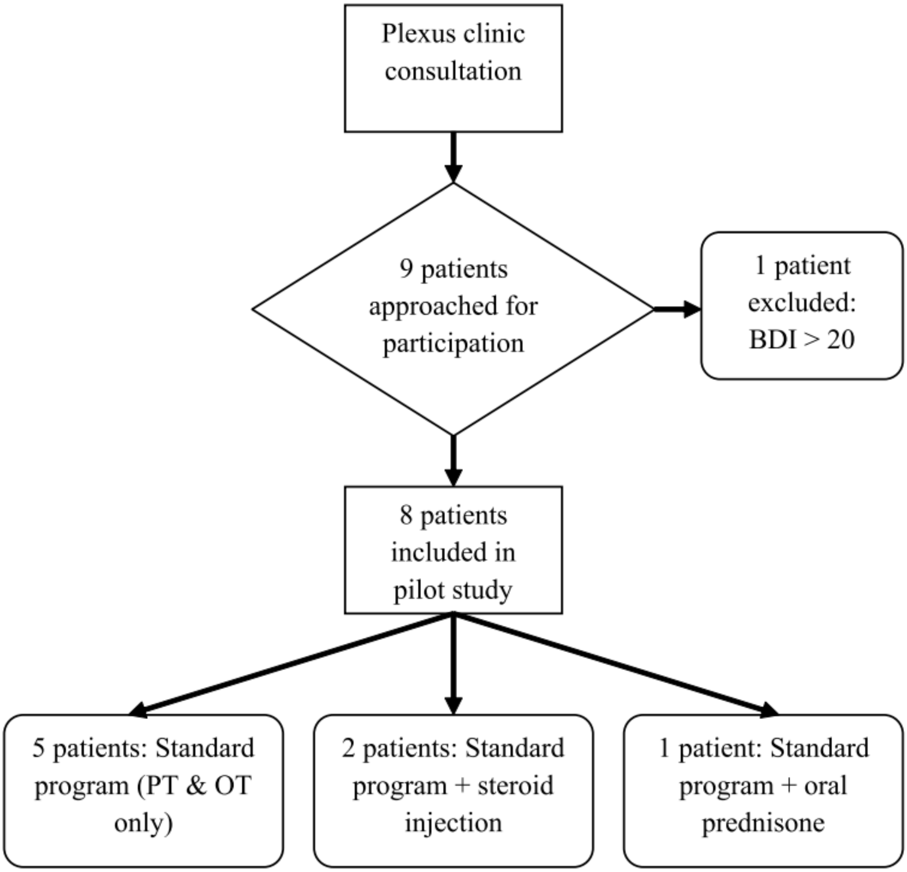

Figure 3: Flowchart procedure of the study
BDI: Beck depression inventory, OT: Occupational Therapy, PT: Physiotherapy

Outcome measures

During the 3-month baseline period before the start of the intervention program none of the patients demonstrated any change in scores of SRQ total, SRQ global or CIS-fatigue subscales.

After intervention, the (mean ± SD) change in SRQ Total score 14.8 ± 8.6, SRQ Global 3.5 ± 1.8, SRQ Pain 4.0 ± 4.9 and SRQ ADL 2.4 ± 2.4 improved significantly. The SRQ total improvement of 30.4% from baseline exceeds the reported minimal clinically important difference (MCID) of 13.5% [32]. Seven patients improved on the

COPM performance subscale (range) 0.2 to 3.2 points. One patient demonstrated a decrease in COPM performance score of -0.3 points. COPM satisfaction scores demonstrated improvement in all patients (range) 0.2-4.8 points. COPM group scores demonstrated a mean improvement of 1.4 ± 1.2 points in performance and 2.3 ± 1.4 points in satisfaction and the mean difference score for satisfaction also exceeded the reported MCID of 2 points [33]. CIS-fatigue scores demonstrated a tendency to improve (i.e. lower scores) in six patients (range) 9.0-12.0, but this was not significant ($p=0.263$). Two patients demonstrated an increase in fatigue scores with 3 and 12 points respectively. Six patients demonstrated an improvement >10 points on the DASH score, exceeding the reported MCID [34]. DASH results demonstrated a tendency to improve, with a drop of 11.3 ± 14.5 points (0.9-23.4) ($p=0.069$). Mean SF-36 scores decreased for health change (-37.5 ± 23.1 points ($p=0.003$)) domains, but not on the other domains. This indicates that, compared to the judgment before treatment, patients found their health state (after the intervention) had more resemblance, compared to their health state a year ago.

HDD measurements only demonstrated a tendency to an increase in strength of the serratus anterior muscle. Values improved in five patients (range) 49.6-187.5 Newtons. Group results for the initial and follow up measurements are shown in table 1.

Table 1: Outcome measurements results

Outcome	Mean Baseline	Mean end of treatment	Paired Differences†				Significance†
			Mean difference	Standard deviation	95% confidence interval		
					lower	upper	
COPM performance	**4.5**	**5.9**	**1.4**	**1.2**	**0.4**	**2.4**	**.015**
COPM satisfaction	**4.3**	**6.6**	**2.3**	**1.6**	**0.9**	**3.7**	**.005**
DASH total‡	62.3	51.0	-11.3‡	14.5	-23.3	0.9	.064
CIS-20 fatigue‡	38.3	36.0	-2.3‡	6.9	-8.0	3.5	.263
SRQ total	**48.7**	**63.4**	**14.8**	**8.6**	**7.4**	**22.0**	**.002**
SRQ global	**5.9**	**9.3**	**3.5**	**1.8**	**1.9**	**5.0**	**.001**
SRQ pain	**19.5**	**26.0**	**4.0**	**4.9**	**2.4**	**10.6**	**.007**
SRQ adl	**12.2**	**14.6**	**2.4**	**2.4**	**.4**	**4.4**	**.025**
SF36 physical functioning	62.5	64.4	1.9	14.4	-10.1	13.9	.723
SF36 social functioning	16.9	25.0	8.1	10.3	-.51	16.8	.061
SF36 role physical	18.8	28.1	9.4	18.6	-6.2	24.9	.197
SF36 role emotional	100	100	0	0			1.00
SF36 mental health	66.0	75.0	-4.4	13.0	-14.7	6.0	.351
SF36 vitality	50.0	45.6	-8.9	12.4	-30.3	12.4	.355
SF36 pain	57.4	48.5	1.9	25.5	-16.3	20.0	.814
SF36 health change	**75.0**	**37.5**	**-37.5**	**23.1**	**-56.9**	**-18.2**	**.003**
SEPECSA	7.3	7.7	0.4	1.1	-.5	1.4	.263
Keygrip*	10.2	8.2	-2.0	2.6	-4.5	0.4	.084
Handgrip*	35.2	32.9	-2.3	5.8	-7.1	2.6	.313
Exorotation*	94.4	97.2	2.8	29.5	-21.8	27.5	.791
Endorotation*	108.4	116.4	8.0	42.5	-27.5	43.5	.611
Elbow flexion*	158.5	165.9	7.4	50.1	-34.5	49.3	.688
Elbow extension*	125.4	105.6	-19.8	33.1	-60.0	20.3	.260
Serratus Anterior*	162.7	210.4	47.7	75.2	-15.2	110.5	.116

** Strength measures of the affected arm*

† Paired statistics based on paired samples T-test

‡ Negative scores relate to functional improvement

***Bold** scores indicate significant results*

COPM: Canadian Occupational Performance Measure, DASH: Disabilities of the Arm, Shoulder and Hand, CIS: Checklist Individual Strength, SEPECSA: Self Efficacy for Performing Energy Conservation Strategies Assessment, SF-36: Short Form (36) health survey

Discussion

Results of this pilot proof-of-principle study indicate the efficacy of our combined PT and OT intervention program for these patients with subacute NA. Patients, who demonstrated no improvement in more than three months prior to the intervention, improved in functioning and even more so in satisfaction with their performance. All patients demonstrated large improvement in SRQ subscales, and the majority in the DASH total score. Even the lower limits of the 95% confidence interval of the SRQ-total and SRQ-global subscales indicate a clear clinically relevant improvement of more than 30%. Strength values of upper extremities obtained by HDD demonstrated no significant change during the treatment period. The serratus anterior muscle that was specifically activated during the program was the only muscle demonstrating improvement but not statistically significant. Even though functioning and satisfaction improved, no significant improvement of experienced fatigue by patients was measured with the CIS-fatigue subscale. As fatigue is a very global indicator of how much energy people have to spend during their daily life, we hypothesize that the learning and training period during our program also cost them extra energy and hence no net effect was present in their energy balance. Further follow up of these patients beyond the treatment period will have to show if in time fatigue will decrease after completion of the intervention program and if persons manage to integrate lifestyle changes automatically.

To our knowledge, this is the first ever rehabilitation intervention described in patients with NA. Even in other peripheral nerve disorders of the shoulder complex, no therapeutic interventions have been researched until now. This makes it difficult to compare our results with other findings. The novelty of the proposed therapy approach does not lie in the therapeutic interventions used, but in the combination of these interventions in complex shoulder problems due to NA. We expect the rather large effects found to be due to the personalized character of this intervention in which problems are approached from a patients perspective.

Study limitations

This study was designed as a proof of principle pilot study and has its limitations. Although patients were controlled in a within subject design, a natural recovery tendency or other confounding may have influenced results [35]. In this design patients may also have reported improvement partly due to a placebo or Hawthorne effect [36]. Especially because patients have been treated in the national reference center for NA, which may have enhanced patient confidence in the treatment program. Another limitation was the group size, although rather large and significant differences were found in this small study population, generalizability may be poor [35].

Two patients received additional treatment because of glenohumeral joint complications during the program. However, primary outcome scores for the group as a whole were no different with or without these subjects.

Conclusions

We did not find indications that our intervention program caused harm or negatively influenced physical and social functioning of our patients. On the contrary, perceived global status in the SRQ and patient satisfaction in the COPM improved extremely well during the treatment period. The relatively small change in muscle strength suggests that improvement in this population is most likely caused by functional and behavioral adaptation to nerve damage and corresponding loss of function of the affected shoulder. Therefore, patients' behavior in relation to complaints, smart alternative ways of carrying out (strenuous) activities, efficient ways of shoulder movement and control and acceptance of limitations appear to be key issues for treatment of these patients. Patients apparently learn to adapt to their limitations and achieve higher efficacy without need for improvement of body functions.

We strongly emphasize the need for a further controlled study, with a larger sample, to provide this multidisciplinary program with a firmer evidence base. Qualitative studies are also recommended to give better insight and understanding of the treatment ingredients that helped patients to deal with problems as a result of NA.

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Chapter 4

Reflections of patients and therapists on a multidisciplinary rehabilitation programme for persons with brachial plexus injuries

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Abstract

Purpose

There is lack of knowledge, evidence and guidelines for rehabilitation interventions for persons with neuralgic amyotrophy or brachial plexus pathology. A first pilot study, evaluating the effect of an integrated rehabilitation program, showed improvements in activity and participation levels. Aim: To gain insight, from the perspective of patients and therapists, into the critical ingredients of the program, that contributed to improvements in activity and participation.

Materials and methods

A qualitative study using semi-structured interviews with eight patients and five therapists (3 occupational therapists and 2 physical therapists). Participants were asked to identify and describe factors regarding the rehabilitation that they perceived as positive and aspects of the program that could be improved. Data were analyzed using a constant comparative approach.

Results

Patients reported 1) Time to diagnose: “Finally I’m in the right place”; 2) Awareness: “They gave me a mirror”; 3) Partnership: “There was real contact with the therapists; we made decisions together”; 4) Close collaboration: “Overlapping scopes of practice; doing the same from a different perspective”; and finally 5) Self-management: “Now I can do it myself”. Therapists reported 1) “Patients knowledge and understanding is critical to success”; 2) “Activate problem solving and decision making”; 3) “Personalize your therapy; it’s more than just giving exercises and information”; 4) “Constant consultation within the team; consistency in messages and approach”; and 5)” Ultimately the patient is in charge”.

Conclusion

The critical ingredients, correspond well with each other and include a person-centered approach, education, support in problem solving and decision making and an integrated team approach. These ingredients provided the patients with confidence to take responsibility to manage their everyday lives, the ultimate goal of the program.

Introduction

Persons with neuralgic amyotrophy (NA) experience severe pain, fatigue and problems in performing movements of the upper extremity [1]. NA limits forward reaching, lifting the arms above shoulder height, maintaining static arm positions and repetitive movements. The combination of limited movement, pain and fatigue compromise the performance of many activities and roles in daily life, making NA a very debilitating condition.

NA is a peripheral nerve disorder characterized by episodes of severe neuropathic pain at onset, followed by multifocal paresis and atrophy of the upper extremity muscles [2, 3]. It can result in impaired humero-scapulo-thoracic coordination and scapula alata (winging of the shoulder blade) and increased fatigability of the muscles, leading to compensatory movements and limitations in everyday life [4, 5]. Recovery is mostly slow and often incomplete [2, 3]. Previously, NA was known as a rare disease (incidence of 2-3 per 100.000 per year [6]), however, recently it has been shown that NA is quite common with an incidence of 1 in 1000 [7]. Still, NA is not well recognized by physicians and therapists and, as a result, treatment provided is often non-specific and sub-optimal. Lack of or incorrect diagnosis, inconsistent or wrong advice, and absence of a clear intervention plan contribute to patients' anxiety that often further aggravates symptoms.

There is limited evidence to guide treatment of NA [3]. While use of prednisolone treatment in the acute phase [8] is showing promising results, evidence and protocols during the sub-acute phase are limited. Therefore, people with NA often receive the message that they 'have to live with it' with no support to manage life with pain and paresis that limits function at work, during sports, leisure and/or self-care activities.

In 2009, the departments of Rehabilitation and Neurology at Radboud university medical center began seeing outpatients at a specialized, multidisciplinary clinic for patients with disorders of the brachial plexus, the so called 'Plexus Clinic'. People with NA form the largest group attending this clinic. Consisting of a neurologist, rehabilitation physician, physical and occupational therapist, the multidisciplinary team has assessed three to four new patients every week for the past seven years. The assessment includes making the diagnosis and providing the patient with a personalized intervention plan. Most patients are then referred to their own region for implementation of this plan, however, patients living in the Nijmegen region are treated by our own multidisciplinary team. Intervention includes physical and occupational therapy and, if necessary, medication and/or orthosis/aids provided by the rehabilitation physician.

As the first integrated rehabilitation program for NA, the limited available scientific evidence was combined with the practice based expertise of the multidisciplinary team to develop a standardized integrated rehabilitation program [9]. The aim of this program is to support patients to gain control over their symptoms in order to manage their life with NA. The focus of physical therapy is to regain scapular muscular balance [10]. Using an individualized adaptation of a fatigue management group intervention [11], occupational therapy supports life balance and self-management strategies known to reduce fatigue and improve quality of life [11, 12]. Both physical and occupational therapist assist patients to identify and adapt activities that provoke pain. The program consisted of a 16-week treatment period during which patients were treated weekly in week 1-4, once every two weeks in week 5-8 and monthly in week 9-16. Each treatment session involved one hour occupational therapy and one hour physical therapy.

In 2013 a pilot study (n=8) was conducted to evaluate the effectiveness of the multidisciplinary rehabilitation intervention for persons with NA [9]. Results showed significant and clinically important differences on participation (performance and satisfaction) scores on the Canadian Occupational Performance Measure [13] as well as significant improvement in self-reported shoulder function, pain and activities of daily living performance. However, patients did not report improvements in strength nor a decrease in fatigue [9]. These results are encouraging and support the need for further studies, with more robust methodology and larger samples. As our ability to diagnose the disorder in a timely and adequate manner improves, the number of patients requiring treatment is increasing as is the need for new multidisciplinary teams to provide care. Understanding the critical ingredients of the programs' effectiveness will facilitate replication at other centers.

The aim of this study was, therefore, to gain insight, from the perspective of both patients and therapists, into the aspects of the integrated rehabilitation program that positively contribute to the improvements in activity and participation. The research question was "what are patient and therapist reflections on the rehabilitation program; how do they identify and value the program ingredients and understand their contribution to their outcomes?"

Materials and methods

Design of the study

This qualitative study employed interpretative epistemology and hermeneutic methodology [14] whereby patients' and therapists' reflections were used to interpret and give meaning to the different ingredients of the rehabilitation program. The study was conducted in 2012 and 2013, using semi-structured interviews.

Participants and context

After receiving ethical approval from the Medical Ethics Committee of Radboud university medical center (registration number 2012/510), participants were recruited. All patients and therapists, who participated in the pilot study to evaluate the effect of our integrated rehabilitation program [9], were approached. All eight patients met the inclusion criteria: 1) diagnosed with NA; 2) uni- or bilateral complaints with pain scores on the numeric rating scale [15] of more than 5; 3) at least 6 months after onset; 4) aged 18 years or over; and 5) able to understand written and spoken Dutch. Each received a telephone call inviting their participation and requesting permission to send information about the study. All gave their permission. Five of the six therapists who delivered the program (two physical and three occupational therapists) also agreed to participate. One physical therapist was unavailable because of maternity leave. All potential participants (patients and health providers) received a letter describing the study. Patients received a follow-up phone call by a research assistant one week later. Willingness to participate was re-confirmed with all providing informed consent. To preserve anonymity, demographic variables of participants (patients and therapists) are band into categories (see table 1 and 2). Patient participants varied in age, sex, affected arm and time between onset of NA and start of the treatment. Six males and two females ranging in age from 34 to 62 years participated. Time between onset of NA and start of the treatment varied from 7 to 156 months; five patients had NA of the dominant arm/shoulder. Therapists also varied; four were females, and years of experience with NA ranged from three to nine years.

Table 1: Demographic data of patients

Patient	**Age in years [30-40]**	**Age in years [40-50]**	**Age in years [50+]**	**Dominant arm also affected arm?**	**Time between onset NA and start treatment in months [0-12]**	**Time between onset NA and start treatment in months [13-24]**	**Time between onset NA and start treatment in months [25+]**
1	X			Yes			X
2	X			Yes			X
3			X	Yes	X		
4	X			No		X	
5			X	No	X		
6			X	Yes	X		
7		X		Yes	X		
8		X		yes		X	

Table 2: Demographic data of therapists

Therapists	**Age in years [20-30]**	**Age in years [30-40]**	**Age in years [40-50]**	**Years of experience in treatment of patients with NA [0-6]**	**Years of experience in treatment of patients with NA [7-12]**
1			X		X
2		X			X
3	X				X
4		X		X	
5		X		X	

Data collection procedures

Two semi-structured interview guides (one each for patients and therapists) were developed. Both used nondirective, open-ended questions. Interviews with patients were held in their chosen environment (typically their home), so they would feel at ease [16, 17]. Two patients preferred an interview at Radboud university medical center, for practical reasons. Interviews with all therapists were held at Radboud university medical center. Duration of the interviews was approximately 1 hour and interviews were performed by four research assistants. Each interview was conducted by two research assistants; one led the conversation and the other made notes, observed and assisted in the use of the recorder. Research assistants are occupational therapy students from the HAN University of Applied Sciences, who received training in conducting qualitative research.

At the beginning of every interview, the aim of the research, procedure of the interview and privacy policy was explained. There was also opportunity to ask questions and informed, signed consent was obtained. Patients were invited to talk about their experience with the integrated intervention program and specifically about their experience with occupational therapy and physical therapy. They were asked to identify and describe aspects of the program that helped them the most and aspects of the program they would like to change. Therapists were also invited to talk about their experiences with the integrated rehabilitation program. Specific topics were perceived effectiveness of the treatment and changes in patients' level of activity and participation during the program. The therapists were also asked to report on factors they perceived contributed to the success of the program and aspects of the program they would like to improve.

Data analysis

Interviews were audio taped and transcribed. For data-analysis, transcripts were imported into Atlas.Ti 7.1.5 software. The constant comparative method was used for the analysis [14, 17]. Analyses of the transcripts were performed by the first and last author.

Analysis consisted of four steps. 1) Familiarization with the interviews was achieved by reading the transcripts several times. 2) This was followed by open coding of each transcript. To improve credibility, two interviews were first coded separately by the first and last author. Codes were then compared and discussed until consensus was reached. The high level of similarity in coding meant other interviews could be coded by only the first author. 3) After the open coding of all interviews, coded text was grouped into categories with patient and therapist text analyzed separately.

4) Finally, comparison and grouping of the categories led to final themes. The created themes were discussed with two other co-authors (with external perspective) and refined as described by the first author [18].

Trustworthiness

To enhance the trustworthiness of the study [19, 20] coding was performed by two researchers, the first and last author. Categories and themes were discussed in meetings with two other co-authors (with external perspective). Triangulation occurred by inclusion of two perspectives; perspective of patients as well as the perspective of therapists.

The research assistants were unfamiliar with the patients they interviewed. They did know one occupational therapist, since she held dual roles of researcher (first author) and participant therapist. Two co-authors provided an ‘outsider perspective’ as they were not familiar with the program and/or organization, while the first and last author, both familiar with the content and organization of the program, provided an ‘insider perspective’. During the analysis, this enhanced the dialogue about the similarities within and differences between the categories, adding additional credibility [19]. The other authors were members of the Plexus Clinic (physical therapist, neurologist and rehabilitation physician) and also contributed to the data, interpretation and review of the manuscript. The physical therapist was also a participant in the interviews from therapists’ perspective, as well as co-author.

Results

Analysis led to five ‘patient themes‘ and five ’therapist themes‘. These themes represented aspects or ingredients of the rehabilitation program that, from the different perspectives, contributed to the improvements in activity and participation (figure 1). Participants placed equal value on all themes, seeing all as required for successful outcomes. Patients and therapists shared the strong view that the overall result of the program finds the patient being in charge and able to self-manage (see final theme for both patients and therapists in figure 1). Each theme will be described, supported by quotes of the participants. Patients and therapists are given a number to ensure anonymity. Following the quotes, the number of participant is put in brackets to show that the quotes are from different participants.

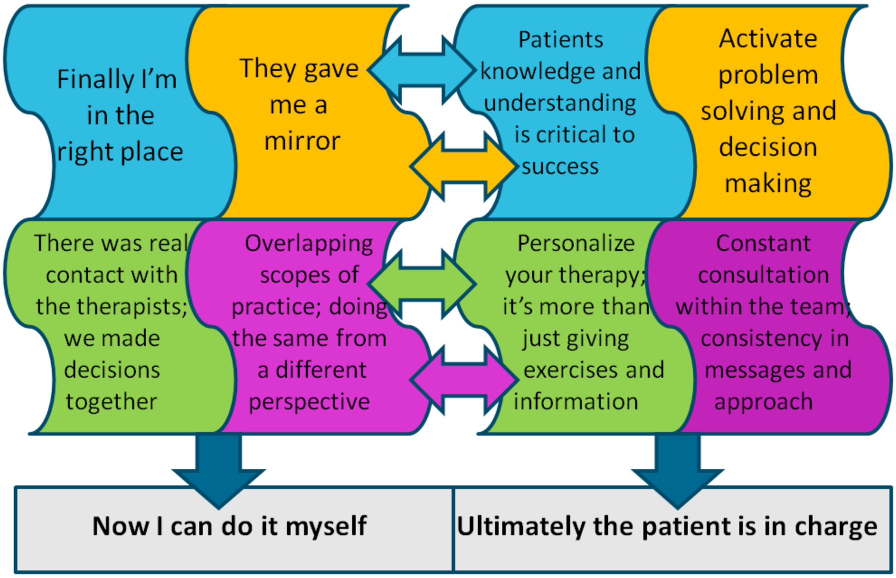

Figure 1: Findings from patients' perspective (pieces with themes on the left side) and from the perspective of therapists (pieces with themes of the right side).

Patients' themes

Time to diagnose: "Finally I'm in the right place"

Nearly all patients talked about the onset of the disease and how long it took for them to receive the right diagnosis. The unfamiliarity with the disease among physicians and therapists elsewhere was often reported, together with the uncertainty and frustration this created. Only a few patients had met physicians and therapists who knew what to do and how to treat their problems. Nearly all described the importance of finally being in the right place when they talked about the Plexus Clinic (i.e. a place where health professionals knew their condition and their problems), which gave them confidence and a sense of being understood.

"You are in the right place, where people know what it is, recognize it and do something about it. They can help you to manage, so you have the least burden" (patient 8)

Knowledge of the team was also reported to be an important aspect of being in the right place. Patients felt taken seriously and reported a sense of trust that therapists had the expertise to support them in the management of their disease.

“There was so much experience, I only had to say something and it was put back to my situation. Nine out of 10 times I was reassured and therefore helped” (patient 7)

Awareness: “They gave me a mirror”

During the interviews patients expressed in different ways how the program helped them to become aware of the relationship between their complaints and the performance of their activities. They gained insight into how their own actions and behaviors could trigger or exacerbate their symptoms. They also learned how to make the changes needed to reduce the pain and fatigue and improve their movements.

"Becoming aware is very difficult. I'm not a disabled person. I can still work, but I realize now that I have limitations" (patient 5)

“They gave me a mirror and taught me to pick up the thread" (patient 8)

Many patients described learning to change their routines. One patient reported that she could “not go on” in the same way she had been doing. She realized her complaints were not going to go away by ignoring them, nor by massaging or strengthening the muscles. Patients became aware of their movement patterns, what they were doing during the day and how they did it; how to lift the groceries, how to sit in the car or how to brush their teeth. Knowing how the performance of tasks could affect their pain was new. They also said that this awareness was exhausting and difficult, but necessary.

Some said that they missed the support of a psychologist during this difficult process.

"An improvement would be to engage a psychologist, because in my case I had to ‘flip a switch’. I thought I was in control of my body, but no, the body is in control of you" (patient 8)

For all patients it was important to learn what to do and what to avoid. The program required patients to adapt many aspects of life, such as changing the performance of their activities and the way they organize their day. One patient said that the information and explanation of the disease in relation to his functioning was enough motivation to change the way he was coping with his problems.

"They explained why it was the way it was, that was enough motivation for me" (patient 6)

Patients also expressed how they had become more conscious about the need to listen to their body, take breaks, analyze, adapt and prioritize their activities and roles.

Patients also mentioned “learning to do things in another way”. To implement the physiotherapy exercises into daily life, they had to continuously focus on “what am I doing? And how am I doing this?”

"Taking breaks, doing things in a different way. Being much more conscious of managing your body and listen carefully [to the body]" (patient 1)

Partnership: “There was real contact with the therapists”

Patients talked about “having real contact with the therapist”. They valued the attention and interest that the therapists showed in them as a person. One patient described how he was not just a number for the therapists, but a real person. Patients said that the therapists gave them the right perspective and made them think about the important and meaningful aspects of life.

"… I have started to think about what is really important …. This happened to me and it made me realize what is most important in my life. Is it important to ride my bike in the evening or do I want to be there for my family?" (patient 8)

Patients also felt they were part of the program that was tailored to their individual needs. There was interaction with the therapists about *their* aims and priorities and what the therapist thought to be important. Decisions were made together.

"We discussed what she thought was important and what I thought was important, there was clear agreement" (patient 4)

Close collaboration: “Overlapping scopes of practice; doing the same from a different perspective”

One of the aspects that almost every patient talked about was the collaboration within the team. They described the program as a “complete package”. Therapists complemented each other and worked across the boundaries of their professions, which was appreciated by the patients. One patient described the importance of getting the same information from different perspectives which helped in applying tips and advice in everyday life.

"The physical therapist and occupational therapist work across the boundaries of their field of expertise; hearing the same from different perspectives has added value" (patient 6)

Several patients expressed that they had experienced how both therapists (physical and occupational) had their specific expertise but worked together towards the patients' goals. They valued the evaluations and the constant dialogue between both therapists during the treatment.

"The talks to transfer the findings in between [consultations] and share this with each other, joint decision making, that is the perfect mix" (patient 6)

The disease specific aspects of therapy were also addressed by the patients; the value of the specific exercises they learned and applied in daily activities, ergonomic advice, the implementation of mini-breaks and the importance of pacing activities during the day and week. This was described as a process of learning to integrate advice and exercises into daily routines. They valued that both the occupational and physical therapist coached them from their own specific expertise. Patients said that this process was difficult but important to reducing their pain and fatigue.

"It involves all those little things, but those are the things giving you the most trouble; for example, cooking is still a burden, however, a lot less than in the beginning "(patient 2)

"Exercises are implemented into the daily movements. If I wash my hair, I'll keep that in mind. You learn a completely different movement pattern "(patient 1)

Self-management: "Now I can do it myself"

Patients described how the therapists provided them with tools to manage themselves in daily life. They reflected how important it was to know the aim of the exercises and to learn to feel whether their movement patterns were correct or incorrect. It was important to link this to learning to pacing and planning.

"You learn to feel when you move incorrectly or when your body needs a break" (patient 1)

One patient said that although she was provided with the right tools to improve functioning, there were still moments when it went wrong. She felt that the tools then helped her to regain control.

There are still times when it goes wrong, but now you know what you can do to make it better" (patient 2)

A few patients said that they had had other expectations of physiotherapy at the start of the treatment. They thought it would be more massage and a physical training program. Some of them expressed the desire to have more massage in the program.

This last theme from the patients' perspective also included their reflections of the importance of being able to live and manage their life with NA. Nearly all patients described how their own role and responsibility in the treatment had gradually increased.

"They teach you to pick up the thread bit by bit, that's why there is gradually more time between the appointments, in order to see how long you can manage yourself" (patient 1)

"Now (when therapy is finished) I need to do it myself" (patient 5)

Patients also expressed difficulties with this responsibility. Some patients said that this way of therapy 'needs to fit you in order to be effective', because it is demanding and not everybody is able to take on this responsibility.

"Both (occupational and physical therapist) expect an 'iron discipline' of the patient, that has to fit you" (patient 6)

A few patients mentioned that they would have appreciated peer support to learn from others and share experiences how to manage themselves.

Therapists' themes

"Patients knowledge and understanding is critical to success"

Most therapists stressed the importance of patients understanding their disease process and its consequences. They said that the effectiveness of the therapy is greater when patients understand why they continue to experience limitations, even when the period of inflammation and neuropathic pain is over. According to the therapists, patients need to understand which factors contribute to the persistence of the symptoms and what they can do to influence these factors. The therapists feel that this is essential in regaining control over the symptoms and the limitations patients experience.

"The effect has to do with whether people understand it; the pain is no longer due to the acute NA, but due to the overload that follows. When people do not understand their contribution to their symptoms, the treatment is less effective " (therapist 2)

Most therapists believe that knowledge and understanding supports patients' motivation to change their behavior.

"People make their own choices, that's why it is very important that they understand why certain things are the way they are; then the motivation to change behavior is completely different " (therapist 2)

"Activate problem solving and decision making"

This theme focused on activating patients; informing them, allowing trial and error and letting them experience where things go wrong and where there is scope for improvement. Therapists reported how they coach their patients to find their own solutions to the problems they experience. This was felt to be the best way to change behavior. Nearly all therapists addressed the value of shared decision making. They reported how they had seen the positive effects when the patient is made a partner in decisions regarding treatment goals and interventions.

"When someone finds his own solution, it will fit best with his strategies" (therapist 1)

Motivational interviewing techniques were reported to be very helpful in this process.
"Let people decide for themselves what they want to work on; make the patient your partner in the treatment, that is the largest advantage of motivational interviewing" (therapist 5)

"Personalize your therapy; it's more than just giving exercises and information"

Therapists stated that all patients are taught similar exercises and strategies, but these are personalized to their specific complaints, daily tasks and life roles.

"The treatment itself is not unique, but it is adapted to the patient. Everyone gets broadly the same, but not exactly the same" (therapist 5)

They said that even though all patients are educated on exercises, ergonomics and finding a balance between activity and rest, there is no 'one size fits all'. Patients are not just given exercises and information, but it is always tailored to the personal situation.

"Most successful is continuously linking [treatment] to someone's specific situation. Not only providing training and giving information" (therapist 2)

"Constant consultation within the team; consistency in messages and approach"

All therapists addressed the value of the multidisciplinary team. Working together towards the same goals, from each professional perspective is seen as a key to success. Therapists said that it is important for the patients to receive the same messages several times. They think that “hearing a similar message, from a different point of view” increases the success of the therapy.

"The strength of the treatment is the collaboration; the power of repetition and approaching something from another perspective in just a different way" (therapist 1)

*"It is the combination of technical exercise therapy with behavioral aspects" (Therapist 5)*Both therapists (occupational and physical) felt that they complemented each other. For example, when the physical therapist trains the scapula position while sitting, the occupational therapist pays attention to the appropriate seating. The therapists described working intensely together and informing each other about the progress, successes and areas of focus so that each can continue to address these aspects from their own perspective.

"I cannot imagine that you would do this separately; one and one is more than two, in this case " (therapist 2)

“Ultimately the patient is in charge”

In this last theme, therapists stressed the responsibility of the patients. Therapists said that they could only provide the patients with information, tools and support. However, in the end, it is the patient who needs to implement the strategies and exercises in his/her daily life in order to regain control.

"You hope that everybody can take matters into their own hands again and can go further by themselves, that they no longer need you" (therapist 2)

It was generally felt by the therapists that giving responsibility to the patients had an empowering and motivating effect on them.

"Success (of the therapy) because you give the responsibility to the patient, they want to get better, we teach them the tools. That motivates" (therapist 4)

However, several therapists felt that not all patients were happy or able to take this responsibility. Some patients continue to expect that the therapist can ‘treat’ the complaints instead of coaching them to become in charge of their own complaints.

Discussion

The current study sought to understand the critical ingredients of an integrated rehabilitation program for patients with NA in order to better understand what contributes to patient outcomes. Three important insights have emerged:

1. Patients and providers identified similar ingredients, though from separate perspectives. These ingredients align with self-management of other chronic conditions.
2. Patients and therapists strongly endorsed shared decision making and a partnership model of care delivery. From a patient perspective this means focusing on their goals and priorities. From a provider perspective it means contributing both professional and disease specific expertise.
3. Patients and providers both recognize that ultimately it is the patient who must take control in order to manage everyday life with a chronic condition.

The ingredients that have been identified by patients and therapists in the themes correspond well with self-management skills as identified by Lorig and Holman [21], which include problem solving, decision making, appropriate resource utilization, forming a partnership with a healthcare provider, and taking necessary actions and self tailoring. Both the patient self-management skills and the method of care delivery are consistent with components of the chronic care model [22]. This model is predicated on the belief that productive interactions between an activated patient and a prepared and proactive team, are essential for positive outcomes. Participants in this study endorsed this view and provide empirical evidence to support the model. In Figure 1 these productive interactions are illustrated by the arrows between the aspects identified by the patients and the aspects identified by the therapists and by the shared fifth theme. Patients valued the "proactive team" identifying how both the occupational and physical therapist contributed their specific expertise while still engaging in close collaboration so that patients received a consistent message from different perspectives. It should also be considered that other therapeutic characteristics, such as taking time with the patients, being open, listening, and being empathic, also can contribute to the perspective of the patients. Recognition by the professional of client values underlying their needs (uniqueness, comprehensiveness, continuity of life, fairness and autonomy) and underlying the care-relationship (equality, partnership and interdependence) has been identified as a central element within the interaction [23]. Feelings of recognition with the client seem to reinforce autonomy, self-esteem and participation. Recognition is optimally felt in a dialogue. Four professional competencies have been identified by Schoot et al. [23] related to recognition: attentiveness (ongoing actions to know and understand the patient); responsiveness (active, committed and responsible care guided by respect of patient identity); being a critical partner in care (giving and grounding professional opinion and discuss boundaries); and being a developer of client competencies (facilitating and developing client participation within care) [23].

The disease specific content of therapy (not specifically identified as a theme) was often alluded to by patients within the different themes. These included the specific exercises, the need for minibreaks, and the planning and pacing strategies they learned and applied in daily activities in order to regain control. However, the first theme strongly emphasized the importance of the expertise of the team. Patients sense of "being in the right place" spoke of their relief in finding knowledgeable and skilled clinicians that was in sharp contrast to the distress they had experienced when searching for a diagnosis, understanding and effective interventions.

There were at least three recommendations to improve the quality of the program. Some patients missed the potential support that a psychologist might offer during the exhausting and difficult process of becoming aware that they needed to change their behavior. Self-management is often described as medical, role and emotional management [21]. This program appears to explicitly support the first two with less explicit emphasis on emotional management an aspect that patients highlighted as important. Future consideration should be given to enhancing the program through additional aspects of emotional support.

The second aspect was the fact that, for some patients, this program's focus on self-management, did not appear to fit their needs. Patients expressed that this approach warranted an iron discipline and several therapists felt that not all patients were able to take this responsibility. Ways to support patients, perhaps with more time or coaching to become ready to change, may need to be considered.

Finally, a few patients would have appreciated peer support, for which a group intervention could be recommended. A large advantage of a group intervention would be that participants would see people similar to themselves manage task demands successfully, which contribute to people's belief in self-efficacy. This is also referred to as vicarious experiences provided by social models and is one of the four main sources of self-efficacy [24]. The other sources include mastery experiences, social persuasion that one has the capabilities to succeed and inferences from somatic and emotional states indicative of personal strengths and vulnerabilities. The final theme from the perspective of both patients and therapists is the ability to manage and be in charge which can be referred to as achieving self-efficacy. To achieve this, people go through a process in which the therapists support them to gain mastery experience. This is achieved by experiences in overcoming obstacles through perseverant effort. As Bandura [24] states, ‘setbacks and difficulties in pursuits serve a useful experience that success usually requires sustained effort. After people become convinced they have what it takes to succeed, they persevere in the face of adversity and quickly rebound from setbacks’. In the current program people go through this process by themselves, whereas a group program would add an additional source of efficacy with peer experiences.

Although the program was individualized in the sense that attention was paid to the personal situation and goals from the patients, the intensity of the program (number of sessions and duration of intervention period) was more or less ‘one size fits all’. This aspect needs more consideration in the future. Audulv [25] has found that self-management does not develop as one uniform pattern. Instead different self-management behaviors are enacted in different patterns, which can be distinguished as consistent, episodic, on demand, and transitional. It is likely that self-management activities require support strategies tailored to each behavior's developmental pattern.

Strength of this study was that all patients from the pilot study [9] participated in this study. Apart from one physical therapist, who was unavailable, all therapists on the team also participated. Collecting the perspective of patients and professionals (physical and occupational therapists) has been done in other studies [26] and allowed strong triangulation [27] of the data and findings. In the future it would be interesting to add the perspective of the neurologist and rehabilitation physician who are also part of the integrated team. Because partners and close family members are also affected, their inclusion would also add a valuable perspective.

We limited our sample to patients involved in the original pilot study, creating a limited sample to draw from. Fortunately, all eight patients and five out of six therapists were available for this current study. During the analysis, we found repeating patterns of the same experiences suggesting that saturation had been reached [27], despite the limited sample.

The fact that the primary researcher was also a member of the Plexus Clinic and integrated rehabilitation program has both strengths and limitations. As part of the team this might have introduced a positive bias into the research process. On the other hand, intimate knowledge of the program brings inside knowledge to the analysis and interpretation of both patient and therapist data. To mitigate potential bias, all interviews were conducted by independent research students trained in interviewing who were at arm's length from the team. In addition, the research team was strengthened with two experienced researchers who participated in the analysis and interpretation of the findings from an outside perspective.

Conclusions

The current study investigated the critical ingredients of an integrated rehabilitation program for patients with NA from the perspective of patients and professionals. The expertise and close collaboration of the team members was an important aspect which contributed to the trust, confidence, understanding, awareness and ability of patients to actively regain control of their everyday activities and participation. Working in partnership coupled with shared decision making led to a personalized approach that was valued by patients and emphasized by therapists as essential to successful outcomes. The critical ingredients can be summarized as a combination of supporting patient self-management skills coupled with disease and profession specific expertise delivered in a collaborative partnership approach. Some patients would have liked more emotional support and some might have needed a more flexible and tailored approach regarding the intensity of the interventions provided. These qualitative results further inform the results of the original pilot study. It appears from both patient and provider perspectives, that the integration of the named ingredients provide the patients with confidence to take responsibility to manage their condition in their everyday lives. For application of the interventions in other health care settings these ingredients are important to consider.

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Chapter 5

Patient-generated graphs to measure pain and fatigue in persons with neuralgic amyotrophy

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Abstract

Background

Patients with neuralgic amyotrophy (NA) often experience limitations in daily activities due to pain and fatigue. Visual analogue graphs with a 24-hour x-axis can be used to rate pain and fatigue severity during a typical day. This study aimed to investigate the reliability and validity of the visual analogue graphs in patients with NA.

Method

Eight patients completed pain and fatigue graphs on three moments to examine inter-rater and test-retest reliability using Intraclass Correlation Coefficients (ICCs). Concurrent validity (n=47) was tested by determining correlations between mean pain graph scores and Numerical Rating Scale for pain (NRS-pain) and between mean fatigue graph scores and checklist Individual Strength-subscale fatigue (CIS-fatigue).

Results

ICC for test-retest reliability varied from 0.72 - 0.93 for pain and 0.67 - 0.85 for fatigue scores. ICC for inter-rater reliability varied from 0.76 - 0.97 for pain and 0.47 - 0.97 for fatigue scores. Correlation between the mean pain graph score and NRS-pain was strong ($r_s = 0.75$, $p<0.000$); correlation between the mean fatigue graph score and CIS-fatigue was moderate ($r_s=0.42$, $p=0.003$).

Conclusion

The visual analogue graph for pain appears reliable and valid in patients with NA. Test-retest reliability and concurrent validity for the fatigue graph warrant further research.

Introduction

Neuralgic amyotrophy (NA) is a common peripheral nervous system disorder with a higher than presumed incidence of 1 per 1,000 per year [1]. Nevertheless, it is often missed and/or misdiagnosed [2]. NA is characterized by episodes of severe neuropathic pain at onset, followed by multifocal paresis and atrophy [2, 3]. More than half of patients with NA are restricted in their daily activities by pain and paresis causing scapular instability and problems with reaching, overhead activities, maintaining static arm positions and repetitive movements. At least 60% of NA patients experience severe fatigue restricting performance of daily activities and roles [4]. The exact onset and pathophysiology of NA are still unknown. Most evidence points to NA being an auto-immune disorder, in which several independent predisposing factors lead to the occurrence of an actual episode. An underlying sensitivity makes patients more vulnerable than the general population. Mechanical factors also seem to play a role as strenuous activity or local trauma can trigger an attack, and NA patients are more often physically active than the general population.

The Radboud university medical center hosts a national expert outpatient Plexus Clinic for patients with complaints and restrictions as a result of brachial plexus pathology, mainly patients with NA. Patients are mostly referred by neurologists or primary care doctors, weeks to years following the onset of their complaints. During their visit to the outpatient Plexus Clinic, patients are seen by a neurologist, rehabilitation physician, physical therapist, and occupational therapist (OT) for assessment and advice regarding self-management and treatment options. The focus of the rehabilitation is to treat secondary complaints caused by loss of muscle function [5]. This loss of muscle function can result in impaired humero-scapulothoracic coordination, scapula alata (winging of the shoulder blade) and increased fatigability of the muscles, leading to compensatory movements, and limitations in everyday life. From clinical experience we know that in more than half of the patients, initial weakness of the serratus anterior muscle leads to compensatory, alternative positioning and movement of the scapula in the post-acute and chronic phase. This puts greater strain on the kinetic chain and causes musculoskeletal pain in the compensating muscles, which are mainly the downward rotators of the scapula. Over time, the strength of the serratus anterior muscle often returns, but this does not automatically lead to a reduction of scapular dyskinesia, compensatory movements and related pain and activity limitations. The persistence of scapular dyskinesia in patients with NA has been researched by our research group in a study done by Lustenhouwer et al. [6] and was linked with cerebral changes, suggesting that these issues are at least in part caused by motor control deficiencies.

Main overall goal of the first OT consultation is to identify whether there is an indication for occupational therapy. A substantial amount of time is spent on explaining and educating about the disease itself, the consequences for the management of the complaints and what an occupational therapist can contribute to support people with NA. The OT interviews the patient to gather insight into the daily life of a person, which is achieved by asking to describe a typical day. Another focus is on understanding and gaining insight into the reciprocal relationship between the symptoms of NA and the performance of daily occupations; i.e. how NA pain and fatigue restrict or impact everyday activities and how everyday activities can themselves exacerbate or prolong NA symptoms. To indicate, and make explicit, the severity of their pain and fatigue, OTs at the Plexus Clinic ask patients to think about their pain and fatigue during a typical day with use of two graphs. The x-axis shows a 24-hour scale, and the Y-axis indicates the severity of symptoms (10-point scale). The patients complete these pain and fatigue graphs, which are clinically very useful as they provide patients and therapists with insight into the pattern and severity of pain and fatigue during a typical day. This visual representation of complaints provides a tangible way to explore and discuss possible relationships between experienced pain and/or fatigue and activities in daily life. By exposing this relationship, options to intervene or alter unhelpful behavioral patterns become explicit. Although there are many instruments for measuring pain and/or fatigue, none of these instruments provide insight into the pattern of these complaints during the day or the relationship to patient-specific daily activities. The pain and fatigue graphs, therefore, go beyond simply measuring perceived pain and fatigue; they provide valuable information to both patient and therapist about the temporal pattern of symptoms during the day. Whether or not these graphs can be used as outcome measures to evaluate effectiveness of interventions aimed at reducing NA-related pain and fatigue has not yet been investigated. A dual role of informing patient/therapist decision-making and measuring effectiveness would add to their value in patient care. The aim of this study, therefore, is to investigate inter-rater and test-retest reliability as well as the concurrent validity of the pain and fatigue graphs in patients with NA.

Methods

Two separate studies were performed:
1. A reliability study to investigate the inter-rater and test-retest reliability, and
2. A validity study using data from an existing prospective cohort study to investigate the concurrent validity of the graphs.

In the *reliability study* the pain and fatigue graphs were completed three times to examine inter-rater reliability as well as test-retest reliability.

For the *validity study*, concurrent validity of the fatigue graph was tested by examining the correlation between the mean fatigue graph score (see below) and the Checklist Individual Strength - subscale fatigue (CIS-fatigue) [7]. Concurrent validity of the pain graph was tested by examining the correlation between the mean pain graph score and the Numeric Rating Scale (NRS) for pain [8].

Participants

Patients were included if aged 18 or older, diagnosed with NA of the brachial plexus by a neurologist and had sufficient command of the Dutch language to understand instructions and complete questionnaires. Patients were excluded if they were diagnosed with concurrent neurological or orthopedic disorders affecting the upper extremities.

In the *reliability study*, eight patients, two OT research students and three OTs, practicing in the Plexus Clinic, participated. All patients and OTs gave written, informed consent. According to the Dutch rules and regulations, ethical approval for the reliability study was not required [9]. For this reliability study, patients already scheduled for the outpatient Plexus Clinic were invited to participate through an information letter (with pain and fatigue graphs added as attachments) and a consent form sent to their home address prior to the appointment at the outpatient clinic. The treating OT of the Plexus Clinic team telephoned the patients and asked permission for the OT research students to contact them by telephone to answer questions about the study, and to ask if they were willing to participate. Eleven patients were contacted, of whom eight gave their informed consent.

For the *validity study*, data was used from 47 patients enrolled in a prospective cohort study approved by the medical ethical committee (CMO 2012/456). Participants in this prospective cohort study, were referred to the Plexus Clinic by their neurologist or general practitioner and each received a set of questionnaires to complete as part of usual care and prior to consultation at the outpatient Plexus Clinic. Together with the questionnaires, patients received an information letter about the cohort study and a consent form. Informed consent was obtained at the outpatient Plexus Clinic appointment.

Instruments

Pain and fatigue graphs

Patients were given a piece of graph paper (1 by 1 cm squares) with 24 hours of the day (starting at 6:00 AM) marked on the X-axis (Figure 1). The Y-axis represented severity of either pain or fatigue, with a scale from 0 (no pain/fatigue) to 10 (maximum pain/fatigue).

Instructions that were given to the patients while completing the graphs, were described in a protocol. Instructed to think about a typical, ordinary day, patients were asked to indicate the severity of pain/fatigue typically experienced upon waking in the morning, by placing a corresponding dot on the graph paper. They were asked to continue placing dots on the graph paper for each hour of the day indicating the severity of their pain or fatigue at each hour of day. The line graph was completed by connecting the dots (figure 1).

To obtain an overall pain or fatigue score, the sum of the hourly scores divided by the number of hours was calculated, referred to as the mean graph score. Hourly pain and fatigue scores were calculated using 0.5 increments from 0.0 to 10.0. When the line on the graph fell between intersecting points, the closest increment of 0.5 was recorded; if there was an equal distance between the closest increments, the highest score was recorded.

Numerical Rating Scale (NRS)

The NRS is a frequently used self-reported measure of pain that reliably measures pain intensity and pain distress in people with persistent pain [8, 10]. Patients give a single score for pain severity at the time of administration (pain at that moment), ranging from 0 (no pain) to 10 (worst possible pain).

Checklist Individual Strength, subscale fatigue (CIS-fatigue)

The CIS-fatigue is a subscale of the CIS20R and measures the self-reported severity of four fatigue dimensions as well as fatigue impact [7, 11]. The CIS-fatigue consists of 8 items, scored on a 7-point Likert scale, assessing fatigue experienced during the previous 2 weeks. A cut-off score of >35 indicates severe experienced fatigue [12].

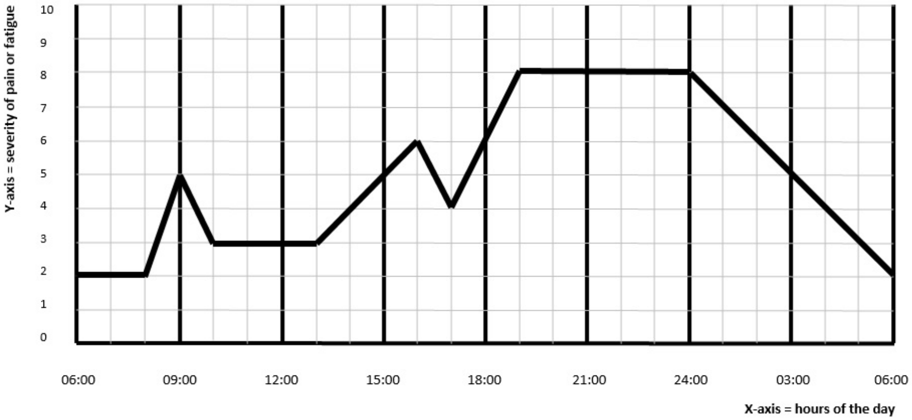

Figure 1. Example of one completed patient-generated fatigue graph

Procedure

For the *reliability study*, graphs were completed three times by each patient (see table 1). Standardized instructions were given to all patients. The first administration was one to five days prior to the first scheduled appointment at the outpatient Plexus Clinic. Patients received a telephone call from one of the OT research students. During this call, the OT research students provided instructions on how to complete the pain and fatigue graphs and asked the patients to bring the completed graphs to the Plexus Clinic appointment.

During the OT consultation at the outpatient Plexus Clinic, the Plexus Clinic OT asked patients to complete the graphs for pain and fatigue for a second time as part of usual care (2nd administration). Finally, directly after the Plexus Clinic consultations (a minimum of one and a maximum of three hours after the 2nd administration), the same OT research student who had previously contacted the patient by telephone (1st administration) asked the patient, face-to-face, to complete the graphs once more (3rd administration).

Table 1. Procedure for administering the pain and fatigue graphs

	Location	**Format**	**Rater**
Administration 1	Patient at home	Telephone	OT research student
Administration 2	Patient at Plexus Clinic	Face-to-face	Occupational Therapist
Administration 3	Patient at Plexus Clinic	Face-to-face	Same OT research student as administration 1

OT = Occupational Therapy

For the *validity study,* patients received a set of questionnaires two weeks before their visit to the outpatient Plexus Clinic. During the OT consultation at the outpatient Plexus Clinic, patients filled out the pain and fatigue graphs once.

Statistical Analysis

To examine *test-retest reliability*, the graphs completed during the 1st and 3rd administration were compared. To test *inter-rater reliability*, the graphs completed during the 2nd and 3rd administration were compared (see table 1). There was blinding from data collection to data analysis. The Intraclass Correlation Coefficient (ICC) (1,k = one-way random effects model) was selected for analysis, because patients were considered to represent the larger population of patients with NA and raters were considered to represent the larger population of raters. Not all raters rated each patient, also indicating the need for a one-way random effects model. Not all data points in the pain and fatigue graphs were consistently available, due to variation in the time patients rose in the morning and went to bed in the evening. Therefore, only the hours for which ratings were available for all 3 administrations across the entire sample were analyzed. In effect, these were the hours from 11.00 AM to 8.00 PM. As each hour was treated as a separate measure of pain or fatigue, there were three ratings per hour (one for each administration). Both test-retest reliability and inter-rater reliability were tested by calculating the ICC at each hour for all three administrations. ICC values less than 0.5, between 0.5 and 0.75, between 0.75 and 0.9, and greater than 0.9 indicated poor, moderate, good, and excellent reliability, respectively [13]. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP. was used for all analysis.

To examine *concurrent validity*, the mean pain graph score at the time of the outpatient Plexus Clinic was compared with the NRS score completed as part of usual care and prior to presentation at the Plexus Clinic visit. Completion of the mean fatigue graph score and the CIS-Fatigue score mirrored these timeframes. Validity was assessed using two-tailed Spearman's Rho correlation coefficients. According to Akoglu [14], values less than 0.4, from 0.4 till 0.7, from 0.7 till 0.9, and greater than 0.9 represent weak, moderate, strong, and excellent concurrent validity, respectively. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. was used for analysis.

Results

Demographics

Patient characteristics for the reliability study and the validity study are shown in table 2. Patients are often referred to the Plexus Clinic for a 1st, 2nd, 3rd (or more) opinion. Therefore, patients arrive at the outpatient Plexus Clinic weeks to years following the onset of their disorder, which results in a large range in their 'duration of complaints'.

Table 2. Descriptive analysis: characteristics of the patients participating in the reliability and validity study

	Reliability study (n=8)	**Validity study (n=47)**
Sex: male/female	3 / 5	23 / 24
Age in years: mean ± SD (range)	45 ± 5.8 (33-53)	48.2 ± 14.4 (18-79)
Affected side(s): right / left / bilateral	5 / 1 / 2	17 / 17 / 13
Duration of complaints in months: mean ± SD (range)	32.6 ± 40.0 (4.5-120)	81.3 ± 128.9 (4-612)

SD = Standard Deviation

Reliability study

Test-retest reliability of the pain graphs (ICC range 0.72 - 0.93) was moderate to excellent and their inter-rater reliability (ICC range 0.76 - 0.97) was good to excellent (table 3).

Table 3. Reliability of pain and fatigue graphs

	Pain Graphs				**Fatigue Graphs**			
	PainTest-retest Reliability: (Administration 1 versus 3)		**PainInter-rater Reliability: (Administration 2 versus 3)**		**FatigueTest-retest Reliability: (Administration 1 versus 3)**		**FatigueInter-rater Reliability: Administration 2 versus 3)**	
Hour	ICC	95% CI	ICC	95% CI	ICC	95% CI	ICC	95% CI
11 AM	0.92	0.64 - 0.99	0.97	0.86 - 0.99	0.85	0.45 - 0.97	0.97	0.86 - 0.99
12 PM	0.82	0.36 - 0.96	0.86	0.50 - 0.97	0.83	0.42 - 0.96	0.96	0.83 - 0.99
1 PM	0.78	0.28 - 0.95	0.76	0.23 - 0.94	0.84	0.43 - 0.97	0.96	0.83 - 0.99
2 PM	0.72	0.13 - 0.94	0.82	0.37 - 0.96	0.84	0.43 - 0.96	0.89	0.59 - 0.98
3 PM	0.85	0.45 - 0.97	0.91	0.64 - 0.98	0.81	0.35 - 0.96	0.82	0.39 - 0.96
4 PM	0.93	0.70 - 0.98	0.91	0.66 - 0.98	0.79	0.32 - 0.95	0.66	0.04 - 0.92
5 PM	0.77	0.21 - 0.96	0.88	0.55 - 0.97	0.80	0.32 - 0.95	0.47	-0.24 - 0.86

Table 3. Continued

	Pain Graphs				**Fatigue Graphs**			
	PainTest-retest Reliability: (Administration 1 versus 3)		**PainInter-rater Reliability: (Administration 2 versus 3)**		**FatigueTest-retest Reliability: (Administration 1 versus 3)**		**FatigueInter-rater Reliability: Administration 2 versus 3)**	
6 PM	0.76	0.23 - 0.95	0.77	0.25 - 0.95	0.67	0.06 - 0.92	0.68	-0.02 - 0.91
7 PM	0.76	0.19 - 0.95	0.87	0.52 - 0.97	0.85	0.46 - 0.97	0.80	0.33 - 0.96
8 PM	0.91	0.64 - 0.98	0.89	0.60 - 0.98	0.82	0.37 - 0.96	0.95	0.78 - 0.99

ICC = Intraclass Correlation Coefficient, CI = Confidence Interval

Test-retest reliability of the fatigue graphs was slightly lower than for the pain graphs, with ICCs ranging from 0.67 - 0.85; within the moderate to good range. The inter-rater reliability (ICC range 0.47-0.97) was moderate to excellent (Table 3) across the day.

Validity study

The correlation between the mean graph score for pain and the NRS-pain score was strong (r_s=0.75, p<0.000). The correlation between the mean fatigue graph score and CIS-fatigue score was moderate (r_s=0.42, p=0.003), see table 4.

Table 4. Spearman Correlation Coefficients between outcomes on pain and fatigue graphs and outcomes with similar constructs

Mean graph score	**NRS-pain / CIS-fatigue**	**Spearman Correlation Coefficient**
Pain: 3.49 (SD 2.23)	3.79 (SD 2.57)	0.75, p<0.000
Fatigue: 4.14 (SD 2.33)	35.15 (SD13.90)	0.42, p=0.003

NRS = Numerical Rating Scale, CIS = Checklist Individual Strength, SD = Standard Deviation

Discussion

This study took the first steps in exploring the measurement properties (reliability and validity) of pain and fatigue graphs that are used as part of usual care in our outpatient Plexus Clinic to assess their value as patient-reported outcome measures.

Results demonstrated moderate to excellent reliability of both graphs. The five lowest (r < 0.75) ICC values (12.5% of all ICC scores) were found late in the afternoon between 4PM and 6PM. Four of the five low ICCs were for the fatigue graphs, particularly regarding inter-rater reliability (three ICC scores). It is possible that fatigue is most variable late in the afternoon, depending on the number and burden of activities completed during the day. However, this notion does not explain why variability of fatigue late in the afternoon would impact inter-rater reliability (assessed on the same day) more than test-retest reliability (assessed on different days). The test-retest interval was 1 to 5 days, which could have resulted in 'biological variability'. However, this source of variability was probably small, as patients were asked to report their average level of pain or fatigue on a 'typical day'. Most patients were experiencing a chronic phase of NA, making it possible for them to picture a 'typical day'. The variation in the inter-rater and test-retest reliability could be due to the level of pain and/or fatigue complaints the patient experiences. If a patient experiences extremely severe complaints or hardly any complaints while filling in the graphs, this could influence the scores of the graphs negatively or positively.

Concurrent validity, as shown by the correlation between the mean pain graph score and NRS pain score was strong (r_s=0.75). In addition, the graphs provide more clinical information than a single NRS score, for patients as well as for OT's. This supports patients and OT's with the opportunity for shared goal setting and action planning to influence the pain levels by addressing the performance of daily activities.

The correlation between the mean fatigue graph score and the CIS-fatigue score was lower than for pain (r_s=0.42), but still moderate. An explanation of the moderate correlation between the mean fatigue graph score and the CIS-fatigue score could be due to the multi-dimensional nature of fatigue [15]. Fatigue can be interpreted as physical or mental fatigue, fatigability or level of energy. This interpretation may have varied among patients when completing the fatigue graphs. For example, one patient may have considered fatigability of the arm during the day, while another may have scored their energy level during the day. Cognitive interviewing methodology [16] would be recommended to further understand how patients have interpreted fatigue when completing the graphs.

Another explanation may be that fatigue scores fluctuate during the day. Heine et al. [17] argued that measuring fatigue at a single time point may not be the best way to gain insight into experienced fatigue. The completion of our graphs took place at one moment in time (as recall), although patients reported the fatigue severity every hour during the day. Although in our current practice this method is valuable, it would be interesting to investigate if the graphs could also be used in a 'real-time format' (e.g. in an app) instead of a 'recall format' and what results this would produce.

This study aimed to explore whether the pain and fatigue graphs can also be used as outcome measures. In the literature, Murphy et al. [18] described how a personalized activity pacing intervention based on patients' recent symptoms and physical activity scores was more effective for reducing pain and fatigue than general activity pacing interventions. This supports the use of the graphs in clinical practice. This study showed that there is also potential for the pain and fatigue graphs to be used for other entities such as Facioscapulohumeral muscular dystrophy (FSHD) or other brachial plexus pathologies.

Study Limitations

One of the limitations of our study was the limited time interval between the two administrations used to assess inter-rater reliability. This time interval was 1 to 3 hours, which may have led to patients remembering the scores from the first measurement. However, patients receive so much information during all the consultations at the Plexus Clinic, it seems unlikely they would remember the scores given during the first administration of the graphs earlier that day.

We used different ways to administer the assessment of test-retest reliability. The first measurement was done by telephone, whereas the third measurement was done face-to-face by the same administrator. Based on the literature, we expected that these administration differences would have little influence on the test-retest reliability. In a study on the influence of various survey methods, there were no differences when comparing paper with online assessment or when comparing face-to-face with telephone assessment [19].

For the reliability study, datapoints from 11.00 AM to 8.00 PM were available in the entire sample. For the other time points (before 11.00 AM and after 8.00 PM) methods or strategies to score the time points while patients were sleeping were discussed but not resolved. Despite the limitations, this exploratory study has shown that standardized instructions are needed.

For the reliability study there was a small sample size. All patients who attended the plexus clinic during a four weeks period were approached to participate in the reliability study (this covered the period of data collection of the OT students conducting their thesis). Therefore, we strived for a representative target population. However, we have not tested if our study population accurately reflects the characteristics of the NA population of the Netherlands.

Conclusions

This article points at a dual purpose for the pain and fatigue graphs: gaining insight into daily patterns of NA-related complaints (clinical use) and obtaining a numerical outcome (evaluation and research purposes). The graphs have already showed their diagnostic value in daily clinical practice. This study is the first to explore whether the pain and fatigue graphs can be used as outcome measures as well. The results showed sufficient test-retest, inter-rater reliability and concurrent validity of the pain and fatigue graphs. Recommendations include further standardization in the scoring of waking and sleeping hours and the use of cognitive interviewing to gather insight into the type of fatigue that is being scored. Further research may also focus on the possibility of using graphs as real-time measurement tools (e.g. with an e-health application) and to assess their responsiveness and minimal clinically important difference in intervention research.

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Chapter 6

Effectiveness of an outpatient rehabilitation programme in patients with neuralgic amyotrophy and scapular dyskinesia: a randomized controlled trial

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Abstract

Background

Neuralgic amyotrophy (NA) is an acute inflammation of nerves within the brachial plexus territory leading to severe pain and multifocal paresis resulting in >60% of patients having residual complaints and functional limitations correlated with scapular dyskinesia. Our primary aim was to compare the effects of multidisciplinary rehabilitation (MR), focused on motor relearning to improve scapular dyskinesia and self-management strategies for reducing pain and fatigue, with usual care (UC) on shoulder, arm and hand functional capability in patients with NA.

Methods

In a non-blinded randomized controlled trial (RCT) patients with NA (aged ≥18 years, scapular dyskinesia, >8 weeks after onset) were randomized to either a MR or UC group. MR consisted of a diagnostic multidisciplinary consultation and 8 sessions physical and occupational therapy. Primary outcome was functional capability of the shoulder, arm and hand assessed with the Shoulder Rating Questionnaire-Dutch language version (SRQ-DLV).

Results

We included 47 patients with NA, due to drop-out there were 22 participants in MR and 15 in UC for primary analysis. The mean group difference adjusted for sex, age and SRQ-DLV baseline was 8.60 (95%CI: 0.26-16.94, p=0.044). The proportion attaining a minimal clinically relevant SRQ-DLV improvement (≥12) was larger for MR (59%) than UC group (33%) with a number needed to treat of 4.

Conclusions

This RCT shows that a MR program focused on motor relearning to improve scapular dyskinesia, combined with self-management strategies for reducing pain and fatigue, shows more beneficial effects on shoulder, arm and hand functional capability than UC in patients with NA.

Introduction

Neuralgic amyotrophy (NA) is a common (incidence 1:1000) [1] yet underrecognized and distinct peripheral nervous system disorder characterized by episode(s) of acute severe pain in the upper extremity [2]. An acute autoimmune inflammation of the nerves in the brachial plexus territory leads to multifocal paresis and recovery is usually slow and incomplete [3-5]. Two to three years after disease onset, 60% of patients have residual paresis, more than 50% are restricted by pain, 63% experience severe fatigue, and 82% have limitations in performing activities of daily living [6]. These residual complaints and functional limitations are strongly correlated with persisting scapular dyskinesia and increased fatigability of the affected muscles.

To date, there are no validated treatment options for NA, [5,7] although corticosteroid treatment in the acute phase appears to be effective [8,9]. Only in selected cases with demonstrated nerve narrowing, so called hourglass constrictions, surgical neurolysis may be indicated [10]. Usual care (UC) in patients with NA typically entails physical therapy with strength training, which in more than 50% has limited to no effect or can even aggravate symptoms [6]. Since More than 60% of patients with NA experience residual complaints [6,11] an effective intervention to improve daily activities and participation is essential.

As a relationship has been shown between scapular dyskinesia, increased fatigability and pain, [6] altered shoulder biomechanics may lead to strain of both paretic and compensating muscles, even when paresis is no longer present [5]. We recently empirically confirmed the clinical suspicion that cerebral (mal)adaptations play a role in this altered motor control and residual complaints in NA [12,13]. In a pilot study we showed a positive effect of a specifically designed multidisciplinary outpatient rehabilitation program (MR) combining physical and occupational therapy to address scapular dyskinesia and to manage residual complaints and limitations [14]. This MR focuses on improving motor control, scapular stability and coordination, combined with training self-management strategies for reducing pain and fatigue.

Here, we report a randomized controlled trial (RCT) to investigate whether the effects of this MR are more beneficial than the effects of UC on shoulder, arm and hand functional capabilities and with regard to residual complaints (pain and fatigue) in patients with NA and scapular dyskinesia.

Methods

Study objectives

Our primary aim was to compare the effects of a targeted MR to UC in patients with NA and scapular dyskinesia, directly after treatment. The primary outcome was self-reported functional capability of the shoulder, arm and hand assessed with the Shoulder Rating Questionnaire – Dutch Language Version (SRQ-DLV) [15]. A variety of secondary outcome measures was selected a priori, representing most domains of the International Classification of Functioning, disability and health (ICF). Our secondary aim was to assess long term effects of this targeted MR on the primary and secondary outcomes.

Design

A single-centre, two-armed RCT (NA-CONTROL study) with repeated measurements was conducted at the Neuromuscular Center of the Radboud university medical center in Nijmegen, the Netherlands. The full study protocol and statistical analysis plan were published [16].

The study was approved by the local medical ethics committee (Medical Ethical Committee region Arnhem-Nijmegen, CMO 2017-3740) and was registered at ClinicalTrials.gov (NCT03441347) before the start. Written informed consent was obtained from all participants in this study.

Participants

Patients were recruited via the outpatient clinic of our Neuromuscular Center which hosts the outpatient Plexus Clinic, a national expert and European referral centre for patients with NA. Inclusion criteria were, diagnosed with NA [1,17] with presence of coordinative motor dysfunction (i.e. scapular dyskinesia), beyond the acute phase of NA (>8 weeks after onset) and aged ≥18 years. Exclusion criteria were previous participation in MR, relevant comorbidities influencing rehabilitation, and in case of a recurrent NA episode during the study. Previous participation in usual care, such as physical or occupational therapy, was allowed.

For full in- and exclusion criteria, selection and enrolment, see our design paper [16].

Randomization and blinding

Participants were randomly (1:1 ratio) assigned to either the MR group or the UC group using a Good Clinical Practice (GCP)-compliant electronic data management system (Castor EDC) with stratified (sex (male/female) and age (18–30, 30–42, 42–54, > 54 years)) and variable (2-4-6) block randomization. After an initial period of 18 weeks receiving UC, the UC group also received the MR in order to not withhold the MR treatment from them and to increase the number of participants for follow up. Both groups were followed up for another 18 weeks after finishing the MR, for a total follow up of 36 weeks after start of MR (see figure 1). Blinding was not possible due to the nature of the intervention (MR at the expert centre versus UC) and self-report character of the primary outcome measure (SRQ-DLV).

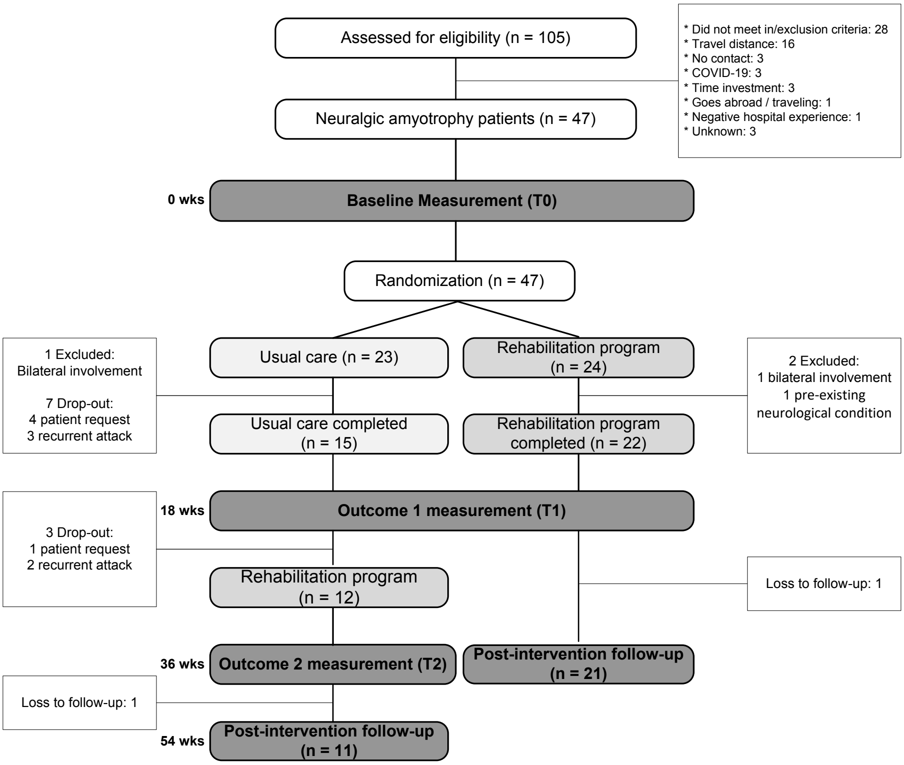

Figure 1. Flowchart of the study design and measurements

Outcomes

The SRQ-DLV, our primary outcome, is a reliable and validated self-report questionnaire measuring functional capability of the shoulder, arm and hand [15]. It has shown to be sensitive to changes in patients with NA [14]. It consists of a visual analogue scale measuring the global assessment of wellbeing (very poor to very well) considering the complaints of the affected shoulder and 19 multiple choice items covering seven domains (pain, daily activities, recreational or athletic activities, work, satisfaction and areas for improvement) [18]. The SRQ-DLV total score ranges from 17 to 100, with higher scores indicating better functioning (range 15-90 if no score in the work domain).

A set of secondary outcomes was pre-specified to cover multiple domains (impairments, activities, participation and personal factors) of the International Classification of Functioning, disability and health (ICF) and are described below [19].

Impairments

Arm muscle strength was measured with a MicroFET2®, digital manual muscle dynamometer, to determine maximal force exerted by the serratus anterior muscle, [20] and during endo- and exorotation of the shoulder. Hand grip was measured using a Jamar® Hydraulic Hand dynamometer. Pinch and key grip were measured with a Baseline® LiTE Hydraulic Pinch Gauge. Dynamometry results were measured in Newtons.

The Checklist Individual Strength - subscale fatigue (CIS-fatigue) was used to assess experienced fatigue [21]. Scores range from 8 to 56, with a score >35 indicating severe experienced fatigue.

The McGill Pain Questionnaire (MPQ) was used to assess the effect of pain on daily life [22]. It uses visual analogue scales for momentary, minimum and maximum pain. Scores range from 0-100, with higher scores indicating higher pain levels.

We used the 3D-reachable workspace as an objective measure of upper extremity active range of motion. It quantifies the relative 3D-surface area representing the portion of a hemisphere that is covered by arm and hand movements during a standardized movement protocol [23,24]. Scores range from 0 to 1, divided over 4 quadrants, with higher scores indicating greater active range of motion.

Activities

The Dutch version of the Disability of Arm, Shoulder and Hand (DASH-DLV) questionnaire was used to assess the capability of the affected upper extremity [25]. The DASH has been used and validated in multiple disorders of the upper extremity [26]. Scores range from 0 to 100, with higher scores indicating more impairment.

Participation

The Utrecht Scale for Evaluation of Rehabilitation Participation (USER-P) was used to evaluate the effect of our MR on social participation in daily activities [27]. The USER-P has four subscales: 1A) time spent on work, education and household; 1B) frequencies of performed activities; 2) restrictions; and 3) satisfaction with current daily life activities. Scores per subscale range from 0 to 100, with higher scores indicating more frequent participation (subscale 1A and 1B), less restrictions (2), or greater satisfaction (3).

Personal factors

The Self-Efficacy for Performing Energy Conservation Strategies Assessment (SEPECSA) tool was used to assess how patients perceived their ability to apply energy conservation strategies in daily life [28]. Scores range from 1 to 10, with higher scores indicating higher confidence or higher self-efficacy in managing energy conservation.

Finally, the Pain Self-Efficacy Questionnaire (PSEQ) was used to assess the confidence that people had in performing activities while being in pain [29]. Scores range from 0 to 60, with higher scores indicating higher confidence or higher self-efficacy in being active even in the presence of pain.

Study procedure

Outcome assessments in both groups were done either by self-report or by a single assessor (RL), not involved in administering the MR. Outcome assessments were completed at baseline (T0), after the initial MR or UC period (T1, 18 weeks after start MR and post baseline), and - for the UC group only - after a second period in which they received the MR as well (T2, 18 weeks after start MR and 36 weeks post baseline). Following T1 (MR group) and T2 (UC group), all patients were asked to complete all questionnaires by e-mail another 18 weeks later (36 weeks after start MR) as a final follow-up assessment (see flow chart; figure 1). Physical outcome measures (dynamometry; 3D-reachable workspace) were not included in the follow-up assessments due to practical constraints.

Interventions

The MR started with a diagnostic visit at our outpatient Plexus Clinic for patients with NA. During this visit they were examined by a multidisciplinary team consisting of a specialized neurologist, rehabilitation physician, physical therapist and occupational therapist. This visit resulted in an individualized (confirmation of the) NA diagnosis, assessment of the resulting impairments, and a personalized rehabilitation treatment advice[16].

This diagnostic outpatient visit was followed by a 16-week outpatient multidisciplinary rehabilitation program that translated the individual treatment advice provided at the diagnostic visit into a personalized treatment plan in a shared decision making approach. This intervention was then carried out in 4 weekly treatment sessions followed by 2 sessions every other week and two monthly sessions. Each of these 8 treatment sessions involved 1 hour of physical therapy and 1 hour of occupational therapy, with both disciplines working closely together, exchanging clinical findings and strategies when possible and appropriate to advance the treatment process.

The MR combines motor learning principles to normalize scapular stability and coordination with self-management strategies for pain and fatigue to enable daily occupations and reduce persisting pain and fatigue, [14,16] see figure 2. The focus and extent to which each of these components were addressed within the intervention depended on individual patient needs.

During the MR, participants were asked to refrain from any additional treatment for their NA-related complaints.

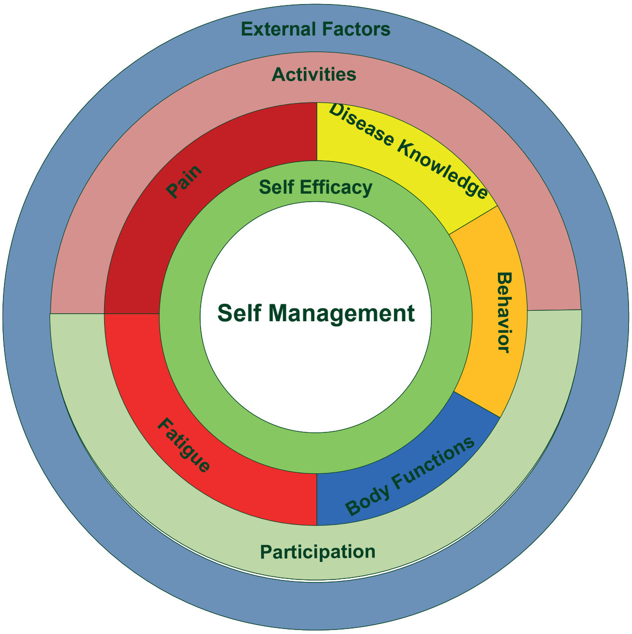

Figure 2. Treatment model which includes the components addressed during the multidisciplinary outpatient rehabilitation program. Issues in the outer two circles (external factors, activities and participation) form the main focus of the occupational therapy sessions. During the physical therapy sessions, the main focus is on improving body functions. All other components (i.e. disease knowledge, fatigue, pain, behaviour, self-efficacy and self-management) are addressed during both occupational and physical therapy sessions. This is accomplished through conveying knowledge of neuralgic amyotrophy and adaptation of behaviour related to daily life functioning. Reproduced with permission from IJspeert et al. NeuroRehabilitation 2013;33:657-665 [14].

Usual care

The general approach of UC in patients with NA typically entails physical therapy with strength training, [6] however because UC may show some variation (e.g. no therapy, only physical therapy, alternative treatments), participants were asked to keep a diary to report the treatment they received during the UC period.

Statistical analysis

For our primary objective, we used an analysis of covariance (ANCOVA), adjusted for sex, age and SRQ-DLV baseline values, to compare the MR with UC regarding all primary and secondary outcome measures. In addition, we calculated group means and mean group differences including 95% confidence intervals (95% CI). All statistical analyses were based on the intention-to-treat principle.

To calculate a number needed to treat, we used a Fisher's exact test to compare the proportion of participants in each group who reached the minimal clinically important difference on the SRQ-DLV total score, defined as a difference of ≥12 points [18]. The number needed to treat was calculated as the reciprocal of the absolute risk reduction [30].

For our secondary objective, we used paired-samples t-tests to assess the retention of the effects of the MR on all primary and secondary outcomes. To this end, we merged both groups into a single intervention group, comparing the outcome directly after completion of the MR (T1 for MR group, T2 for UC group) with the outcome at 18 weeks follow-up (T2 for MR group, T3 for UC group).

All statistical analyses were performed with SPSS (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp).

Results

Inclusion, data acquisition and compliance

A total of 105 patients with established NA and scapular dyskinesia were screened for eligibility between March 1st 2018 and March 16th 2020. After applying all inclusion and exclusion criteria, 47 patients were included and randomly assigned to the MR (n=24) and UC (n=23) group. Due to the COVID-19 pandemic, we fell slightly short of the intended inclusion of 50 participants. Three out of 47 participants were excluded after the baseline measurement (T0) and randomization: 2 because of late recognition of bilateral involvement (one in each group) and 1 due to late recognition of pre-existing neurological condition (MR group). Ten participants dropped out during the study (all UC group): 5 due to a recurrent NA episode, and 5 on own request. Data from 3 drop-outs could still be used for primary analysis since time of dropout was after T1. Hence, we had 22 participants in the MR and 15 in the UC group for primary analysis. Another 2 participants were lost to follow-up (1 in each group) after T1 (figure 1).

Due to the COVID-19 pandemic, physical measurements (3D-reachable workspace and strength measurements) were not possible for approximately 2 months during the trial and, as a consequence, those outcomes were missing in 5 participants.

As for therapy adherence in the MR group, 12 participants received at least 1 MR session online due to COVID-19 pandemic (supplementary data table 1). In the UC group, there were 2 diaries missing of participants who dropped out. Five participants in the UC group received no treatment at all and the other 7 received mainly a general approach physical therapy that involved either massage, exercises, strength and/or aerobic training (4-29 consultations per participant in total) (supplementary data table 2).

No (serious) adverse effects related to the study and/or intervention were reported.

Baseline characteristics

Baseline characteristics for both groups are shown in table 1. There were no group differences for age, sex, education or work status between both groups. A marked group difference, however, was found for the time since onset of NA. Participants in the MR group had a significantly longer period between the onset of NA and their inclusion compared to UC (t=1.620; p=0.007). In the MR group, there was 1 outlier with a duration of 204 months, but even without this outlier the time since onset of NA in the MR group was on average 15.3 months and significantly longer compared to UC (t=1.691; p<0.001).

Table 1. Baseline characteristics

	Usual care (n=23)	**Multidisciplinary rehabilitation (n=24)**
Age (years)	42.9 (18-60)	44.3 (20-76)
Sex (n)		
Male	13 (56.5%)	16 (66.7%)
Female	10 (43.5%)	8 (33.3%)
Time since onset NA (months)	8.7 (3-17)	23.9 (2-204)*
Education (n)		
Lower	1 (4.3%)	2 (8.3%)
Middle	8 (34.8%)	8 (33.3%)
Higher	14 (60.9%)	14 (58.3%)
Work (n)		
Fulltime education	1 (4.3%)	1 (4.2%)
Fulltime work	10 (43.5%)	10 (41.7%)
Partially ill/sick	5 (21.7%)	7 (29.2%)
Fully ill/sick	3 (13.0%)	4 (16.7%
Incapacitated	2 (8.7%)	-
Other	2 (8.7%)	2 (8.3%)

*Values for age and time since onset are means (ranges). Values for sex, education and work are numbers (percentages). NA, neuralgic amyotrophy. *, significantly different (p<0.01).*

Effectiveness of MR compared to UC

Primary outcome

Absolute and adjusted group means for SRQ-DLV outcomes at different time points (T0-T1) are presented in table 2. At T1 the group means adjusted for sex, age and baseline SRQ-DLV values were 61.92 (95% CI: 55.52-68.33) for the UC group and 70.53 (95% CI: 65.25-75.80) for the MR group, with a significant mean group difference of 8.60 (95% CI: 0.26-16.94) (F(x,y)=4.414, p=0.044).

Because of baseline difference in ‘time since onset NA’, we performed a post-hoc ANCOVA with time since onset NA as additional covariate with no difference in outcome (F(x,y)=4.457 p=0.043).

The proportion of participants who attained the minimal clinical important difference on the SRQ-DLV score (≥12 points) at T1 was larger for the MR group (13/22; 59%) than UC group (5/15; 33%) (Fisher’s exact test: p=0.184), resulting in an absolute risk reduction of 26% (95% CI: -6-58%). The number needed to treat is 4, this means that about one in every four patients will benefit from the MR.

Table 2. Results of primary outcome measure (SRQ-DLV)

Group	Absolute mean		Adjusted mean	Mean group difference
	T0	T1	T1	
Usual care (n=15)	58.69 (47.38-70.00)	64.11 (53.69-74.53)	61.92 (55.52-68.33)	
Multidisciplinary rehabilitation (n=22)	54.49 (47.73-61.24)	69.03 (60.73-77.33)	70.53 (65.25-75.80)	8.60* (0.26-16.94)

*Values are means (95% confidence intervals) for the Shoulder Rating Questionnaire-Dutch Language Version (SRQ-DLV). Absolute means at baseline (T0) and directly after usual care or multidisciplinary rehabilitation (T1). Adjusted means at T1 (adjusted for age, sex and baseline values). Mean group difference between usual care and multidisciplinary rehabilitation at T1. *, significant difference (p<0.05).*

Secondary outcomes

Absolute and adjusted group means for all secondary outcome measures at different time points (T0-T1) are presented in table 3 and 4. The group means adjusted for age, sex and baseline values at T1 showed a significant difference in favour of the MR group for the USER-P subscale 3, satisfaction with current daily life activities (F(x,y)=6.072, p=0.019). In addition, a significant difference in favour of the UC group was found for the pinch grip measurement (F(x,y)=2.372, p=0.025). No other group differences were found to be significant.

Table 3. Results of secondary outcome measures, reachable workspace and strength measurements

Outcome measure	Group	Absolute mean		Adjusted mean (95% CI)	Mean group difference (95% CI)
		T0	T1	T1	
3D-reachable workspace					
Quadrant 1	UC	0.114	0.128	0.128 (0.100-0.157)	
	MR	0.116	0.141	0.141 (0.118-0.164)	0.013 (-0.024-0.049)
Quadrant 2	UC	0.135	0.130	0.144 (0.131-0.157)	
	MR	0.130	0.142	0.144(0.133-0.155)	-0.001 (-0.018-0.016)
Quadrant 3	UC	0.162	0.183	0.196 (0.174-0.218)	
	MR	0.183	0.206	0.197 (0.179-0.216)	0.002 (-0.027-0.031)
Quadrant 4	UC	0.232	0.231	0.196 (0.1740-0.218)	
	MR	0.225	0.235	0.197 (0.179-0.216)	0.005 (-0.003-0.013)
Total	UC	0.642	0.689	0.230 (0.224-0.236)	
	MR	0.654	0.724	0.235 (0.230-0.240)	0.023 (-0.043-0.090)
Strength measurements (N)					
SA muscle Hand	UC	192.2	210.3	209.2 (182.4-235.9)	
	MR	196.7	223.1	223.8 (201.7-245.9)	14.7 (-20.1-49.5)
SA muscle Elbow	UC	188.0	201.3	200.3 (174.6-226.1)	
	MR	189.2	208.3	208.9 (187.6-230.2)	8.6 (-24.9-42.0)
Exorotation	UC	93.2	98.1	99.7 (87.3-112.2)	
	MR	97.5	113.4	112.3 (102.0-122.5)	12.5 (-3.6-28.7)
Endorotation	UC	146.4	166.3	171.7 (152.7-190.6)	
	MR	157.0	162.9	159.2 (143.5-174.8)	-12.5 (-37.2-12.2)
Hand grip	UC	41.0	42.1	42.2 (38.2-46.1)	
	MR	40.9	42.4	42.4 (39.1-45.6)	0.2 (-5.0-5.3)
Pinch grip	UC	6.0	6.3	6.2 (5.8-6.7)	
	MR	5.8	5.5	5.5 (5.1-5.9)	-0.7* (-1.3-1.0)
Key grip	UC	10.7	11.3	11.2 (10.5-12.0)	
	MR	10.6	11.3	11.3 (10.6-11.9)	0.0 (-1.0-1.1)

*Values are means. Absolute means at baseline (T0) and directly after usual care or multidisciplinary rehabilitation (T1). Adjusted means (95% confidence intervals (95% CI)) at T1 (adjusted for age, sex and baseline values). SA, serratus anterior. UC, usual care. MR, multidisciplinary rehabilitation. Mean group difference (95% CI) between usual care and multidisciplinary rehabilitation at T1. *, significant difference ($p<0.05$).*

Table 4. Results of secondary outcome measures, questionnaires

Outcome measure	**Group**	**Absolute mean**		**Adjusted mean (95% CI)**	**Mean group difference (95% CI)**
		T0	**T1**	**T1**	
Checklist individual strength - subscale fatigue (CIS-fatigue)					
	UC	35.5	33.3	33.5 (27.7-39.5)	-6.2 (-13.9-1.5)
	MR	35.8	27.5	27.4 (22.5-32.2)	
McGill Pain Questionnaire (MPQ)					
VAS momentary	UC	28.6	23.2	24.8 (17.6-32.0)	
	MR	33.1	22.5	21.5 (15.5-27.4)	-3.3 (-12.6-6.1)
VAS minimum	UC	18.0	13.4	13.0 (7.4-18.6)	
	MR	16.5	8.2	8.4 (3.8-13.0)	-4.6 (-11.9-2.7)
VAS maximum	UC	67.6	61.1	59.5 (46.9-72.1)	
	MR	64.4	50.9	52.0 (41.6-62.4)	-7.5 (-23.8-8.8)
Disability of Arm, Shoulder and Hand (DASH)					
	UC	36.1	28.7	30.1 (23.4-36.8)	
	MR	39.0	27.0	26.1 (20.6-31.6)	-4.0 (-12.7–4.6)
Utrecht scale for evaluation of rehabilitation - participation (USER-P)					
1A (frequencies)	UC	29.0	28.0	28.8 (24.5-33.1)	
	MR	30.5	31.1	30.6 (27.1-34.2)	1.8 (-3.7-7.4)
1B (frequencies)	UC	45.0	44.2	43.6 (37.5-49.8)	
	MR	43.2	45.5	45.8 (40.8-50.9)	2.2 (-5.8-10.2)
2 (restrictions)	UC	79.0	81.2	81.1 (74.7-87.6)	
	MR	78.8	83.7	83.8 (78.5-89.1)	2.7 (-5.7-11.1)
3 (satisfaction)	UC	61.3	64.0	64.4 (58.3-70.5)	
	MR	62.0	74.2	73.9 (68.9-78.9)	9.5* (1.6-17.4)
Self-efficacy for performing energy conservation strategies assessment (SEPECSA)					
	UC	6.6	7.1	7.3 (6.7-7.9)	
	MR	7.4	7.8	7.6 (7.1-8.1)	0.3 (-0.5-1.1)
Pain self-efficacy questionnaire (PSEQ)					
	UC	41.6	45.3	45.6 (42.1-49.0)	
	MR	42.3	48.6	48.5 (45.6-51.3)	2.9 (-1.5-7.4)

*Values are means. Absolute means at baseline (T0) and directly after usual care or multidisciplinary rehabilitation (T1). Adjusted means (95% confidence intervals (95% CI)) at T1 (adjusted for age, sex and baseline values). VAS, visual analogue scale. UC, usual care. MR, multidisciplinary rehabilitation. Mean group difference (95% CI) between usual care and multidisciplinary rehabilitation at T1. *, significant difference (p<0.05).*

Retention of effects

Primary outcome

The mean SRQ-DLV score at the end of the MR for all participants combined (MR group (T1) and UC group (T2), n=34) was 69.41 (95% CI: 62.41-75.31) versus 71.69 (95% CI: 65.14-77.24) at follow-up (mean difference 2.28, 95% CI: -1.68-6.23). This means that over a 18 week follow-up period after the MR there is a retention of the effect on the functional capability of the shoulder, arm and hand.

Secondary outcomes

There were no significant time effects during 18 weeks of follow-up in any of the secondary outcome measures (supplementary data table 3).

Discussion

This RCT showed that MR was more effective than UC to improve shoulder, arm and hand functional capability, as assessed with the SRQ-DLV, in patients with NA and scapular dyskinesia. Moreover, the observed improvements were retained after a follow-up period of 18 weeks (36 weeks from start MR). MR focused on motor relearning of scapular stability and coordination combined with self-management strategies to cope with and reduce persisting pain and experienced fatigue. The overall goal is to improve daily functioning and reduce activity limitations in daily life. Based on a pre-determined minimal clinically relevant improvement (SRQ-DLV ≥12), the number needed to treat was 4. These results are in line with our previously published pilot and reported clinical and patient experiences [4,5,14,31].

The positive effect of our MR on the primary outcome was not reflected in the secondary outcomes However, although not significant, there seemed to be a visible trend in almost all secondary outcomes in favour of MR compared to UC, reflecting better functioning, less pain and fatigue, and better self-management and participation. The absence of significant changes or group differences in the strength measurements, with exception of pinch grip, was coherent with the focus of physical therapy within our MR, specifically aimed at restoring motor control, scapular stability and coordination, whereas physical therapy in UC mainly had a focus on strength training and massage.[6] Another large difference in our MR compared to UC was occupational therapy focused on improving self-management strategies to cope with and reduce persisting pain and experienced fatigue which was clearly underrepresented in UC. Although the effect of occupational therapy was not reflected in the secondary outcomes (e.g. SEPESCA, PSEQ or CIS-fatigue), this was also included in the SRQ-DLV domains such as sleep, leisure, work and daily activities. Therefore, the primary outcome measure (SRQ-DLV) covered multiple domains which our MR, with combined physical and occupational therapy, addresses.

A significant difference in the time since onset NA was found between both groups. Post hoc analysis showed no difference in results of the primary outcome measure when 'time since onset NA' was added as covariate. Nevertheless, there was difference in time since onset which on average was 15 months longer in the MR compared to the UC group. We believe that the difference may have led to an underestimation of the observed effect size. Since patients shortly after an NA episode are more likely to show spontaneous nerve recovery, [4] and this can be expected to coincide with better functional improvement. Furthermore, for patients who have been struggling with the functional consequences of NA for a longer period of time, it was probably more difficult to normalize motor control, reverse maladaptive movement patterns, [12,13] and change behaviour to self-manage NA symptoms. Most of these patients will have had some kind of usual care, mostly physical therapy, before inclusion with insufficient effect on their residual complaints as previously reported [6]. Therefore, we expect that a comparable time since onset of NA in both groups would have led to a larger effect size in favour of MR. The lower time since onset may have been a reason for the higher drop-out rate in the UC compared to the MR group, since in five UC participants the reason for drop-out was a recurrent NA episode and recurrence rate of NA is larger in the first year after an initial NA episode [3].

The effect of spontaneous recovery in UC, with a lower time since onset of NA, raises the question on the optimal timing of MR. Should we start as soon as possible to supercharge functional recovery or should we wait and see until residual complaints impede daily activities or participation? Furthermore, we need to identify outcome measures, beside the SRQ-DLV, which address these residual complaints and their effects on activities and participation and are sensitive to change during spontaneous recovery and MR. And lastly, we need to review and optimize the content of our MR relating to the results of this RCT on the primary and secondary outcomes combined with our recent findings of cerebral (mal)adaptations after NA [13].

Strengths and limitations

Due to restrictions related to the COVID-19 pandemic we were unable to include the intended 50 participants. Nevertheless we found a significant effect on our primary outcome that was retained at follow-up. Nevertheless, a lack of power might have influenced the effect on the secondary outcomes.

It could be that patients think that MR is more helpful and rate it more successful than UC since it is a more intensive program . If this possible bias was present, it should emerge in all outcome measures and not only in the positive effect of our primary outcome measure.

A potential confounder might be the use of analgesics or muscle relaxants, for which we did not control. However, only 6 out of 24 patients with NA in MR and 1 out of 23 in UC used a kind of analgesics and only 1 out of 23 in UC used a muscle relaxant. We therefore believe that a possible confounding effect, if any, of potential medications will be limited.

A strength of this study is the fact that the MR was executed within daily clinical practice and was customized to the participants individual needs and goals, which implies that the external validity of our results is high and their clinical implementation relatively easy.

Conclusions

This RCT showed that an outpatient multidisciplinary rehabilitation program focusing on improving motor control, scapular stability and coordination, combined with training self-management strategies for reducing pain and fatigue, is more effective than usual care to improve shoulder, arm and hand functional capabilities in patients with NA and scapular dyskinesia. Future research should confirm our findings, focus on mechanisms of change, and address cost-effectiveness.

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Supplementary tables

Supplementary table 1. Number and type of online consultations due to COVID-19 pandemic

Participant	Number of online consultations during MR
MR Group	
1	1 OT and 1 PT
2	2 OT and 2 PT
3	5 OT and 4 PT
4	5 OT and 4 PT
5	5 OT and 5 PT
UC Group	
6	2 OT and 2 PT
7	4 OT and 4 PT
8	4 OT and 4 PT
9	4 OT and 4 PT
10	Plexus clinic and 1 OT and 1 PT
11	Plexus clinic and 1 OT and 1 PT
12	Plexus clinic

MR, multidisciplinary rehabilitation program. UC, usual care. OT, occupational therapy consultation. PT, physical therapy consultation. Plexus clinic, multidisciplinary diagnostic outpatient expert clinic for patients with neuralgic amyotrophy (NA).

Supplementary table 2. Content of usual care (UC) in the UC group

Participant	Type and number of session	Content
1	1x General physician 4x Physical therapy	Other health issue Combination of massage and exercises
2	1x General physician 29x Physical therapy 4x Occupational therapy	Other health issue Strength training and aerobic training Activities
3	13x Physical therapy 2x Sleep expert center	Medical fitness
4	2x General physician 10x Physical therapy 9x Psychologist	Influenza vaccination and sleeping problems Unknown No relation with NA
5	3x General physician 5x Physical therapy	Unknown Unknown
6	2x General physician 8x Physical therapy	Other health issue Massage, exercises, trigger point and tape
7	1x General physician 11x Physical therapy	Unknown Unknown

Multidisciplinary rehabilitation consisted of a multidisciplinary diagnostic visit followed by 8 sessions of physical and occupational therapy, one hour each, working closely together.

Supplementary table 3. Long term effects (18 week follow-up) of multidisciplinary rehabilitation (MR) on secondary outcome measures

Outcome measure	**Absolute mean**		**Mean group difference(95% CI)**
	End of MR	**Follow-up**	
Checklist individual strength - subscale fatigue (CIS-fatigue)			
	26.5	24.6	-1.9 (-5.9-2.0)
McGill Pain Questionnaire (MPQ)			
VAS momentary	22.3	21.8	-0.5 (-7.1–6.2)
VAS minimum	8.9	10.2	1.2 (-1.5 –4.0)
VAS maximum	47.9	41.0	-6.9 (-15.5–1.7
Disability of Arm, Shoulder and Hand (DASH)			
	26.3	23.8	-2.5 (-6.3–1.2)
Utrecht scale for evaluation of rehabilitation - participation (USER-P)			
1A (frequencies)	30.9	27.3	-3.6 (-6.7–-0.5)
1B (frequencies)	44.1	43.8	-0.4 (-3.7–3.0)
2 (restrictions)	84	87.4	3.2 (-0.7–7.2)
3 (satisfaction)	73.2	75.0	1.8 (-3.1–6.7)
Self-efficacy for performing energy conservation strategies assessment (SEPECSA)			
	7.7	7.9	0.1 (-0.2-0.5)
Pain self-efficacy questionnaire (PSEQ)			
	48.5	49.5	1.0 (-2.1-4.0)

Values are means. Absolute means at end of multidisciplinary rehabilitation (MR) and after 18 weeks of follow-up. VAS, visual analogue scale. Mean group difference (95% confidence interval (95% CI)) between end of MR and follow-up.

Chapter 7

Summary and general discussion

Part A: Summary

In this thesis we describe the development and evaluation of our multidisciplinary outpatient rehabilitation program for patients with neuralgic amyotrophy (NA). Until now, there were no evidence based interventions available for patients with NA in the chronic phase. There is limited information about physical therapy for patients with NA reporting that “standard physical therapy” is ineffective or even aggravates symptoms in more than 50% of the cases. With this thesis we fill a gap regarding effective multidisciplinary rehabilitation treatment for patients with NA.

In **chapter 1** we give a description of NA, the impact of NA on people’s daily lives, and of the outpatient multidisciplinary rehabilitation program. NA is an acute autoimmune inflammation of (most often) the proximal nerves in the brachial plexus distribution. It is characterized by one or more episode(s) of acute severe pain, leading to multifocal paresis and atrophy of the upper extremity muscles. It appears to be a common disease with an incidence of 1 in 1000 persons per year. Patients with NA experience long-term residual complaints and activity limitations in daily life. The most common residual complaints are severe pain, general fatigue, and muscle atrophy and/or residual paresis. These symptoms cause movement restrictions, increased muscle fatigability, and altered - often compensatory - movement patterns.

In 2009 we started our “Plexus Clinic” for patients with brachial plexus pathology, mostly due to NA. The multidisciplinary Plexus Clinic team consists of a neurologist, rehabilitation physician, occupational therapist and physical therapist, collaborating closely together and providing rehabilitation as a team. Our rehabilitation program was established through best practice. The two main goals of the rehabilitation program are: 1) improving upper extremity motor control, scapular stability and coordination, combined with 2) training of self-management strategies to reduce pain and fatigue

Chapter 2 is a review focusing on recent insights and developments in NA. NA is a clinical diagnosis first and foremost with a typical history and specific clinical phenotype. NA has a broad phenotypic spectrum with the ‘classic’ presentation present in about 70% of the patients. Other presentations include involvement of other brachial plexus nerves, lumbosacral plexus affection in 10%, phrenic nerve involvement leading to diaphragm dysfunction in 8%, and a painless onset in about 4% of the patients.

Multiple case series and reports suggest that oral corticosteroids and intravenous immunoglobulin can be effective in the acute phase of NA, as soon as possible, but at least within 2 weeks. Nevertheless, the majority of patients with NA is left being restricted in their daily activities because of residual pain and fatigue. These symptoms are persistent due to inefficient motor control of the affected shoulder/arm, loss of endurance in the affected muscles, and strain of the compensating musculature. Physical therapy for NA focuses on regaining motor control. Patients are trained to maintain their scapular position in a subtle posterior tilt while using the arm selectively, with supportive feedback on posture and movement control from their therapist. Occupational therapy for NA focuses on management of pain and fatigue with the use of energy conservation strategies. Key elements include ergonomics during activities such as self-care, household, work, education, sports and leisure and on an optimal arm and shoulder position at rest.

Recent findings show that nerves who fail to recover usually exhibit focal hourglass constrictions that can lead to severe nerve narrowing. When there is a (near-) complete paralysis without recovery after 6 months, surgical neurolysis is indicated within 6–12 months to allow reinnervation. In patients for whom neurolysis is not an option, but who suffer from residual impairments, other surgical options such as nerve transfer or secondary surgery using tendon transfers should be considered. Patients with phrenic neuropathy may benefit from nocturnal non-invasive mechanical ventilation and coordinative inspiratory muscle training, and may benefit from diaphragm plication when no spontaneous nerve recovery occurs.

Chapter 3 reports the results of a within-subject proof-of-principle pilot study. This study was the first to evaluate the efficacy of a combined physical and occupational therapy intervention for patients with NA. The program consisted of a 16-week intervention period during which patients were treated weekly in week 1–4, once every two weeks in week 5–8, and monthly in week 9–16. Each treatment session involved one hour of physical therapy and one hour of occupational therapy. Eight patients with NA participated in the study. Measurements were carried out during a baseline period – three months prior to the intervention – as well as at start and at completion of the multidisciplinary rehabilitation program. Outcome measures covered several domains of the International Classification of Functioning, disability and health (ICF). Primary outcome measures were the Shoulder Rating Questionnaire - Dutch Language Version (SRQ-DLV) and the Canadian Occupational Performance Measure (COPM) to evaluate occupational performance and satisfaction with performance of the patients' most important daily occupations. Secondary outcome measures included the Disabilities of Arm Shoulder and Hand (DASH) questionnaire, strength measurements, and the Self-Efficacy for Performing Energy Conservation Strategies Assessment (SEPECSA). The short form 36 (SF-36) questionnaire was used to measure health-related quality of life and the Checklist Individual Strength 20 (CIS-20) to measure fatigue.

The results showed significant improvements (mean (95% CI)) on the COPM performance (+2.3 (0.9/3.7)) and satisfaction (+1.4 (0.4/2.4)) scores, and on the SRQ-DLV (+14.8 (7.4/22.0)) and the health change sub-scale of the SF-36 (−37.5 (−56.9/−18.2)). Strength measurements demonstrated a tendency to an increase in strength only of the serratus anterior muscle. These findings suggests that improvement is most likely caused by functional and behavioral adaptation to nerve damage and corresponding loss of function of the affected shoulder. This pilot study showed that patients with NA may improve in their activity and participation levels after multidisciplinary rehabilitation.

The aim of **chapter 4** was to gain insight - from the perspectives of patients and therapists - into critical ingredients of the rehabilitation program that contributed to the improvements in activity and participation levels as reported in chapter 3. A qualitative study was conducted using semi-structured interviews. Participants were the same eight patients who participated in the pilot study of chapter 3, complemented with five of their therapists: three occupational and two physical therapists. Data were analyzed using a constant comparative approach.

Patients and therapists identified similar critical ingredients from diverse perspectives. The expertise and close collaboration of the team members was an important aspect that was mentioned to contribute to the trust, confidence, understanding, awareness, and ability of patients to actively regain control of their everyday activities and participation. Working in partnership coupled with shared decision making led to a personalized approach that was valued by patients and emphasized by therapists as essential to successful outcomes. The critical ingredients were summarized as a combination of supporting self-management skills and delivering disease- and profession-specific expertise in a collaborative partnership. Some patients recommended more options for personalization of the intensity and duration of rehabilitation, and the possibility to consult a psychologist or receive peer support.

Chapter 5 is a clinimetric study focusing on the pattern of experienced pain and fatigue that patients with NA experience during the day. The occupational therapy consultation and treatment focuses on understanding and gaining insight into the reciprocal relationship between the symptoms of NA and the performance of daily occupations; i.e. how pain and fatigue restrict or impact everyday activities and how everyday activities themselves can exacerbate or prolong NA symptoms.

Although there are many instruments for measuring pain and/or fatigue, none of these instruments provide insight into the pattern of complaints during the day or the relationship with patient-specific activities. To fill this void, we developed pain and fatigue graphs where patients indicate the 24-hour pattern of their complaints on the X-axis and the severity of their symptoms (10-point scale) on the Y-axis. A dual role of informing patient-therapist decision-making and measuring effectiveness would add to their value in patient care. The aim of this study, therefore, was to investigate inter-rater and test-retest reliability as well as concurrent validity of the pain and fatigue graphs in patients with NA.

Inter-rater and test-retest reliability (n=8) were examined using intraclass correlation coefficients (ICCs). Concurrent validity (n=47) was tested using the Numerical Rating Scale (NRS) for pain and the Checklist Individual Strength (CIS)-subscale fatigue. ICCs of test-retest reliability varied from 0.72 to 0.93 for pain and from 0.67 to 0.85 for fatigue, while ICCs of inter-rater reliability ranged from 0.76 to 0.97 for pain and from 0.47 to 0.97 for fatigue. Correlations of mean pain and fatigue graph scores with the NRS-pain and CIS-fatigue scores were strong ($r_s = 0.75$, $p<0.000$) and moderate ($r_s = 0.42$, $p=0.003$), respectively. It was concluded that this explorative study showed sufficient reliability and validity of pain and fatigue graphs to assess NA-related complaints during the day.

Chapter 6 reports the results of a Randomized Controlled Trial (RCT). The primary aim was to compare the effects of our multidisciplinary rehabilitation program to usual care in patients with NA and scapular dyskinesia. Our secondary aim was to assess long-term effects of the rehabilitation program on the primary and secondary outcomes. The primary outcome was self-reported functional capacity of the shoulder, arm and hand assessed with the SRQ-DLV. A variety of secondary outcome measures were selected a priori, representing most domains of the ICF.

In total 47 patients with NA were included. Due to drop-out, there were 22 participants in the rehabilitation group and 15 in usual care group for primary analysis. Despite randomization, a marked group difference was found for the 'time since onset of NA'. Participants in the rehabilitation group had a significantly longer period since disease onset compared with those who received usual care. The mean group difference of the SRQ-DLV post-treatment, adjusted for sex, age and baseline score was 8.60 (95%CI: 0.26 -16.94, p=0.044). The proportion attaining a minimal clinically relevant SRQ-DLV improvement (≥12) was larger for the rehabilitation group (59%) than for the usual care group (33%) with a number needed to treat of 4. The observed improvements were retained after a follow-up period of 18 weeks. Because of a baseline difference in 'time since onset of NA', we performed a post-hoc analysis with 'time since onset of NA' as additional covariate yielding no difference in outcome (F(x,y)=4.457 p=0.043). Most secondary outcome measures did not show significant changes, although there seemed to be a visible trend in almost all secondary outcomes in favor of the rehabilitation group, reflecting better functioning, less pain and fatigue, and better self-management and participation.

Part B: General discussion

This thesis describes the development and evaluation of an outpatient multidisciplinary rehabilitation program for patients with neuralgic amyotrophy (NA). We showed our newly developed rehabilitation program to be effective. After rehabilitation, patients with NA experienced less pain and their impairments of the shoulder, arm and hand improved, as well as the limitations in daily activities, leisure/sport activities and work. In this chapter I will discuss our outpatient multidisciplinary rehabilitation program for patients with NA from the perspectives 'why', 'how' and 'what' according to Simon Sinek's golden circle [1] (see figure 1).

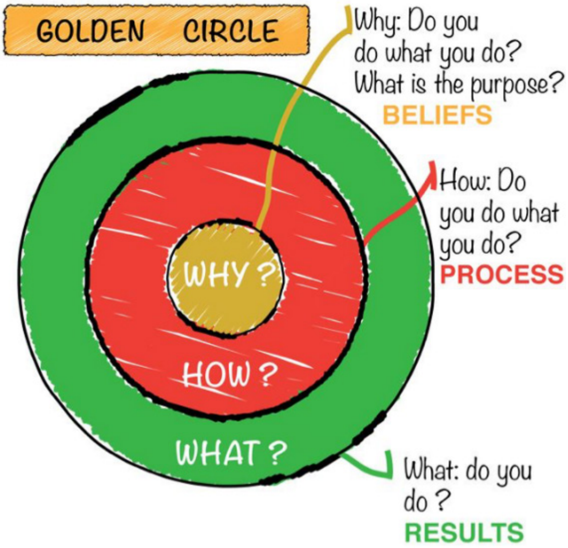

Figure 1: Golden Circle from Simon Sinek [1]

The golden circle has been developed to explain successful leadership and business. The success of businesses and inspiring leaders is mostly based on why they are doing what they are doing [1]. Starting at the core by knowing what drives and motivates a person is also important in healthcare. Why do we as healthcare providers do what we do? And why do patients do what they do? According to Sinek, the answers to these 'why' questions are the key to success. I will use Sinek's format to discuss the beliefs and goals regarding the treatment (why), the delivery of the program (how), and the content of the program (what).

Why

As an interdisciplinary team we aim to have a significant impact on people's daily life by improving patient participation and by reducing patients' complaints. In the golden circle, the 'why' is related to meaning, feeling and passion (from a patient's perspective) and clinical reasoning (from a professional perspective). As a team, we work with patients to find out what is valuable for them in their daily lives to set personalized rehabilitation goals.

Persons with NA come to our Plexus Clinic with multiple questions, hopes, goals and expectations. Overall, they hope to get a better understanding about the disease, about what to expect from nerve recovery, how to deal with complaints and activity limitations, and how to self-manage their limitations in daily life. Most patients experience continuous pain and fatigue and limited to no control over their complaints. They try to reduce their complaints and activity limitations by intensive physical therapy sessions in the community, where the primary focus often is to strengthen the weakened muscles. Most of the time, such strength training does not lead to improvement and might even worsen the symptoms and complaints [2]. Patients expect us to give them therapy advice and guidance and they frequently ask what they can safely do despite their complaints.

Another reason why patients come to our Plexus Clinic is often for a (definite) medical diagnosis. Over the years, the knowledge of NA has increased among general practitioners, neurologists and physical therapists; the professionals that patients with NA most often turn to. Still, it often takes too much time before the diagnosis NA is made. In many cases, professionals doubt whether or not NA is the appropriate diagnosis. For these cases, the Plexus Clinic serves as a tertiary referral center. It is important for these patients to know what condition they have to better understand how to cope with the consequences of NA. Decision making is based on having enough and appropriate information [3].

From our clinical point of view, we want to find out what is meaningful for NA patients. Which activities and societal roles are important for them to regain? And why are specific activities and roles meaningful to an individual patient? The answers to these questions help to determine patient specific treatment goals based on shared goal setting. The Canadian Occupational Performance Measure (COPM) can be used to prioritize activities and set personal goals. The COPM is a validated and reliable instrument for evaluating performance and satisfaction with performance of participation in prioritized meaningful activities [4, 5]. Accordingly, we aim to tailor the intervention towards these priorities, which helps to explain to patients what rehabilitation can accomplish, and why we offer certain treatment strategies.

To get a better understanding of why patients with NA are motivated for rehabilitation and which activity limitations are most troublesome for them, it is interesting to get insight into their priorities identified with the COPM. Do these priorities correspond with other populations or are there typical concerns specific for the NA population? In literature there are not many studies that have reported the priorities identified with the COPM. Only two studies have identified categories of the COPM priorities. One study with 161 individuals receiving occupational therapy in primary care identified a total of 656 priorities [6]. Most priorities were in the domain self-care (38%), followed by productivity (35%) and leisure (27%). Another study with 65 individuals with chronic upper-extremity paresis following stroke reported 319 priorities [7] in five categories: instrumental activities of daily living (IADL) (40%), activities of daily living (ADL) (37%), general upper extremity movement (12%), leisure (9%) and work/productivity (2%).

For the 27 individuals with NA who received our rehabilitation program (chapter 6), 115 priorities were identified (additional unpublished data to chapter 6). The priorities could be divided into seven categories: ADL (20%), IADL (20%), leisure (17.4%), work/productivity (13%), sports (12.2%), general upper extremity movement (12.2%), and sleep (5.2%). The COPM itself contains three categories: self-care (ADL and IADL), productivity and leisure. The study of Waddell et al. [7] added 'general upper extremity movements' to these domains, based on the "Occupational Therapy Practice Framework". For our study we also added 'sports' and 'sleep', since patients with NA experience problems in both of these categories and mentioned them frequently in COPM priorities. The priorities were well distributed over the different categories. Most of the patients had been active in all life domains. There were no big differences from the population in primary care as described above. Compared with the study of Waddell et al. [7], work/productivity goals were much more common in our NA population than in the population with post-stroke upper-extremity paresis.

This may be due to a lower average age of patients with NA compared to post-stroke patients, as patients with NA are more likely to participate in work/productivity.

Personalizing priorities for rehabilitation using the COPM contributed to a positive effect of our rehabilitation program according to the patients (chapter 4) who valued our personalized care. Therefore, it is interesting to look at the effect of our rehabilitation program on the performance and satisfaction scores of the COPM priorities. COPM scores of all participants (n=27) were used to compare the outcome before and after the intervention. Paired samples t-test (significance level 0.05) were performed and showed statistically significant improvements on COPM performance scores with a mean difference of 1.8 points (SD 2.0) as well as on COPM satisfaction scores with a mean difference of 2.5 points (SD 2.0). The clinically relevant difference of the COPM has not yet been investigated in the NA population. Recently it was discussed whether the commonly accepted clinically relevant difference of 2 points might be different in different populations [8]. Nevertheless, our findings appear to be clinically relevant, when compared with a heterogeneous population in the Netherlands [9] and compared to a group of persons with heterogeneous neuromuscular disorders [10].

How

In the golden circle, 'how' represents the process to realize the desired outcome of the intervention. In daily practice and in the literature, the focus of an intervention is often on the 'what' [1]. However, research shows that 'how' you design an intervention may have a significant impact on its effect as well [11]. The 'how' can be found in the entire process of development, feasibility, and evaluation of a complex intervention, as described in the UK Medical Research Council (MRC) framework [12].

Process of development, feasibility and evaluation of a complex intervention

The UK-MRC framework was used as an underlying methodological framework for our research studies. In this thesis we describe the results of its first three phases; i.e. the development (chapter 1), feasibility (chapters 3, 4 and 5) and evaluation (chapter 6) phase. In the newest version of this framework [12], there is an extended focus on understanding 'how' and under what circumstances interventions bring about change. Thus, research on complex interventions should take into account the complexity that arises from both the intervention's components and the interaction with the context in which it is being implemented [12].

The first aspect – complexity of the intervention components – was addressed in the general introduction of this thesis (chapter 1). The second aspect – complexity of the interaction within the context in which the intervention is being implemented – was not yet investigated. The context of implementation of our rehabilitation program was the outpatient Plexus Clinic of the Radboud university medical center, with the team working in interdisciplinary collaboration. This way of collaboration seemed to be a critical ingredient when it comes to the delivery of the program. It was a common topic in the qualitative study of chapter 4. Patients reported that therapists complemented each other and worked across the boundaries of their profession. They valued the evaluations and constant dialogue between the therapists during the rehabilitation. One patient said “hearing the same from different perspectives has added value”.

A process evaluation of the Randomized Controlled Trial (RCT) – chapter 6 – could provide us with more insight in the aspects that are important for further implementation of our rehabilitation program. Such a process evaluation can answer questions about fidelity and quality of implementation (what is implemented and how?), mechanisms of change (how does the delivered intervention produce change?), and context (how does context affect implementation and outcomes?) [13].

When we want to implement our rehabilitation program to other contexts, the question arises whether the program can be performed in the way we developed it. Our program does not need to be provided in a specialized rehabilitation setting. It would – generally – also suit in primary care. Related to the high incidence rate of 1:1000 new patients per year [14] and the large variability in nerve recovery, there are many patients with less physical impairments and complaints – requiring a shorter and less intensive trajectory – which would fit well in primary care.

But how do we ensure that all important aspects of our program can be transferred to other contexts, such as primary care? This requires implementation research which involves “deliberate efforts to increase impact and uptake of successfully tested health innovations”, which is described by Skivington et al. [12] (see figure 2).

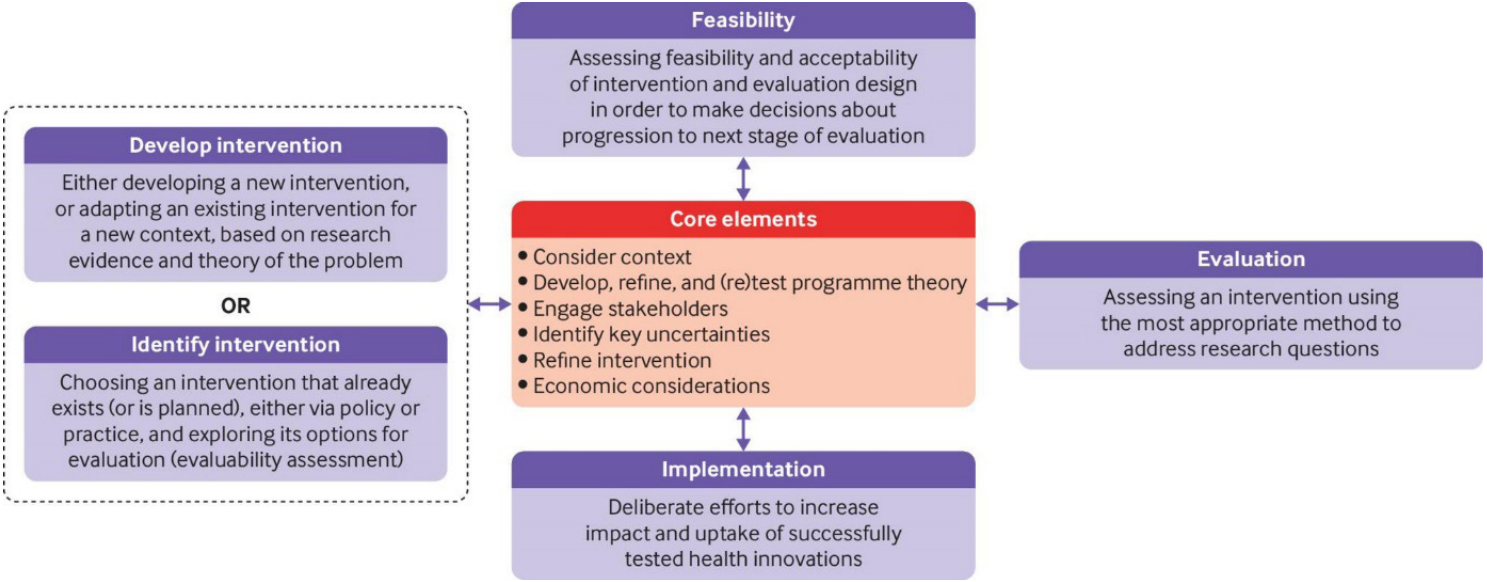

Figure 2: Medical Research Council (MRC) framework for the development and evaluation of complex interventions [12].

Delivery of the multidisciplinary rehabilitation program

It is often assumed that - when the content of an intervention has clearly been described and educated - the intervention is applied in the same way by every therapist [15]. However, it appears that some therapists consistently achieve better results than others [16]. This is coherent with our experience ever since we started delivering our treatment in 2015 by providing training to therapists and teams. We learnt that there is a difference in how therapists apply knowledge and skills into practice, even though they have all attended the same training. To gain more insight into these differences, again a process evaluation would be useful. Was the intervention implemented as intended? How was the compliance of the patients in applying the intervention? And how did patients and therapists experience the intervention? In chapter 4, we examined the critical ingredients of our rehabilitation program according to the patients' and therapists' perspectives. It was interesting to see that most themes in this study were about the delivery of the program (how), and not about the content (what). From both perspectives, the focus was on disease knowledge, creating awareness, activating problem solving, personalization of therapy, and close collaboration (within the team and with the patient). Here, I will discuss several aspects regarding the delivery of our multidisciplinary rehabilitation program for patients with NA.

Role of the therapist

Several ways of giving instructions and coaching were used in our rehabilitation program and may have influenced its effect. These instructional differences concerned training the correct movement pattern (e.g. exercises and ergonomics) and coaching the necessary behavioral changes to help patients getting control over their complaints.

Regarding training, there are various possibilities to improve and adopt a movement pattern, including education, instruction, experiencing, providing physical guidance, learning to feel (possibly with the use of taping), and using photos and videos.

With regard to achieving behavioral change, the role and coaching skills of the therapist are critical [3]. Patients first need to understand why change is needed and what they need to change. Achieving such understanding is an intensive process. To this end, several techniques can be used such as motivational interviewing [17], a strength-based approach [18], or an acceptance commitment therapeutic approach [19]. Therapists can also use their own qualities to enable behavioral change. This is called "therapeutic use of self" and involves the deliberate application of personal behaviors, insights, perceptions, judgments, skills, knowledge and personal qualities such as creativity and humor [20]. When it comes to delivery, it depends on whether a patient is coached to manage him/herself using the above-mentioned techniques or whether a therapist tells a patient what to do. Self-efficacy is a strong predictor of success in goal setting and achieving behavioral change [21]. There are four ways self-efficacy can be improved, the first being the most impactful: 1) successfully perform a (new) skill, 2) seeing someone else successfully complete a task, 3) social persuasion, giving positive feedback and encouragement, and 4) re-interpreting physiological and emotional reactions, creating a positive focus on the problem [22]. In our rehabilitation program we mainly used the first and third way of enhancing self-efficacy. So, we could improve our intervention by including the second and fourth way as well, which would be consistent with the findings of our qualitative study (chapter 4). Firstly, patients reported that creating awareness was exhausting and difficult but necessary. Some missed the support of a psychologist during this process. Secondly, a few patients would have appreciated peer support, for which a group intervention could be an option. An example of such a group intervention is the ‘Energetic’ group program from our rehabilitation department [10]. Energetic is an effective self-management interdisciplinary group program, in which a combination of aerobic exercise training and energy conservation management are provided based on individual goals of patients with a neuromuscular disease [10]. This could also apply to our rehabilitation program for patients with NA, as we offer a combination of physical exercise training - improving motor control - and training of self-management skills as well. In a mixed method study of the Energetic intervention, the group setting was considered to be essential [23]. Patients learned from one another and encouraged each other. When starting a group intervention for patients with NA, we can learn from the Energetic group intervention that all participants has enough time for individual questions, that therapists need education to guide a group and promote behavioral change and to take into account the mental strain of evaluating and reflecting on one’s own behavior.

Personalized care

Our multidisciplinary rehabilitation program is not ‘one size fits all’. Although all components of the program need to be addressed, its implementation is personalized. For research purposes we standardized our treatment into eight therapy sessions. Each session contained one hour of physical therapy and one hour of occupational therapy. We experienced that the number of sessions someone needed to apply all strategies into daily practice varied per person. Sometimes the fixed eight therapy sessions were insufficient and sometimes they were excessive. Personalizing an intervention should therefore not only apply to its content but also to the number of sessions. The stage of behavioral change someone is in may also influence the number of sessions needed. Some patients go straight into action after they have received information and advice. Others need step-by-step guidance through the entire process of behavioral change.

Process-wise, there are opportunities to improve our rehabilitation program. We could consider a selection procedure and offer different program pathways for patients in different stages. Prochaska and Velicer [24] advocated proactive recruitment combined with programs that match the stage of change a patient is in. A large amount of persons is expected to be in the precontemplation (40%) or contemplation (40%) phases. Hence, according to Prochaska and Velicer [24], proactive recruitment and stage-matched intervention will lead to better participation. With a selection procedure and a screening interview we can assess whether patients are 'ready' for the rehabilitation program as we provide it. The earlier mentioned Energetic program is an example of a rehabilitation program using an individual screening of patients' readiness to change before inclusion. They used the Patient Activation Measure (PAM13) [25] and classified almost all (27 out of 29) participants in the categories "becoming aware", "taking action" and "maintaining behavior and pushing further" [23], reporting a high willingness to change already at the start of the program. This example supports the idea of a screening prior to the rehabilitation program. However, patient screening also raises the problem what to do with those who do not meet the criteria? Regarding Energetic, after negative selection, some patients receive individual treatment instead of participating in the intended group program. For our individual NA rehabilitation program, a screening would be valuable to decide which pathway would be most suitable for a patient. We recommend one pathway for patients who are in the preparation or action phase; and one for patients who are in the precontemplation or contemplation phase and who need more information, education and time to make the necessary behavioral changes and take action.

In the current rehabilitation program, we already detect in what stage of change a patient is in and – if necessary – we coach the patient to reach the next stage. Coaching patients is more than just giving information and advice [3]. Education alone does not suffice. Patients also need to acquire skills, experiment with actions, and obtain confidence to implement behavioral change in their daily lives [26]. Indeed, Murphy et al. [27] found that tailored instructions may be a more effective symptom-management approach than giving general instructions. This finding corresponds well with the study results of chapter 5, in which we used patient-generated graphs to obtain insight into the pattern of pain and fatigue during a typical day. These graphs provide a tangible way to explore possible relationships between experienced pain and fatigue and daily activities. This enables personalized interventions to be deployed.

In my collaboration with other occupational therapists who treat patients with NA, I have learnt that there are differences in the effect of occupational therapy for people with NA. Two reasons seem to be of influence: 1) the treatment being not shoulder-specific enough in the practical aspects of the intervention (i.e. activity analysis, ergonomics, posture, and implementation into daily practice), and 2) the therapist not adequately connecting to the patient's stage of behavior change. Often, when therapy is not effective, this may be because the therapist is in the preparation or action phase, whereas the patient is in the (pre)contemplation phase. Hence, they are unlikely to apply the well-intended advices in daily practice. In literature this is referred to as the "righting reflex" [28], which is addressed in motivational interviewing techniques. The righting reflex is the tendency of health professionals to advise patients about the right path for good health. This can often have a paradoxical effect in practice, inadvertently reinforcing the argument to maintain the status quo [28]. The above-mentioned critical issues need to be carefully taken into account when further implementing our rehabilitation program for patients with NA in different healthcare settings.

What

Our multidisciplinary rehabilitation program focuses on improving motor control and scapular coordination, combined with training self-management strategies for reducing pain and fatigue. The different components of the intervention have been described in chapter 1. Our rehabilitation program proved to be effective for patients with NA (chapters 3 and 6). They valued the combination of receiving disease-specific information, learning self-management skills, and training motor control in a collaborative partnership using a personalized approach (chapter 4).

To further disseminate knowledge and promote implementation, it is useful to clearly describe the content of our treatment. Up to now, we developed so called "tip sheets" focusing on 1) education about NA, 2) education about finding a balance between activity and rest and, 3) ergonomics. In addition, we use the app "Physitrack" for video instructions on adequate exercise therapy. The next step is to develop a guideline for multidisciplinary rehabilitation for patients with NA.

Even though our rehabilitation program has proven to be effective, there are possibilities for further improvement:

- One of the six core self-management skills is 'taking action' [3]. Taking action may seem more like a decision than a skill but, in fact, there are skills involved in learning how to change a behavior. Coping and action plans [29] support patients

in both their behavioral change process and in applying their personal actions in daily life. Patients are asked to rate their confidence to reach their goals and their action plans. There is a common belief that the minimum level of self-efficacy for taking actions is 7 out of 10. This is important to evaluate when setting goals and making a plan of action. It is recommended to either set smaller goals or revise the action plan if a patient rates his/her confidence level lower than 7 [30].
- At the end of our rehabilitation program, we address the maintenance of the attained behavioral change and prepare patients for a possible relapse. It is important for them to know that a relapse will likely occur, but they are supported to gain confidence in their resilience how to deal with such a relapse. We can support this 'confidence in resilience' more specifically by creating a personalized retention and relapse plan together with patients.
- A recent study of our group has shown abnormal cerebral sensorimotor representations of the upper extremity after peripheral nerve damage in persons with NA, which can recover towards normality [31, 32]. As such adaptations occurred in visuomotor brain areas, our rehabilitation program could be further optimized by applying visuomotor strategies, where the focus is on visual feedback [32].

Assessment

Despite the positive primary outcomes of our rehabilitation program, some secondary outcome measures did not show change. In both studies (chapters 3 and 6), we did not find significant changes in self-efficacy nor in self-management. The Self-Efficacy for Performing Energy Conservation Strategies Assessment tool (SEPECSA) was used to assess how patients perceived their ability to apply energy conservation strategies in daily life [33]. The Pain Self-Efficacy Questionnaire (PSEQ) was used to assess the confidence that patients had in performing activities while being in pain [34]. We expected to find differences on these outcome measures, since training self-management strategies to cope with pain and fatigue constitute a key topic of our program.

Reason why the PSEQ showed no change may be because the construct that the PSEQ measures does not fit our intervention. The PSEQ measures a person's confidence in performing activities *despite* pain. In our intervention, we focus on pain as a *signal to reduce overuse* and not to continue activities despite pain. Therefore, on reflection, the PSEQ does not seem to be an appropriate measurement tool for our rehabilitation treatment.

The SEPECSA however, does correlate with our intervention because the SEPECSA measures the confidence a person has to apply the energy conservation strategies in daily practice. The absence of significant change in the SEPECSA could have been due to the fact that patients are "unconsciously incompetent" at the beginning of the program. We have learnt that some patients initially think that they have certain competencies, but during the program they gain insight that they did not yet have the appropriate knowledge and skills. This resulted in overestimation of their competencies, leading to higher initial scores on the SEPECSA than justified, leaving little opportunity for improvement.

Clinical experience has learnt that many occupational therapists who attended our training find it difficult to observe shoulder movement patterns during relevant activities. The Upper Limb Performance Assessment (ULPA) is an ecologically valid, criterion-referenced, two-stage assessment of upper-limb contributions to daily life task performance [35]. In the future, it would be interesting to investigate if the ULPA can be used as a tool to support the observations of shoulder and arm movements during daily activities.

Muscle fatigability and scapular dyskinesia are two important impairments that influence patients' complaints and activity limitations. Quantifying scapular dyskinesia might allow better tailoring of the treatment to an individual and monitor the effect of the rehabilitation program. Unfortunately, quantifying scapular dyskinesia is very complex and, currently, no validated tools exist to assess shoulder kinematics, scapular posture, movement and dysfunction [36, 37]. Regarding muscle fatigability, it would be interesting to gain more insight into possibilities to quantify muscle fatigability for patients with NA.

Our patient-generated graphs for the assessment of pain and fatigue (chapter 5) have already proven their value in clinical practice. Chapter 5 is the first study to explore whether these pain and fatigue graphs can be used as outcome measures as well. The results showed sufficient test-retest, inter-rater reliability, and concurrent validity. In future studies, it would be interesting to investigate if these graphs can be used as real-time assessment tools, possibly in combination with digital technologies such as an app or activity tracker.

Future perspectives and next steps

Implementation

Almost all patients visiting the Plexus Clinic actually have or have had physical therapy, often with no effect or even an increase in symptoms (50% of the cases) [2]. Strength training often causes symptom worsening, as it increases the dyskinetic movement pattern. Remarkably, an occupational therapist is involved in only a small proportion of patients, which was evident in the control group of our RCT (chapter 6) of whom only 1 out of 13 participants reported to have had occupational therapy during the usual care period. The results of this thesis support the notion of a substantial role for the occupational therapist next to the physical therapist. How can it be that this role is not yet recognized?

One of the reasons could be that occupational therapists usually do not participate in shoulder networks in the Netherlands. These networks typically consist of physical therapists and physicians. Occupational therapists are primarily focused on activities and participation and may feel less connected with function-oriented working groups or networks. As a result, they remain unaware of their possible role in the interdisciplinary treatment of patients with NA, especially when it comes to shoulder-specific aspects (see chapter 1). Complementing the occupational therapists' focus on activities and participation with disease- and shoulder-specific aspects will enhance their importance for the effectiveness of NA rehabilitation.

In addition to the unfamiliarity among occupational therapists themselves, there is also unfamiliarity among other healthcare providers with the possible role of occupational therapists. As stated before, the knowledge of NA has increased over the last years among general practitioners, neurologists and physical therapists (the professionals that patients with NA most often turn to). Still, the time it takes to make the right medical diagnosis is often too long. It is reasonable to expect that unfamiliarity with the disease itself implies unfamiliarity with possible treatment as well. This could prevent healthcare providers from referring patients to occupational therapy in combination with specialized physical therapy, which emphasizes the importance of further dissemination of knowledge of NA and of our multidisciplinary rehabilitation program.

In 2015, we started training courses for physical and occupational therapists and multidisciplinary rehabilitation teams. We experienced that it is much more difficult to find occupational therapists for this training than involving physical therapists. This could be due to the above-mentioned 'unfamiliarity' or it may be that occupational therapists are 'unconsciously incompetent' when it comes to the treatment of patients with NA. Most occupational therapists may believe they have sufficient knowledge and skills when it comes to generic topics such as ergonomics, posture, activity-rest balance, activity analysis, and behavioral change, but they may be unaware of their possible skills and role in the treatment of shoulder-specific aspects? So how can we involve occupational therapists who do not know that they need to be part of the rehabilitation team for patients with NA and who may (or may not) realize that they have insufficient knowledge and skills when it comes to the shoulder-specific aspects of NA rehabilitation? Until now, we found occupational therapists through 1) physical therapists in the community who attended our training and wanted to collaborate with an occupational therapist, 2) multidisciplinary rehabilitation teams who are interested in our rehabilitation program, and 3) by referring patients to primary care for occupational therapy. In the future, we may consider other ways to actively recruit occupational therapists. Interviewing trained occupational therapists could be a good starting point. We can learn from their experiences, needs and wishes. How did they get involved in the treatment of the NA population? What makes it attractive? What are the difficulties, and how to engage more occupational therapists?

NA-Network

We have a great interest in creating a solid NA-network of therapists in primary care and in rehabilitation settings in the Netherlands. We already started to create a map (Google maps) showing therapists and teams we have trained over the years and/or who have interest in - and experience with - the treatment of patients with NA. There are challenges in further expanding this network, keeping the network up-to-date and connecting the people involved more effectively. To make the network more effective, it may be necessary to organize peer review moments, to offer additional training modules, and to create an online platform where questions can be asked to each other.

In addition to the previously proposed process evaluation, we recommend a qualitative study among therapists and rehabilitation teams who have had our training and are part of the NA-network. It would be good to learn from them about the implementation of the training into their daily practice. Have they been able to perform the program as intended? And – especially in primary care – have physical and occupational therapists been able to collaborate? And to what extent is this collaboration experienced as interdisciplinary? What expectations do these therapists have from an NA-network? The answer to these questions could provide us with insight in how to further implement our NA rehabilitation program into different healthcare contexts.

Clinical practice and research

- According to the UK MRC-framework [12], costs (resources), consequences (outcomes, impact), and implementation aspects should be core components of intervention research. Outcomes of our program have already been evaluated in chapter 6 and implementation has partly been evaluated in chapter 4 by evaluating the treatment delivery in a rehabilitation context. Costs – in terms of resources used – have not yet been investigated. Therefore, a cost-effectiveness would be needed in addition to the previously mentioned process evaluation. In clinical practice, we see many patients who attended - prior to their visit to the Plexus Clinic - many physical therapy sessions, reporting no effect or even an increase in symptoms. It would therefore be interesting to investigate the financial consequences of these excessive physical therapy sessions and how this relates to the costs of our rehabilitation program.

- Our rehabilitation program has been developed and evaluated for patients with NA, but it might be useful for the treatment of shoulder complaints and disabilities of different origin as well, for instance other plexopathies or neuromuscular disorders (e.g. facioscapulohumeral muscular dystrophy and myotonic dystrophy).

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Chapter 8

Nederlandse samenvatting

In dit proefschrift beschrijven we de ontwikkeling en evaluatie van onze poliklinische multidisciplinaire revalidatie behandeling voor patiënten met neuralgische amyotrofie (NA). NA is een onbekende, maar veel voorkomende aandoening. Tot nu toe zijn er nog geen behandelingen beschikbaar voor patiënten met NA in de chronische fase. In de literatuur is alleen beperkte informatie te vinden over fysiotherapie voor patiënten met NA, waarin wordt beschreven dat 'standaard fysiotherapie' geen effect heeft of de klachten – in meer dan 50% van de gevallen – zelfs verergert. Met dit proefschrift presenteren we een effectieve multidisciplinaire revalidatie behandeling voor patiënten met NA.

In **hoofdstuk 1 geven** we een beschrijving van de aandoening NA, de impact die NA heeft op het dagelijks leven van mensen en geven we een beschrijving van de ontwikkeling en inhoud van ons revalidatie programma. NA is een acute auto-immuun ontsteking van (meestal) de zenuwen die zorgen voor aansturing van de spieren in de schoudergordel, arm en hand (zenuwen vanuit de 'plexus brachialis'). NA wordt gekenmerkt door één of meerdere aanvallen van acute hevige pijn, die leiden tot zenuwschade, waardoor verzwakking van de desbetreffende spieren optreedt. Het blijkt een veel voorkomende aandoening te zijn, waarbij 1 op de 1000 mensen per jaar in Nederland deze aandoening krijgt. Patiënten met NA ervaren langdurig restklachten en beperkingen in het uitvoeren van hun dagelijkse bezigheden. De meest voorkomende restklachten zijn ernstige pijn, algemene vermoeidheid en spierzwakte. Deze klachten veroorzaken bewegingsbeperkingen, verminderde duurbelasting (snellere vermoeidheid van de aangedane spieren) en een veranderd beweegpatroon van de schouder (dyskinesie).

In 2009 zijn de afdelingen Revalidatie en Neurologie van het Radboudumc gestart met een zogenaamde "Plexuspoli". Dit is een specialistische polikliniek speciaal voor patiënten met NA of andere aandoeningen aan de zenuwen van de plexus brachialis. Het multidisciplinaire team van de plexuspoli bestaat uit een neuroloog, revalidatiearts, fysiotherapeut en ergotherapeut, die nauw met elkaar samenwerken. De inhoud van onze revalidatie behandeling is gebaseerd op 'best practice' (ervaring van het plexuspoli-team). De twee belangrijkste doelen van de revalidatie behandeling zijn: 1) het verbeteren van het bewegingspatroon van de schouder (stabiliteit en coördinatie van het schouderblad), gecombineerd met 2) het trainen van zelfmanagement-strategieën om pijn en vermoeidheid te verminderen.

Hoofdstuk 2 is een review gericht op recente inzichten en ontwikkelingen in NA. NA is in de eerste plaats een klinische diagnose die te stellen is met een duidelijke anamnese, in combinatie met lichamelijk onderzoek. De 'klassieke' vorm van NA, waarbij de zenuwen van de plexus brachialis beschadigd raken en de spieren van de schoudergordel, arm en hand aangedaan zijn, komt het meeste voor (ongeveer 70% van de patiënten met NA). Andere varianten zijn, beschadiging van de 'plexus lumbosacralis' (uitval rondom de heup en in het been) in 10% van de gevallen en/of betrokkenheid van de 'nervus phrenicus', waardoor zwakte van het diafragma (middenrif), wat lijdt tot benauwdheid en problemen met ademhaling. Er is ook een variant die pijnloos begint in ongeveer 4% van de patiënten met NA.

Er zijn meerdere casus beschrijvingen en onderzoeken die suggereren dat medicatie (orale corticosteroïden) en/of infuus (intraveneus immunoglobuline) effectief kunnen zijn in de acute fase van NA (start medicatie zo snel mogelijk, maar in ieder geval binnen 2 weken). Toch blijft de meerderheid van de patiënten met NA beperkt in hun dagelijkse activiteiten door pijn en vermoeidheid. Deze klachten blijven bestaan door een inefficiënte manier van bewegen (verminderde motorische coördinatie) van de aangedane schouder/arm (scapulaire dyskinesie), verlies van duurvermogen in de aangedane spieren en overbelasting van de compenserende spieren. Fysiotherapie voor NA richt zich op het verbeteren van de motorische controle. Patiënten worden getraind om de positie van hun schouderblad te corrigeren en gecontroleerd te bewegen. Ze leren de houding en bewegingscontrole te vergroten tijdens het inschakelen van de schouder, arm en hand. Ergotherapie voor NA richt zich op het leren omgaan met pijn en vermoeidheid met behulp van energiebesparende strategieën. Belangrijke elementen zijn het aanleren van een juiste houding/ergonomie tijdens dagelijkse activiteiten zoals zelfverzorging, huishouden, werk, onderwijs, sport en vrije tijd en het aanleren van een optimale schouder- en armpositie in rust.

Recente bevindingen tonen aan dat zenuwen die niet herstellen insnoeringen of constricties kunnen vertonen, wat zorgt voor een beschadiging van de zenuw. Wanneer er sprake is van een (bijna-)volledige uitval van een spier, zonder herstel na 6 maanden, kan aan deze insnoeringen gedacht worden. Dan kan overwogen worden om binnen 6-12 maanden de insnoering operatief op te heffen (chirurgische neurolyse) om herstel van de beschadigde zenuw mogelijk te maken. Bij patiënten voor wie een neurolyse geen optie is, maar die wel last blijven houden van restverschijnselen, kunnen in tweede instantie andere chirurgische behandelingen overwogen worden, zoals zenuw- of peestranspositie(s). Patiënten met uitval van het middenrif kunnen baat hebben bij nachtelijke niet-invasieve mechanische beademing en coördinatieve inspiratoire ademtraining. Chirurgisch pliceren (strak trekken) van het middenrif kan overwogen worden als er geen spontaan herstel optreedt.

Hoofdstuk 3 beschrijft de resultaten van een pilotstudie. Dit was de eerste studie die het effect van een revalidatie behandeling met gecombineerde fysio- en ergotherapeutische behandeling voor patiënten met NA onderzocht. Het betrof een 16 weken durend programma waarin patiënten wekelijks werden behandeld in week 1 tot en met 4, eenmaal per twee weken in week 5 tot en met 8 en maandelijks in week 9 tot en met 16. Elke behandelsessie bestond uit één uur fysiotherapie en één uur ergotherapie. Acht patiënten met NA namen deel aan het onderzoek. Er werden metingen uitgevoerd drie maanden voorafgaand aan de behandeling, bij de start en bij afronding van de behandeling. Primaire uitkomstmaten waren de *Shoulder Rating Questionnaire - Dutch Language Version* (SRQ-DLV) en de *Canadian Occupational Performance Measure* (COPM) om zowel de uitvoering als tevredenheid met deze uitvoering van belangrijke dagelijkse activiteiten te evalueren. Secundaire uitkomstmaten waren onder andere de *Disabilities of Arm Shoulder and Hand* (DASH) vragenlijst, krachtmetingen en de *Self-Efficacy for Performing Energy Conservation Strategies Assessment* (SEPECSA). De 36 item *Short Form Health Survey* (SF-36) vragenlijst werd gebruikt om de gezondheid gerelateerde kwaliteit van leven te meten en de *Checklist Individual Strength* 20 (CIS-20) om vermoeidheid te meten.

Resultaten toonden significante verbeteringen (gemiddelde; 95% betrouwbaarheid interval) op de COPM uitvoering (2,3; van 0,9 tot 3,7) en tevredenheid (1,4; van 0,4 tot 2,4) scores, op de SRQ-DLV (14,8; van 7,4 tot 22,0) en de subschaal voor gezondheidsverandering van de SF-36 (-37,5; van -56,9 tot -18,2). Krachtmetingen lieten een trend zien in de richting van krachttoename van alleen de serratus anterior spier (verantwoordelijk voor de stabilisatie van het schouderblad op de romp). Deze pilotstudie toonde aan dat patiënten met NA verbeteren op activiteiten- en participatieniveau na onze multidisciplinaire revalidatie behandeling.

Het doel van **hoofdstuk 4** was om - vanuit het perspectief van patiënten met NA en therapeuten - inzicht te krijgen in de 'kritische ingrediënten' van onze revalidatie behandeling, die ertoe hebben bijgedragen dat patiënten verbeterd zijn op activiteiten- en participatieniveaus, zoals gerapporteerd in hoofdstuk 3. Er werd een kwalitatief onderzoek uitgevoerd door middel van semigestructureerde interviews. Deelnemers waren dezelfde acht patiënten die deelnamen aan het onderzoek van hoofdstuk 3, aangevuld met vijf van hun therapeuten: drie ergotherapeuten en twee fysiotherapeuten. De gegevens werden geanalyseerd met behulp van de methode van 'constante vergelijking'.

De bevindingen lieten zien dat patiënten en therapeuten vergelijkbare kritische ingrediënten weergaven, vanuit verschillende perspectieven. De expertise en nauwe samenwerking van de behandelaars was een belangrijk onderdeel dat werd genoemd als bijdragend aan het vertrouwen, het begrip, de bewustwording en het vermogen van patiënten om weer controle te krijgen over hun dagelijkse activiteiten en participatie. Samenwerking tussen therapeut en patiënt in partnerschap, gecombineerd met gezamenlijke besluitvorming leidde tot een persoonlijke benadering die door patiënten werd gewaardeerd en door therapeuten werd benadrukt als essentieel voor een succesvolle behandeling. De kritische ingrediënten werden samengevat als een combinatie van het ondersteunen van zelfmanagementvaardigheden en het leveren van NA-specifieke en beroeps-specifieke expertise. Sommige patiënten hadden graag meer opties gehad om de intensiteit en duur van de behandeling te personaliseren, en om een psycholoog te kunnen raadplegen of steun te krijgen van lotgenoten.

Hoofdstuk 5 is een klinimetrisch onderzoek dat zich richt op het in kaart brengen van het patroon van ervaren pijn en vermoeidheid van patiënten met NA gedurende de dag. De ergotherapeut richt zicht op het verkrijgen van inzicht en het begrijpen van de relatie tussen de restklachten van NA (pijn en vermoeidheid) en het uitvoeren van dagelijkse activiteiten. Dat wil zeggen; hoe pijn en vermoeidheid dagelijkse activiteiten beperken of beïnvloeden en hoe dagelijkse activiteiten zelf NA gerelateerde klachten kunnen verergeren.

Hoewel er veel meetinstrumenten zijn om pijn of vermoeidheid te meten, geeft geen van deze meetinstrumenten inzicht in het *patroon* van de klachten gedurende de dag of de relatie met activiteiten. Daarom hebben we pijn- en vermoeidheidsgrafieken ontwikkeld waar patiënten op een 24-uur schaal (X-as, horizontaal) aangeven hoe hun klachten (Y-as, verticaal) over de dag verlopen op een 10-puntsschaal. Deze grafieken hebben hun waarde in de dagelijkse praktijk al bewezen. Het zou een aanvulling zijn als deze grafieken ook als meetinstrument gebruikt zouden kunnen worden, om het effect van de behandeling te evalueren. Het doel van deze studie was daarom het onderzoeken van de interbeoordelaars en test-hertest betrouwbaarheid en de concurrente validiteit van de pijn- en vermoeidheidsgrafieken bij patiënten met NA.

Interbeoordelaars en test-hertest betrouwbaarheid (n=8) werden onderzocht met behulp van intraclass correlatiecoëfficiënten (ICC's). Concurrente validiteit (n=47) werd getest met behulp van de *Numerical Rating Scale* (NRS) voor pijn en de *Checklist Individual Strength* (CIS)-subschaal vermoeidheid. ICC's van test-hertest betrouwbaarheid varieerden van 0,72 tot 0,93 voor pijn en van 0,67 tot 0,85 voor vermoeidheid, terwijl ICC's van interbeoordelaars betrouwbaarheid varieerden van 0,76 tot 0,97 voor pijn en van 0,47 tot 0,97 voor vermoeidheid. De correlaties van de gemiddelde pijn- en vermoeidheidsgrafiekscores met de NRS voorpijn en

CIS vermoeidheidsscores waren respectievelijk sterk (r_s = 0,75, p<0,000) en matig (r_s = 0,42, p=0,003). Geconcludeerd werd dat deze exploratieve studie voldoende betrouwbaarheid en validiteit van de pijn- en vermoeidheidsgrafieken aantoont om NA-gerelateerde klachten gedurende de dag te beoordelen.

Hoofdstuk 6 rapporteert de resultaten van een gerandomiseerd gecontroleerd onderzoek (*randomised controlled trial* (RCT)). Het primaire doel was om de effecten van onze multidisciplinaire revalidatie behandeling te vergelijken met gebruikelijke zorg bij patiënten met NA. Ons secundaire doel was het beoordelen van de langetermijneffecten van de revalidatie behandeling op de uitkomstmaten. De belangrijkste uitkomstmaat was de door de patiënt zelf gerapporteerde functionele capaciteit van de schouder, arm en hand gemeten met de SRQ-DLV. Vooraf werden verschillende overige uitkomstmaten geselecteerd, op de domeinen van functies, activiteiten en participatie.

In totaal deden 47 patiënten met NA mee aan deze RCT. Door uitval waren er voor de analyse 22 deelnemers in de interventiegroep (multidisciplinaire revalidatie) en 15 in de gebruikelijke zorggroep. Ondanks randomisatie hadden de patiënten in de interventiegroep een langere periode sinds het begin van NA, vergeleken met de gebruikelijke zorg groep. Het gemiddelde groepsverschil van de SRQ-DLV na de behandeling, gecorrigeerd voor geslacht, leeftijd en begin score, was 8,60 (95% betrouwbaarheid interval: 0,26 -16,94, p=0,044). Het aantal patiënten dat een 'klinisch relevante' verbetering (≥12) op de SRQ-DLV lieten zien was groter voor de interventiegroep (59%) dan voor de gebruikelijke zorggroep (33%), met een '*number needed to treat*' van 4. De gemeten verbeteringen bleven behouden na een langetermijn periode van 18 weken. Ondanks het verschil in tijd sinds het begin van NA tussen de 2 groepen, had dit bij een extra analyse geen effect op de uitkomsten. De meeste overige uitkomstmaten lieten geen veranderingen zien. Wel leek er een trend te zijn bij bijna alle overige uitkomstmaten in het voordeel van de interventiegroep, wat kan duiden op beter functioneren, minder pijn en vermoeidheid, en betere zelfmanagement en participatie.

Appendices

Dankwoord

Wat zijn er veel mensen betrokken geweest bij de ontwikkeling van dit proefschrift. Officieel 5 jaar, maar onofficieel heeft het proces 12 jaar in beslag genomen. Ik ben trots op het eindresultaat, wat er niet was geweest zonder de hulp, ondersteuning en betrokkenheid van velen. Ik wil iedereen bedanken die in welke vorm dan ook onderdeel is geweest van dit proces; een aantal mensen in het bijzonder.

Als eerste wil ik alle **deelnemers** bedanken die mee hebben gedaan aan de verschillende onderzoeken. De bereidheid, betrokkenheid, inzet en het enthousiasme om mee te doen aan de verschillende onderzoeken heeft indruk op mij gemaakt. Vooral jullie motivatie om bij te dragen aan het verkrijgen van meer inzicht, kennis en focus op neuralgische amyotrofie (NA) en (delen van) de revalidatiebehandeling. Jullie ervaringen met de behandeling zijn zeer waardevol geweest in het verder ontwikkelen en vormgeven van de behandeling. De deelnemers zijn betrokken geweest bij alle stappen in het proces om uiteindelijk de specifieke revalidatiebehandeling te kunnen vergelijken met de reguliere zorg. Daarom kunnen we nu een effectieve behandeling publiceren, waar alle mensen met NA, nu en in de toekomst, mee geholpen zijn.

Dan wil ik mijn **promotieteam** bedanken. Ik heb me in de afgelopen jaren ontzettend gesteund gevoeld. **Maud,** wat heb ik een bewondering voor alles wat jij doet. Toen jij hoogleraar ergotherapie werd, was direct duidelijk dat jij mijn eerste promotor zou worden. Het is een eer onder de vlag van een ergotherapie leerstoel te mogen promoveren. Je ergotherapeutische kennis en visie zijn een inspiratie. Dank dat je deze met mij wilde delen. **Sander,** wat heb ik veel van je mogen leren. Je wijze raad als het gaat om methodologie en statistiek. Ik kan me een teambespreking herinneren die uitdraaide op een les in statistiek. Dat heb ik erg gewaardeerd en heeft mij ontzettend geholpen. Ook je kritische blik en feedback zijn erg van meerwaarde geweest. Naast een statistiek les heb ik ook een schriftelijke taalles ontvangen ten behoeve van het schrijven van mijn discussie. Bewonderenswaardig hoe je overkoepelend, toch concreet feedback kunt geven, om mijn schrijven te verbeteren. **Jan**, dank voor je betrokkenheid bij alle verschillende facetten; patiëntenzorg, onderzoek en onderwijs. Je feedback, meedenken, kansen zien en je vermogen om te relativeren zijn waardevol geweest. Ik wil je nog extra bedanken voor je begeleiding bij het klinische deel van de NA-CONTROL studie, hoofdstuk 6 van dit proefschrift. Dat jij het 'laatste stukje' naar publicatie van dit artikel wilde waarnemen toen ik met zwangerschapsverlof ging, heb ik zeer gewaardeerd. En dan mag ik je ook nog eens extra feliciteren met de stappen die jij in de tussentijd hebt gezet in je eigen carrière: Prof. dr. Jan. **Edith**, van begin af aan al betrokken bij mijn traject, ook al lang voordat het een officieel promotietraject werd: als collega ergotherapeut (op de plexuspoli), voormalig leidinggevende en copromotor. Jij bent iemand waar ik altijd op kan rekenen en bij terecht kan, voor inhoudelijke vragen, dilemma's, twijfels of onzekerheden. Je weet mij altijd weer verder te helpen en te coachen. Niet alleen werk gerelateerd, maar ook met privé kwesties kan ik bij jou terecht. De balans tussen werk en privé is voor mij op verschillende momenten in dit traject een uitdaging geweest. Dit bracht de nodige dilemma's en uitdagingen met zich mee. Ik wil je bedanken voor alle keren dat ik bij je terecht kon om even stoom af te blazen, maar ook voor de gezelligheid, je luisterend oor en geruststelling. Dank je wel!

En dan mijn fysio en ergo NA-maatjes. Wat ben ik blij dat jullie mijn **paranimfen** zijn! **Jos**, mijn werk partner. Wat trekken wij al lang samen met elkaar op. Dat begon in de patiëntenzorg op de plexuspoli. We waren op hetzelfde moment allebei bezig met afstuderen van onze master studies. Vanuit dezelfde interesse was het niet meer dan logisch dat we ons afstudeeronderzoek samen bij de plexuspoli gingen doen, elkaar aanvullend vanuit onze verschillende discipline. Ik zie ons nog samen (ook wel op een vrije zaterdag) data invoeren, analyseren of schrijven; vaak met veel onderbreking en geklets tussendoor. Na ons afstuderen ging het zo verder. Vanuit enthousiasme rolden we van het ene project of onderzoek in het andere; allen met het doel om de NA behandeling verder vorm te geven en te onderzoeken. Naast patiëntenzorg en onderzoek voegden we daar vanaf 2015 - geheel volgens de speerpunten van het Radboudumc - nog onderwijs aan toe. Na een leuke en intensieve lesdag, altijd even samen afschakelen. In al die jaren hebben we natuurlijk privé ook veel van elkaar meegekregen. Het vinden van een partner, krijgen van kinderen. Qua werk en leven lopen we aardig gelijk op, zelfs onze promotiedatums liggen nog geen 2 maanden uit elkaar. Maar qua persoonlijkheid zijn er ook verschillen. We vullen elkaar aan en dat is waardevol. Waar ik bezig ben met structuur, planning en voorbereiding, ben jij van de nieuwe ideeën, inspiratie en 'het komt wel goed'. Ik heb bewondering voor je kennis, kunde, enthousiasme en je relaxte instelling. Daar kan ik veel van leren. Die relaxte houding en het feit dat je mij vertrouwen geeft is heel fijn in het voortraject naar mijn verdediging toe. Dank dat je mijn paranimf bent en op naar nog veel fijne jaren samenwerken! **Yvonne,** lange tijd hebben wij vanuit de ergotherapie de plexuspoli gedraaid. Samen hebben we onze ervaring met ergotherapie bij NA opgebouwd. Sparren, ideeën delen en nieuwe inzichten verkrijgen. Dit heeft een waardevolle bijdrage geleverd aan de ontwikkeling van de ergotherapie behandeling zoals deze nu is. Naast productief en constructief, is het ook altijd ontzettend gezellig met jou en ben je meer dan alleen een collega. We hebben veel gemeen en je loopt vaak net een stapje vooruit. We zeiden allebei dat we niet zouden gaan promoveren. Jij promoveerde in 2022 en nu ben ik aan de beurt. We dachten dat het onmogelijk was om te functioneren met een minimaal aantal uren slaap per nacht (vanwege het moederschap). Toen jij moeder werd, zag ik dat jou dat toch lukte. En dat gaf mij vertrouwen toen ook ik moeder werd. Als ik mijn verdediging net zo goed mag doen als jij, dan ben ik apetrots.

Vanzelfsprekend ben ik ook veel dank verschuldigd aan mijn collega's van de **plexuspoli.** Toen ik 3 maanden in dienst was bij het Radboudumc kwam de vraag of ik mede de plexuspoli wilde opzetten. Ik had nog geen idee wat dit precies ging inhouden en waar het toe zou leiden. Ik mocht dit doen onder begeleiding van jou, **Allan.** Het was een hele uitdaging en een waar avontuur. Het feit dat de plexuspoli er is, is aan jou te danken **Nens**. NA is jouw 'uit de hand gelopen hobby'. Jij hebt NA op de kaart gezet en samenwerking gezocht met de afdeling revalidatie. Ik zie jou als onofficiële mede-promotor. Je bent mede auteur van letterlijk alle artikelen uit mijn proefschrift. Ik bewonder je efficiëntie. De snelheid waarmee ik feedback op mijn stukken kreeg is onbegrijpelijk. En ik ben blij dat je - ondanks je nieuwe 'hobby' - nog steeds op woensdagochtend de plexuspoli met ons draait. Jouw vermogen om de patiënt echt als geheel te zien en precies de vinger op de juiste plek te leggen is bijzonder. Dat is een kracht en mooi om te zien. Ook de andere collega's van de plexuspoli wil ik hier noemen**; Jan, Jessica**, **Judith en Manouk**. Ik ervaar de plexuspoli als een warm bad. Er is veel expertise opgebouwd, respect voor elkaar en voor elkaars kunnen, we vullen elkaar aan. Daarnaast is er (soms te?) veel lol tijdens de voor- en nabespreking van de plexuspoli. Dank aan dit fijne team! Ik wil hier ook de mensen noemen die in de afgelopen jaren kort of lang betrokken zijn geweest bij de plexuspoli of de behandeling van plexus patiënten: **Sander, Harmen, Daphne, Tamara, Jasper, Yvonne, Edith, Jacqueline, Maaike en Yolanda.** Dank voor jullie bijdrage!

Mijn **ergotherapie collega's en oud-collega's.** Wat een geweldig bevlogen team hadden en hebben wij en wat ben ik daar trots op. Ik heb altijd gezegd dat ik de beste baan heb die er is. En daar sta ik nog altijd achter; mede dankzij jullie. Een groot deel van mijn werkplezier komt voort uit de samenwerking in en met een team van fijne mensen. Dank voor de leuke gesprekken, lekkere kopjes koffie, gezelligheid binnen en buiten het werk. De steun en betrokkenheid die ik in dit team ervaar zijn hartverwarmend. Eigenlijk is de hoeveelheid aan woorden in dit dankwoord niet in overeenstemming met hoeveel jullie als ergo-team voor mij betekenen. Dank jullie wel voor alles!

Dank aan iedereen van het **Netwerk Ergotherapie Onderzoekers Nijmegen (NEON).** Wat een kennis, ervaring en kunde zit er in deze groep mensen. De bijeenkomsten zijn altijd nuttig en inspirerend. Voortkomend uit NEON, wil ik ook de PhD-students van **jong-NEON** bedanken. Het is fijn met gelijkgestemde laagdrempelig contact te hebben over alle verschillende facetten die bij het promoveren komen kijken.

Patiëntenzorg secretariaat, het plannen van de patiënten van de verschillende onderzoeken is niet altijd makkelijk geweest. Het was soms puzzelen, schuiven en creatief zijn om ervoor te zorgen dat de uitvoering van de behandeling kon plaatsvinden op de manier die nodig was voor het onderzoek. Jullie kregen het steeds weer voor elkaar. Dank voor jullie inzet! En niet onbelangrijk, dank voor jullie tijd en de gezelligheid als ik even binnen kom waaien. **Staf secretariaat** en **Laurien**, jullie zijn onmisbaar als het gaat om de ondersteuning bij het organiseren van de cursus Plexus management. Dank voor het regelen en al jullie werk 'achter de schermen'.

Marianne Dees, toen ik je benaderde of je mijn mentor wilde zijn, gaf je aan dat je dat wilde doen als je onderdeel kon zijn van mijn proces / inhoudelijk kon meedenken. En dat is gebeurd. We hebben niet heel frequent contact gehad (en ook niet hoeven hebben). Toch was elke bijeenkomst nuttig en waardevol. Dan waren er nieuwe invalshoeken of inzichten die we konden bespreken. Juist de input en jouw visie vanuit een andere 'tak van sport' van de gezondheidszorg hebben een bijdrage geleverd aan het proces. Dank daarvoor.

Er hebben veel mensen meegewerkt en/of mee geschreven aan de verschillende hoofdstukken. Dank voor jullie input en begeleiding. The Packer managing fatigue program is used as guideline for the occupational therapy treatment for patients with NA. We were thrilled that you, **Tanya Packer** - founder of that program - was willing to be keynote speaker at our symposium in 2014. Afterwards, you became a visiting professor at our rehabilitation department. It was an honor that you supervised me on the qualitative study (chapter 4) and on the graph article (chapter 5). Your enthusiasm, commitment and positive way of giving feedback brought me a lot in my role as a junior researcher. I wish all PhD students such a great person during their PhD process. **Renee**, je hebt de NA-CONTROL studie op een gedegen manier tot een succesvol einde gebracht. Ik ben dankbaar dat ik het klinische gedeelte van de Randomized Controlled Trial (RCT) heb mogen oppakken. De samenwerking met jou hierin was altijd prettig en leerzaam! Ik heb veel van je geleerd, onder andere over MATLAB en Castor EDC. Vanuit je nieuwe rol als assistent professor aan de Universiteit Utrecht zijn er plannen om verder te gaan met onderzoek en NA. Hopelijk kunnen we in de toekomst onze samenwerking nog verder uitbreiden! **Ton**, ik weet niet of jij het je nog kunt herinneren, maar dankzij jou ben ik in 2008 bij het Radboudumc begonnen. Daarvoor heb je mij begeleid bij het afstudeeronderzoek van de opleiding ergotherapie aan de HAN. Ik heb opnieuw van je begeleiding mogen profiteren bij hoofdstuk 4 van dit proefschrift. Dank je wel voor alles wat ik van jou heb mogen leren als het gaat om het doen van kwalitatief onderzoek. Mijn dank gaat ook uit naar **alle studenten** die betrokken zijn geweest bij het uitvoeren van verschillende onderzoeken. Ik dank **Marianne Jonker** voor haar statische bijdrage aan de RCT van hoofdstuk 6.

Dank ook voor de fijne samenwerking met alle andere collega's van de **afdeling revalidatie,** collega's van het **Spierziekten Centrum Radboudumc** en de verenigingen **Spierziekte Nederland** en **Ergotherapie Nederland**.

Alle **deelnemers aan de cursus Plexus management**. Wat zijn jullie een enthousiaste en leergierige groep van fijne collega's. Dank dat jullie de cursusdagen zo inspirerend en interactief hebben gemaakt. Mooi om te zien hoe jullie het geleerde in de praktijk brengen, en alle kennis en vaardigheden in het werkveld verspreiden!

Margo, jij hebt een belangrijke rol gespeeld in het begin van mijn carrière. Als voormalig leidinggevende heb jij mij aangenomen in het Radboudumc en verwelkomd bij de afdeling ergotherapie. Je hebt mij de kans gegeven mijn interesse in het doen van onderzoek te exploreren. Hoe mooi dat je nu in de manuscriptcommissie zit van mijn proefschrift.

Yette, wat prijs ik mij gelukkig dat het mijn werk is in contact te zijn met zulke mooie mensen. Ik vind het prachtig dat ik van jouw vakbekwaamheid gebruik mag maken. Het is een eer dat je de voorkant van mijn proefschrift hebt ontworpen.

Buiten het werk om zijn er ook een aantal mensen die ik hier graag wil noemen. Als eerste mijn lieve vriendinnengroep, 'de systems'**. Laura, Janna, Juul, Anouk, Paula, Lise en Chantal**. Ik wil jullie bedanken voor alle fijne momenten samen, de borrels, uitjes, feestjes en weekendjes weg. Dank voor de afleiding en gezelligheid in de afgelopen jaren, en voor jullie luisterend oor op de nodige momenten. Ik ben blij dat er nu meer vrije tijd komt én dat we (weer) dichterbij een aantal van jullie zijn gaan wonen in Groesbeek. Laat de volgende borrels en uitjes maar komen!

Brigit, dankzij de vriendschap van onze ouders, ben jij mijn 'oudste vriendin'. Ik ben dankbaar dat we ons hele leven al vriendinnen zijn en voor de vele kopjes koffie, thee, wijntjes, etentjes en goede gesprekken. Inmiddels hebben we allebei 2 dochters. Wie weet ontstaat er tussen die meiden ook zo'n mooie vriendschap.

Lonneke, Marloes en Lisa, mijn lieve 'froomies'. In het 'oranje huis' hebben we lief en leed gedeeld. Jullie waren er voor mij aan het begin van mijn carrière, tijdens mijn master studie en alles wat daarna volgde. Wat een geluk dat jullie mijn huisgenootjes waren!

Marsha, Paula en Gerbrig. Na de opleiding ergotherapie zijn we allemaal onze eigen weg gegaan, maar het blijft fijn om vriendinnen te hebben uit het ergo-wereldje.

Bert en Anke, Marie-Suzanne, Wilfred, Maartje en Marijn. Toen ik Toine 10 jaar geleden leerde kennen, kreeg ik jullie er gratis bij. Je schoonfamilie kun je niet kiezen, maar als ik had kunnen kiezen, had ik jullie gekozen. Bedankt voor jullie oprechte interesse en betrokkenheid. Zowel bij mijn promotie als bij het reilen en zeilen van ons gezin. Ik vind het mooi om te zien en te mogen ervaren hoe warm jullie familie is. Bert en Anke, dank voor alle uren in de auto om bij ons te komen oppassen en voor de lekkere gekookte maaltijden van Anke.

Sabine, mijn grote zus. Ik heb in mijn leven veel van jou geleerd. Ik kan me aan jou optrekken. Jij bent diegene waar ik bij terecht kan als ik ergens mee zit, wat dat ook mag zijn. Ik heb bewondering voor hoe jij je eigen huisartsenpraktijk runt, er voor je gezin bent en de balans kunt houden. Heerlijk dat we beide in dezelfde sector werken, om over patiëntenzorg, onderzoek, mijn promotie en alles wat daarmee samen hangt te kunnen sparren. Dank je wel daarvoor. En natuurlijk voor alle super gezellige momenten, gezamenlijke interesses en idolen ;) **Julian, Mirte en Guido, j**ullie zijn een verrijking voor Sabine en voor ons allemaal. Bedankt dat we ons altijd thuis voelen bij jullie. Norah en Romy blijven maar vragen: wanneer gaan we weer naar Mirte en Guido? (ook al hebben we jullie een paar dagen daarvoor nog gezien).

Peter en Annemieke, lieve pap en mam. Dank voor het warme en fijne thuis dat wij als kinderen hebben gehad. Jullie onvoorwaardelijke liefde, steun en vertrouwen hebben mij een sterke basis mee gegeven. Door jullie sta ik hier vandaag. Altijd enthousiast als er weer nieuwe ontwikkelingen waren op het werk of privé. Jullie stimuleerden mij in mijn ontwikkeling en gaven mij vertrouwen in de keuzes die ik maakte. Dank dat jullie in mij geloven, op de kinderen passen, helpen met klussen, en nog heel veel meer. Dank dat jullie er altijd zijn voor mij en voor ons gezin.

En dan als laatste, Toine, Norah en Romy. **Norah en Romy**, wat een prachtige meiden zijn jullie. Ik ben zo trots dat jullie in ons leven zijn gekomen. Jullie hebben mij geleerd om mindfull en in het moment te zijn. Ik kan niet anders als ik met jullie samen ben. Jullie laten mij relativeren en beseffen wat er belangrijk is in het leven. Jullie zijn twee verschillende en geweldige meisjes. Dank dat jullie zijn wie jullie zijn! **Toine**, voordat mijn traject overging in een officieel promotietraject hebben we het daar samen over gehad. Ik weet niet of je toen hebt kunnen inschatten wat het allemaal voor voeten in aarde zou hebben. Ik kan niet genoeg benadrukken hoe geweldig ik het vind wat je allemaal voor mij en voor ons doet. Je bent mijn steun en toeverlaat. Moeiteloos pakte je er extra taken en klusjes bij op de momenten dat ik daar geen tijd en ruimte voor had. Dank voor je vertrouwen in mij, je liefde en voor het feit dat ik altijd bij jou terecht kan; om even uit te huilen of om de mooie momenten te vieren. En last but not least, dank voor je geduld om met een gestreste vriendin om te gaan. Ik ben trots op ons en onze meiden en ik kijk er naar uit om, nu dit traject is afgelopen, nog meer tijd met jullie drieën door te brengen.

Curriculum Vitae

Renske Janssen was born in Nijmegen on April 9th, 1987. After graduating from secondary school (Nijmeegse Scholengemeenschap Groenewoud, HAVO) in 2004, she started the bachelor Occupational Therapy at the HAN University of Applied Sciences. In 2008 she got her bachelor degree and started working as an occupational therapist in the Radboud university medical center. She became interested in neurological conditions, neuromuscular diseases and pain and fatigue management. In 2009 the departments of Neurology and Rehabilitation started a multidisciplinary outpatient Plexus clinic for patients with complaints and restrictions as a result of brachial plexus pathology, mainly patients with neuralgic amyotrophy (NA). Renske was part of the plexus team since the beginning. Her interest and expertise about this unknown condition grew. In 2010 - besides her work as occupational therapist - she started the master Physical Activity and Health at Maastricht University. Her graduate research focused on investigating the efficacy of the combined occupational and physical therapy intervention for patients with NA, developed within the Plexus clinic. After receiving her master degree in 2012 she continued the development of the multidisciplinary rehabilitation program for patients with NA, specifically the occupational therapy intervention. Carrying out this rehabilitation program started with the organization of a symposium in 2014 (*Behandeling van plexus brachialis letsel: een nieuwe aanpak*). Since 2015 she teaches the Plexus Management course twice a year together with physical therapist Jos IJspeert and in cooperation with prof. dr. Nens van Alfen and prof. dr. Jan Groothuis. In 2019 this all continued in an official PhD program, further developing and testing the multidisciplinary rehabilitation program for patients with NA. During her PhD program Renske kept working part-time as occupational therapist at the department of Rehabilitation of Radboudumc.

List of publications

Cup EH, IJspeert J, **Janssen RJ**, Bussemaker-Beumer C, Jacobs J, Pieterse AJ, van der Linde H, van Alfen N. Residual complaints after neuralgic amyotrophy. *Archives of Physical Medicine and Rehabilitation*. 2013;94(1):67-73. doi: 10.1016/j.apmr.2012.07.014.

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Janssen RMJ, Satink T, IJspeert J, van Alfen N, Groothuis JT, Packer TL, Cup EHC. Reflections of patients and therapists on a multidisciplinary rehabilitation programme for persons with brachial plexus injuries. *Disability and Rehabilitation.* 2019;41(12):1427-1434. doi: 10.1080/09638288.2018.1430175.

IJspeert J, Kerstens HCJW, **Janssen RMJ**, Geurts ACH, van Alfen N, Groothuis JT. Validity and reliability of serratus anterior hand held dynamometry. *BMC Musculoskeletal Disorders*. 2019;20(1):360. doi: 10.1186/s12891-019-2741-7.

IJspeert J*, **Janssen RMJ***, van Alfen N. Neuralgic amyotrophy. *Current Opinion in Neurology*. 2021;34(5):605-612. doi: 10.1097/WCO.0000000000000968.

IJspeert J, Lustenhouwer R, **Janssen RM**, Han JJ, Hatch MN, Cameron I, Helmich RC, van Engelen B, van der Wees P, Geurts ACH, van Alfen N, Groothuis JT. Reachable workspace analysis is a potential measurement for impairment of the upper extremity in neuralgic amyotrophy. *Muscle Nerve*. 2022;66(3):282-288. doi: 10.1002/mus.27651.

Janssen RMJ*, Lustenhouwer R*, Cup EHC, van Alfen N, IJspeert J, Helmich RC, Cameron IGM, Geurts ACH, van Engelen BGM, Graff MJL, Groothuis JT. Effectiveness of an outpatient rehabilitation programme in patients with neuralgic amyotrophy and scapular dyskinesia: a randomised controlled trial. *Journal of Neurology, Neurosurgery and Psychiatry.* 2023;94(6):474-481. doi: 10.1136/jnnp-2022-330296.

Janssen RMJ, IJspeert J, Groothuis JT, van Alfen N, Geurts ACH, Graff MJL, Packer TL, Cup EHC. Reliability and validity of patient-generated graphs to measure daily pain and fatigue in persons with neuralgic amyotrophy. Accepted in: *The Open Journal of Occupational Therapy.* 2024.

**Shared first authorship*

PhD portfolio

Name PhD candidate: Renske MJ Janssen
Department: Rehabilitation
PhD period: 13/05/2019 – 27/11/2024
PhD Supervisor(s): Prof. dr. M.J.L. Graff, Prof. dr. A.C.H. Geurts, Prof. dr. J.T. Groothuis
PhD Co-supervisor(s): Dr. E.H.C. Cup

Training activities	**Hours**
Courses	
• Motivational interviewing, basisvaardigheden (2009)	24.00
• Atlas.ti voor beginners (2014)	16.00
• Motivational interviewing, vervolgtrainingPlus (2015)	24.00
• Praktijk opleiding handtherapie (2015)	152.00
• Radboudumc - Scientific integrity (2020)	20.00
• DGS - Introduction day (2020)	7.00
• eBROK course (2020)	42.00
• Statistics for PhD's by using SPSS (2020)	60.00
• Scientific writing for PhD candidates (2021)	84.00
• Defending your thesis (2022)	1.25
• Basistraining kwalitatief onderzoek (2023)	12.00
• Re-registration eBROK (2023)	5.00
• Presenteren en promoveren (2023)	8.00
• Webinar slaapproblemen: slaapcycli en de relatie met activiteiten overdag (2023)	2.00
• Omgaan met vermoeidheid: "Managing fatigue" (2023)	4.00
Seminars	
• Schoudersymposium orthopedie Amphia. Oral presentation (2021)	3.00
Conferences	
• Council of Occupational Therapists for the European Countries (COTEC) congress of occupational therapy, Stockholm. Poster presentation (2012)	32.00
• Vereniging Revalidatieartsen (VRA) annual congress. Oral presentation mini-symposium (2013)	8.00
• Symposium: Behandeling van plexus brachialis letsel; een nieuwe aanpak. Organisation and oral presentations (2014)	12.00
• Congres ergotherapierichtlijn multiple sclerose. Oral presentation workshop (2017)	3.00
• Jaarcongres Ergotherapie Nederland. Oral presentation (2019)	8.00
• ParkinsonNet congres. Oral presentation workshop (2019)	8.00
• Dutch Congress of Rehabilitation Medicine (DCRM). Poster presentation and pitch (2021)	3.00
• World Federation of Occupational Therapists (WFOT) congress, Paris. Oral presentation (2022)	32.00
• Spierziektencongres voor patienten. Oral presentation (2022)	3.00
• Jaarcongres Ergotherapie Nederland. Oral presentation workshop (2024)	8.00

Other	
• Leertraject: begeleiden praktijkgericht onderzoek voor docenten (2013)	60.00
• Academische dag voor ergotherapeuten (2015)	8.00
• Consulentenmiddag Spierziekten Nederland. Oral presentation (2018)	6.00
• Matlab skills training (2021)	4.00
• Refereer bijeenkomsten afdeling ergotherapie Radboudumc (2008 - 2024)	65.00
• Member of the Occupational Research Network Nijmegen (NEON) (2012 - 2024)	72.00
Teaching activities	
Lecturing	
• Cursus plexusmanagement. Organisation and lecturing. 2 times per year (2015 - 2024)	128.00
Supervision of internships / other	
• Praktijkbegeleiding opleiding ergotherapie: stage begeleiding (2015)	17.00
• Begeleiding praktijkgericht onderzoek: Meten van pijn en vermoeidheid op de plexuspoli (2015)	21.00
• Praktijkbegeleiding opleiding ergotherapie: stage begeleiding (2016)	17.00
• Praktijkbegeleiding opleiding ergotherapie: stage begeleiding (2017)	17.00
• Praktijkbegeleiding opleiding ergotherapie: stage begeleiding (2018)	17.00
• Begeleiding Praktijkgericht Onderzoek: ondersteuning bouwen CASTOR-database (2020)	10.00
Total	**1023.25**

Research data management

General information about the data collection

This research followed the applicable laws and ethical guidelines. Research data management was conducted according to the FAIR principles. The paragraphs below specify in detail how this was achieved.

Ethics and privacy

Chapters 3, 4, 5 and 6 were based on the results of human subject data. These chapters were conducted according to the principles of the Declaration of Helsinki (version 64th WMA General Assembly, Fortaleza, Brazil, October 2013) and in accordance with the Dutch Medical Research Involving Human Subjects Act (WMO). The principles of Good Clinical Practice were followed throughout. Written informed consent was obtained from all study participants, prior to any study procedure.

The local Medical and Ethical Review board Committee of the region Arnhem Nijmegen, Nijmegen, The Netherlands (CMO) has given approval to conduct these studies (file numbers: chapter 3; CMO2011/481, chapter 4; CMO2012/510, chapter 5; CMO2012/456, and chapter 6; CMO2017/3740). The work described in chapter 6 was part of the NA-CONTROL study and was registered at ClinicalTrials.gov (NCT03441347).

The privacy of the participants in all studies of this thesis was warranted using encrypted unique individual subject codes. The encrypted keys were stored separately from the research data and were only accessible to members of the project who needed access based on their role within the project.

FAIR principles

Findable: Data were stored on a shielded part of the server of the Rehabilitation department at the Radboudumc on the Q-location (chapter 3, 4, 5: Q:\Research\075 NA Onderzoek). For the NA-CONTROL study (chapter 6) clinical data (questionnaires (.csv) and reachable workspace files (.mat) were stored in a Castor EDC database and on a shielded part of the server of the Rehabilitation department at the Radboudumc on the Q-location (Q:\Research\066 NA Project\Data). The paper CRF files were stored at the departments archive.

Accessible: The anonymous datasets that were used for analysis are available on reasonable request.

By contacting the corresponding author (Renske.Janssen@radboudumc.nl).

Interoperable: Data were stored in the following formats: .XLSX (Microsoft Office Excel), .SAV and .SPS (SPSS) and .hpr (Altlas Ti). No existing data standards were used such as vocabularies, ontologies or thesauri.

Reusable: All studies are published open access. The data will be archived for 15 years after termination of the study. Reusing the data for future research is only possible after renewed permission by the study participants.

Theses Spierziekten Centrum Radboudumc

The work described in this thesis was conducted in the Neuromuscular Center of the Radboud university medical center.

Year	PhD	Title thesis	Supervisors
2002	Drs M van Beekvelt	Quantitative near-infrared spectroscopy in human skeletal muscle. Methodological issues and clinical application	Prof dr RA Wevers Prof dr GWAM Padberg Dr ir WJNM Colier Dr BGM van Engelen
2004	Drs J Hiel	Ataxia telangiectasia and Nijmegen Breakage syndrome, neurological, immunological and genetic aspects.	Prof dr FJM Gabreëls Prof dr BGM van Engelen Dr CMR Weemaes Dr LPJW van den Heuvel
2005	Drs G Hengstman	Myositis specific autoantibodies, specificity and clinical applications.	Prof dr BGM van Engelen Prof dr WJ van Venrooij
2005	Drs M Schillings	Fatigue in neuromuscular disorders and chronic fatigue syndrome, a neurophysiological approach.	Prof dr MJ Zwarts Prof dr BGM van Engelen Prof dr G Bleijenberg
2006	Drs B de Swart	Speech therapy in patients with neuromuscular disorders and Parkinson's disease. Diagnosis and treatment of dysarthria and dysphagia.	Prof dr BGM van Engelen Prof dr GWAM Padberg Dr BAM Maassen
2006	Drs J Kalkman	From prevalence to predictors of fatigue in neuromuscular disorders. The building of a model.	Prof dr G Bleijenberg Prof dr BGM van Engelen Prof dr MJ Zwarts
2006	Drs N van Alfen	Neuralgic amyotrophy.	Prof dr BGM van Engelen Prof dr FJM Gabreëls
2007	Drs G Drost	High-density surface EMG, pathophysiological insights and clinical applications.	Prof dr MJ Zwarts Prof dr ir DF Stegeman Prof dr BGM van Engelen
2009	Drs M van der Linden	Perturbations of gait and balance: a new experimental setup applied to patients with CMT type 1a.	Prof dr J Duysens Prof dr BGM van Engelen Dr HT Hendricks
2010	Drs J Trip	Redefining the non-dystrophic myotonic syndromes. Phenotypic characterization based on genetic testing.	Prof dr BGM van Engelen Dr G Drost Dr CG Faber
2010	Drs C Horlings	A weak balance, balance and falls in patients with neuromuscular disorders.	Prof dr BR Bloem Prof dr BGM van Engelen Prof dr biomed eng JHJ Allum
2011	Drs E Cup	Occupational therapy, physical therapy and speech therapy for persons with neuromuscular diseases. An evidence based orientation.	Prof dr RAB Oostendorp Prof dr BGM van Engelen Prof dr GJ van der Wilt Dr HT Hendricks
2011	Drs A Tieleman	Myotonic dystrophy type 2, a newly diagnosed disease in the Netherlands.	Prof dr BGM van Engelen Dr H Scheffer

Year	PhD	Title thesis	Supervisors
2011	Drs N Voermans	Neuromuscular features of Ehlers-Danlos syndrome and Marfan syndrome, expanding the phenotype of inherited connective tissue disorders and investigating the role of the extracellular matrix in musle	Prof dr BGM van Engelen Prof dr BC Hamel Prof dr A de Haan
2012	Drs A Pieterse	Referral and indication for occupational therapy, physical therapy and speech-language therapy for persons with neuromuscular disorders.	Prof. Dr RAB Oostendorp Prof dr BGM van Engelen Prof dr GJ van der Wilt Dr HT Hendricks
2012	Drs B Smits	Chronic Progressive External Ophthalmoplegia. More than meets the eye.	Prof dr BGM van Engelen Prof. Dr LPWJ van den Heuvel
2012	Drs I Arts	Muscle ultrasonography in ALS.	Prof dr ir DF Stegeman Prof dr BGM van Engelen Dr HJ Schelhaas Dr S Overeem
2013	Drs M Minis	Sustainability of work for persons with neuromusclar diseases.	Prof dr MWG Nijhuis-van der Sanden Prof dr BGM van Engelen Dr YF Heerkens Dr JA Engels
2014	Drs W Leen	Glucose transporter-1 deficiency syndrome.	Prof dr M Willemsen Prof dr BGM van Engelen
2014	Drs M Jansen	No use is disuse: physical training in Duchenne muscular dystrophy	Prof dr ACH Geurts Dr IJM de Groot Dr N van Alfen
2015	Drs B Janssen	Magnetic Resonance Imaging signature of facioscapulohumeral muscular dystrophy.	Prof dr A Heerschap Prof dr BGM van Engelen
2015	Drs N Rijken	Balance and gait in facioscapulohumeral muscular dystrophy, relations with individual muscle involvement.	Prof dr ACH Geurts Prof dr BGM van Engelen Dr VGM Weerdesteyn
2016	Drs F Seesing	Shared medical appointments for neuromuscular patients and their partners.	Prof dr BGM van Engelen Prof dr GJ van der Wilt Dr G Drost
2016	Drs A Bergsma	The upper limb in neuromuscular disorders: from basic function to daily life performance	Prof dr ACH Geurts Dr IJM de Groot Dr EHC Cup

Year	PhD	Title thesis	Supervisors
2017	Drs N Voet	Aerobic exercise and cognitive behavioral therapy in facioscapulohumeral muscular dystrophy: a model based approach.	Prof dr ACH Geurts Prof dr BGM van Engelen Prof dr G Bleijenberg
2017	Drs B van der Sluijs	Oculopharyngeal muscular dystrophy (OPMD) in the Netherlands, beyond dysphagia and ptosis.	Prof dr BGM van Engelen Dr NC Voermans
2018	Drs S Knuijt	Prevalence of dysarthria and dysphagia in neuromuscular diseases and an assessment tool for dysarthria in adults.	Prof dr ACH Geurts Prof dr BGM van Engelen Dr BJM de Swart Dr JG Kalf
2018	Drs M Wohlgemuth	A family based study of in facioscapulohumeral muscular dystrophy. Lessons learnt from mild and severe phenotype	Prof dr GWAM Padberg Prof dr BGM van Engelen Dr NC Voermans Dr RJ Lemmers
2019	Drs. Karlien Mul	The many faces of facioscapulohumeral muscular dystrophy: opportunities and challenges on the road to therapies	Prof dr BGM van Engelen Prof dr ir SM van der Maarel Dr GC Horlings Dr NC Voermans
2019	Drs. J van Vliet	Myotonic dystrophy type 2. The challenging diagnosis of a complex disease.	Prof dr BGM van Engelen Dr A Verrips Dr AA Tieleman
2019	Drs K Bhansing	Clinical aspects and muscle ultrasound in polymyositis and dermatomyositis.	Prof dr PLCM van Riel Prof dr BGM van Engelen Dr MC Vonk
2019	Drs L Peeters	The trunk in neuromuscular disorders: a neglect part of the chain	Prof dr ACH Geurts Prof dr JH van Dieën Dr IJM de Groot Dr I Kingma
2020	Drs L Heskamp	Quantitative muscle MRI to unravel the physiology of dystrophic and healthy muscle.	Prof dr A Heerschap Prof dr BGM van Engelen
2020	Drs R Goselink	Growing up with FSHD. Characteristics of early-onset FSHD and childhood FSHD.	Prof dr BGM van Engelen Dr CE Erasmus Dr NC Voermans
2020	Drs S Lassche	Contractile function in facioscapulohumeral muscular dystrophy.	Prof dr BGM van Engelen, Prof dr CAC Ottenheijm Dr NC Voermans
2020	Drs J van Eijk	Antecedent infections in neuralgic amyotrophy, a prominent role for hepatitis E virus.	Prof dr BGM van Engelen Prof dr B Jacobs Dr N van Alfen
2020	Drs N Bin Abu Bakar	Glycomics by mass spectrometry for the diagnosis of congenital disorders of glycosylation (CDG)	Prof dr DJ Lefeber Prod dr RA Wevers Dr M van Scherpenzeel
2021	Drs A Rietveld	Anti-cN-1A reactivity in JDM	Prof dr BGM van Engelen Prof dr GJM Pruijn Dr CGJ Saris

Year	PhD	Title thesis	Supervisors
2022	Drs Y Veenhuizen	Aerobic Exercise Training and Energy Conservation Management to improve social participation in people with a neuromuscular disease. Effectiveness and cost-effectiveness of the Energetic group program.	Prof dr ACH Geurts Prof dr BGM van Engelen Dr EHC Cup Dr JT Groothuis
2022	Drs C Ausems	First steps towards a pericyte-based muscle therapy for myotonic dystrophy	Prof dr JHLM van Bokhoven Prof dr BGM van Engelen Dr DG Wansink
2022	Drs M Lagarde	The added value of instrumented measurements in pediatric dysphagia	Prof dr ACH Geurts Dr L van den Engel-Hoek Dr N van Alfen
2023	Drs R Lustenhouwer	Recovery in neuralgic amyotrophy: an interplay between peripheral nerve damage, motor dysfunction, and the brain.	Prof dr BGM van Engelen Dr JT Groothuis Dr IGM Cameron Dr RCG Helmich
2023	Drs B Stunnenberg	N-of-1 trials for personalized treatment, the case of muscle channelopathies.	Prof dr BGM van Engelen Prof dr GJ van der Wilt Dr G Drost Dr J Raaphorst
2023	Drs K Okkersen	The brain in myotonic dystrophy type 1, Hammer & Anvil.	Prof dr BGM van Engelen Prof dr JA Knoop Dr J Raaphorst
2024	Drs C Seijger	Respiration in myotonic dystrophy: characteristics and therapeutic interventions	Prof dr PJ Wijkstra Prof dr BGM van Engelen
2024	Drs J Molenaar	Focus on muscle relaxation in health and disease. From in vivo to in vitro and back again.	Prof dr BGM van Engelen Prof dr NC Voermans Dr J Doorduin
2024	Drs K Bouman	Optimization of clinical care and trial readiness of two rare muscle diseases: LAMA2-related muscular dystrophy and SELENON-related congenital myopathy	Prof dr NC Voermans Prof dr BGM van Engelen Dr JT Groothuis Dr CE Erasmus
2024	Drs R Janssen	Development and evaluation of an integrated multidisciplinary rehabilitation program for patients with neuralgic amyotrophy	Prof dr MJL Graff Prof dr ACH Geurts Prof dr JT Groothuis Dr EHC Cup