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The effects of hand training in patients with Welander distal myopathy and Myotonic dystrophy type 1

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Stockholm 2009

”That man, through the use of his hands
as they are energized by mind and will,
can influence the state of his own health”

M. Reilly, In AJOT 1962; XVI, 1: 1-9.

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ABSTRACT

The overall aim was to study and gain knowledge about the effects of hand training on both functional capacity such as hand function and Activities of Daily Living (ADL) in patients with Welander distal myopathy (WDM) and Myotonic dystrophy type 1 (DM1). The thesis comprises three interventional studies regarding the effects of hand training in patients with WDM (Study I) and DM1 (Studies II & IV), and one reliability study (Study III) including test-retest and inter-rater reliability of four hand function testing instruments used in Study IV. Study IV was a single-blinded longitudinal randomised control trial (RCT) with a crossover design, i.e. a follow-up on the changing-criterion single-case study with five DM1 patients (Study II). Functional data were collected by using different hand function testing instruments including the Grippit® (Studies I-IV), Grip Ability Test (GAT) (Studies III-IV), hand-held Myometer (Microfet2™) (Studies II-IV), Purdue Pegboard (Studies II-IV), Manual Muscle Testing (MMT; 0-5 scale) (Study I) and finger goniometer (Study I). Self-rated myotonia using a VAS scale was added as an outcome measure in Study II. ADL were evaluated using the areas of the ADL taxonomy in a structured verbal interview (Study I), and the Canadian Model of Occupational Performance (COPM) (Studies II and IV). Assessment of Motor and Process Skills (AMPS) was evaluated in Study IV. Life satisfaction was evaluated using a modified version of the Life Satisfaction Checklist (LiSat9) in Study I. Fourteen WDM patients were included in Study I, five DM1 patients were included in Study II, 16 WDM patients and 16 DM1 patients, respectively, participated in Study III and 35 DM1 patients were enrolled in Study IV. The reliability study (Study III) showed mainly good–very good (intra-class correlation coefficient ≥ 0.61) intra-rater and inter-rater (test-retest) reliability in three out of four instruments, specifically the Grippit®, the hand-held Myometer (Microfet2™) and the Purdue Pegboard. The three interventional studies (Studies I-II & IV) all included a period of three months of hand training with resistance putties, both guided and self-training. The results of these studies show that hand training in WDM and DM1 patients is safe, with minor but significant improvements in hand function.

LIST OF ABBREVIATIONS

ADL	Activities of Daily Living
AMPS	Assessment of Motor and Process Skills
ANOVA	Analysis of variance
CC	Complete cases
COPM	Canadian Occupational Performance Measure
CMOP	Canadian Model of Occupational Performance
DIP	Distal interphalangeal joint
DM1	Myotonic dystrophy type 1
EMG	Electromyography
GAT	Grip Ability Test
GLM	General linear model
I-ADL	Instrumental-ADL
ICC	Intra-class correlation coefficient
ICF	International Classification of Functioning, Disability & Health
ITT	Intention-to-treat
MCP	Metacarpophalangeal joint
MD	Muscular dystrophy
MMT	Manual Muscle Testing
NMD	Neuromuscular diseases
OT	Occupational therapist/therapy
P-ADL	Personal-ADL
PIP	Proximal interphalangeal joint
RA	Rheumatology patients
RC	Repeatability coefficient
RCT	Randomised control trial
ROM	Range-of-motion
SCI	Spinal cord injury
WDM	Welander distal myopathy

LIST OF PUBLICATIONS

I. Sandin-Aldehag A, Jonsson H
Evaluation of a hand training programme in patients with Welander distal myopathy. Scand J Occup Ther 2003; 10:188-92
http://www.informaworld.com/10.1080/11038120310017354

II. Sandin-Aldehag A, Jonsson H, Ansved T
Effects of a hand training programme in patients with myotonic dystrophy type 1. Occup Ther Int 2005; 12 (1):14-27
http://www3.interscience.wiley.com/journal/112224151/abstract

III. Aldehag SA, Jonsson H, Littorin S, Ansved T
Reliability of hand function testing instruments in patients with muscular dystrophies. Inter J of Ther and Rehab 2008; 15(5):211-219
http://www.ijtr.co.uk/cgi-bin/go.pl/library/abstract.html?uid=29232

IV. Aldehag SA, Jonsson H, Lindblad J, Kottorp A, Ansved T
Specific hand training in patients with myotonic dystrophy type 1.
Submitted

CONTENTS

PROLOGUE

When I came back to work at the Karolinska University Hospital's Department of Neurology in August 1998, after having worked in the United States for a few years, I started to work with patients with a variety of neuromuscular disorders (NMD) in outpatient care. This was a totally new area of expertise for me; I had previously worked mostly with spinal cord injury (SCI) and stroke patients. The job as an Occupational Therapist (OT) for NMD patients included mostly teaching compensatory strategies, prescriptions of technical devices, home adaptations etc. Many patients asked if hand training could help them to maintain or even increase muscle strength and functional capacity, as there are no cures for the diseases themselves. Two patient groups caught my interest especially, namely Welander distal myopathy (WDM) and Myotonic dystrophy type 1 (DM1) patients. They demonstrate, in general, muscle weakness and wasting in the distal hand and wrist muscles. Being an OT with SCI and stroke rehabilitation background, I felt that hand training was a natural part in patients' management. It turned out that colleagues before me had been using hand training exercises for patients with or without resistance and with individual follow-ups, but these regimes had not been scientifically validated. In a literature search I found out that this area had hardly been studied at all. Only a few articles appeared regarding training effects on lower extremities, and only one article addressed hand training. The existing research had conflicting results regarding the effects of training with positive effects, no effects or even negative effects. Some training studies had also combined patients with different muscular dystrophies (MD) diagnoses. This is not optimal as the diseases differ in the severity of symptoms, the rate of progression, and the muscles affected.

In this thesis patients with WDM or DM1 have been studied, using hand training with resistance putty (Studies I, II & IV). The hand function testing instruments used to evaluate the effects of hand training have also been tested regarding their reliability for test-retest, and in addition for inter-rater reliability for DM1 patients only (Study III). Therefore, my belief is that the four explorative studies in this thesis contribute to the understanding of hand training and its effects in WDM and DM1 patients and to an enhanced knowledge about the possible clinical usefulness of hand training for these patients.

1. INTRODUCTION

1.1 Muscular dystrophies

The term muscular dystrophy was introduced in the mid-19th century and has been accepted internationally for 150 years (Kuhn, 1990). The muscular dystrophies (MD) are a heterogeneous group of inherited disorders that are characterized by muscle weakness and wasting, but the severity and distribution of symptoms may vary considerably (Ansved 2003). In an extensive Swedish population study, the total prevalence of MD was 39/100,000 persons (aged 5-79 years), which gives an estimated total of 3,200 persons with MD in Sweden (Ahlström 1994). This figure is probably an underestimation since there are numerous individuals with only minor clinical signs and symptoms who have never been to a neurologist for correct diagnosis. The cardinal symptom of all MD is a progressive degeneration of muscle fibre, and different muscle groups are involved in the different types of MD (Brooke, 1986; Walton & Gardner-Medwin, 1988). The two MD groups studied in this thesis are Welander distal myopathy and Myotonic dystrophy type 1 patients, and both show muscle wasting and weakness in distal muscles of the hands, wrists and feet.

1.1.2 Welander distal myopathy (WDM)

Distal myopathies are a group of muscle disorders with different inheritance patterns and variable progression rates that are characterized clinically by a slow progression of muscle weakness and atrophy beginning in the hands or feet (Ansved, 2003). ***Welander distal myopathy (WDM)*** represents a clinically homogenous form with late adult onset characterized by slow progression of distal muscle weakness (Åhlberg, 1998). The disease was first described by a Swedish neurologist, Lisa Welander, in her dissertation where she described 249 patients from 72 Swedish families under the title of ***Myopathia distalis tarda hereditaria*** (Welander, 1951). Even though WDM is the most prevalent of the distal myopathies, it occurs hardly anywhere except in Sweden and parts of Finland. Onset is usually between the ages of 30 and 60 years. The prevalence is estimated at 1/10 000 in Sweden. However, in the Swedish town of Hedesunda the prevalence was estimated to as high as 1/70 and therefore WDM is sometimes called “Hedesunda-sjukan” [the Hedesunda disease] (Åhlberg, 1998). Weakness of the thumb and index finger is the initial symptom in the vast majority of patients and later on it spreads to the other fingers (Åhlberg, 1998; von Tell, 2004). WDM is linked to chromosome 2p13, but the disease-causing gene has not yet been identified (von Tell, 2004). The results in the von Tell (2004) dissertation indicate that WDM originates from one single ancestor. WDM is almost always presented as a distal muscular dystrophy and it is extremely rare for the muscles of the thighs and hips to be affected (Åhlberg, 1998). Lisa Welander (1951) separated the disease into three different categories depending on clinical symptoms. In the "typical form", the disease progressed slowly and remained distal to the elbows and knees. A "moderately atypical group" shows weakness of the finger and the toe extensors/or of proximal muscles at relatively early stages of the disease and had a much more rapid progression compared to the typical group. In a "grossly atypical group" muscle weakness started in the legs and the course of the disease was much more rapid. These few cases are very rare and the patients Welander described in her dissertation are no longer alive (von Tell, 2004). In the patient group studied in the von Tell dissertation (2004) there were two such cases. However, in this thesis no patients with proximal weakness were included.

A WDM patient trying to perform full finger extension.

1.1.3 Myotonic dystrophy type 1 (DM1)

DM1 (Steinert´s disease) is the commonest form of muscular dystrophy in adults with a prevalence of 1/8000 in most populations and is associated with muscle weakness, wasting and myotonia (see 1.6 Myotonia in DM1 patients) as the main symptoms. It is multisystemic with involvement of other organs, such as the brain, eyes, smooth muscles, heart and the endocrine system (Ahlström 1994; Harper, 2001; Machuca-Tzili et al., 2005). In the limbs, weakness is initially distal and the finger and wrist flexors are particularly affected, causing substantial disability (Machuca-Tzili et al., 2005). Wasting of the intrinsic hand muscle is frequent but occurs later and less prominently than wasting of the long flexors and extensors of the fingers (Harper, 2001). Myotonic dystrophy consists of at least two phenotypically similar syndromes, DM type 1 (DM1) and DM type 2 (DM2), of which DM1 is the commonest. Unlike several other MDs, the progressive muscle wasting in both forms of DM is not the result of a mutation in a structural protein encoding gene, but the exact pathophysiological mechanism is still unclear. DM1 patients have a pathological cytosine-thymine-guanine (CTG) expansion at the myotonic dystrophy protein kinase (DMPK) locus on chromosome 19q13.3 (Brook et al. 1992; Fu et al. 1992; Mahadevan et al. 1992).

DM1 can be divided into four main categories, each representing specific clinical features and management problems: (1) *congenital*, (2) *childhood-onset*, (3) *adult-onset*, and (4) *late-onset/asymptomatic*. In reality, no absolute distinction between the four categories exists, although understanding the particular clinical features of each of the four categories aids the diagnosis and awareness of particular complications. *In the congenital* form the newborn child is hypotonic, has talipes (club feet) and other contractures, and has sucking, swallowing and respiratory problems. Most survive, but they have significant morbidity and mortality and show delayed motor and mental development. *The childhood-onset* form is also characterized by facial weakness but without the tented upper lip that is usually seen in the congenital form. Slurred speech is common. Low IQ and other psychosocial problems are often the major management problems. *The adult-onset* (classic) form is characterized by limb or facial muscle weakness, myotonia, cardiac rhythm abnormalities, respiratory failure, excessive daytime sleepiness and bowel disturbances. *The late-onset/asymptomatic* (mild) form shows few or no symptoms. A typical family with DM1 would consist of a congenitally affected child, a mother with adult-onset disease, and a grandparent with few or no symptoms. This progression of symptoms with progressively earlier onset of symptoms is called anticipation, and is typical of DM1 (Harper, 2001; Machuca-Tzili et al., 2005). No patients with the congenital form were included in this thesis.

A DM1 patient trying to perform full finger flexion.

1.2 Theoretical framework for the description of hand function, occupation and ADL

The International Classification of Functioning, Disability and Health (ICF) (WHO, 2001) is a useful framework for describing and analysing different aspects of functioning and disability in the rehabilitation process, and for understanding the impact of the disease on the patients’ Activities of Daily Living (ADL). The classification consists of two parts, *Functioning and Disability*, and *Contextual factors*. Functioning is an umbrella term including all body functions and structures, activities and participation, while disability serves as an umbrella term for impairments, activity limitations or participation restrictions. *Body functions and structures* refers to the physiological and anatomical aspects of the body, *activities* are the performance of a task or action, and *participation* is the involvement in a life situation. Contextual factors consist of Environmental factors and Personal factors, which are not classified. This thesis focuses on the Functioning and Disability part, and the aspects targeted are hand function, occupational performance in ADL and participation. In the ICF (WHO, 2001) range-of-motion (ROM) and muscle strength are classified as body functions, while grip function and dexterity are classified as activities. In this thesis hand function is defined as the overall function of the hands and wrists, including mobility, fine motor control (dexterity), wrist and grip force and is in line with the ICF viewed as body function. The Canadian Model of Occupational Performance (CMOP) (Townsend, 2002) constitutes an additional framework used for describing and analysing occupational performance and participation problems in this thesis.

1.3 Hand function, hand function evaluation and hand training

1.3.1 Hand function

The wrist and hand form a functional unit and should be considered together (Harris 1993). The hand has a very complex anatomy. Most of the hand muscles are located in the forearm i.e. muscles for finger flexion and extension. The muscles of the hand can be subdivided into two groups, the extrinsic and intrinsic muscle groups. The muscles that are located in the hand are called intrinsic muscles. The extrinsic muscles are the long flexors and extensors and are called extrinsic muscles because the muscle belly is located on the forearm. The intrinsic muscles are the thenar and hypothenar muscles (thenar referring to the thumb, hypothenar to the small finger), the interosseus muscles (between the metacarpal bones, four dorsally and three volarly) and the lumbricals, which originate in the deep flexor (and are special because they have no bony origin) and insert on the dorsal extensor hood mechanism. The fingers have two long flexors, located on the volar side of the forearm. They attach by tendons to the phalanges of the fingers. The deep flexor attaches to the distal phalanx, and the superficial flexor attaches to the middle phalanx. The flexors allow for the actual bending of the fingers. The thumb has one long flexor and a short flexor in the thenar muscle group. The thumb also has other muscles i.e. opponens and abductor muscle, moving the thumb in opposition, making grasping possible. The extensors are located on the dorsal side of the forearm and are connected, in a more complex way than the flexors, to the dorsum of the fingers. The tendons unite with the interosseous and lumbrical muscles to form the extensor hood mechanism. The primary function of the extensors is to straighten the fingers. The thumb has two extensors in the forearm; the tendons of these form the anatomical snuff box. The index finger and the little finger also have extra extensors, used for pointing. The extensors are divided into six separate compartments. The first compartment contains abductor pollicis longus and extensor pollicis brevis. The second compartment contains extensors carpi radialis longus and brevis. The third compartment contains extensor pollicis longus. The extensor digitorum indicis and extensor digititorum communis are within the fourth compartment. The extensor digiti minimi is in the fifth, and extensor carpi ulnaris is in the sixth.

The muscles that flex the wrist are flexor carpi radialis respective ulnaris and palmaris longus and those extending the wrist are extensor carpi radialis longus respective brevis, and extensor carpi ulnaris (Netter, 2003).

There are many aspects of hand function, such as anatomical integrity, mobility, muscle strength, sensation, grasp patterns, precision and accuracy, coordination and dexterity, unilateral and bilateral tasks and ADL. Effective use of the hands depends on, among other things, skills involving motion, strength and dexterity, which are essential for the grasping function (McPhee, 1987). Hand function is one aspect within the person component that is an important contributor to the performance of ADL (Kimmerle et al., 2003).

The prerequisite for the majority of ADL is a functioning grip. This can be obtained with about 60% of available motion of the metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints, 45% of available distal interphalangeal joints (DIP) and only 32% of thumb mobility (Hume et al., 1990).

The importance of a normally functioning hand needs to be emphasized, whether it is used for earning a living, practising a hobby or allowing independence in ADL. The hand is capable of the strongest grasp and the most delicate touch; its rich and complex sensory innervations allow the finest judgement of texture, volume and temperature. Hand function is complex in its nature with intact motor and sensory functions of the hand, in addition to the absence of pain, as prerequisites for a well-coordinated grip function. A functioning hand is of great importance for a person’s well-being, for his/her ability to pursue a variety of ADL and to participate in society. Injury, disease or surgical interference, therefore, do much more than interfere with grip or touch; they affect the personality itself. Hand function is important in the performance of ADL and is more than just a tool for coping with day-to-day life (Runnquist et al., 1992; Lundborg, 1999).

1.3.2 Hand function evaluation

Clinicians should have a number of functional hand tests at their disposal, as no single evaluation method covers all aspects of hand function (McPhee, 1987). Different measurements to evaluate functions like ROM, muscle strength and fine motor control are used to show effects of interventions, such as hand training (Runnquist et al., 1992; Lundborg, 1999). Measuring full hand function can be a time-consuming task for the therapist and the patient (Tyler, et al., 2005). In this thesis, the hand function testing instruments that were used included the Grippit®, Grip Ability Test (GAT), hand-held Myometer (Microfet2™) and Purdue Pegboard. They assessed wrist force, grip force, pinch grip, fine motor control (dexterity) and three practical tasks. Manual Muscle Testing (MMT; 0-5-scale) and standard finger goniometer was used as outcome measures in Study I only (see 3.3 Hand function testing instrument).

1.3.3 Hand training

The American College of Sports Medicine (ACSM) (1998; 2002) has guidelines regarding training regimes for healthy persons. This includes setting up an individualized program that is progressive in nature. The training should provide stimulus to all major muscles (8-10) with at least one set of 8 to12 repetitions and with a frequency of 2-3 days a week. The exercises should be performed at least three times a week for a minimum of 10 weeks. However, one should observe that it cannot simply be applied to all patients with MD (Cub et al., 2007). ACSM (1997) guidelines for patients with conditions like MDs are to focus on maintaining muscle endurance, peak power and strength. They recommend that for most cases only a moderate resistance exercise regime should be used. The hand training regime in this thesis (see 3. Patients and Methods) fulfilled the guidelines of ACSM (1997; 1998; 2002). Hand training should be seen as part of ADL, which implies that the patients should be able to perform the exercises in their homes. Home treatment such as hand training allows financial savings in health care as well as minimizing intrusion into the patient's everyday life. OTs have traditionally been concerned with hand function and the use of activities involving the hand (Wade, 1992). Functional training is an essential part of hand rehabilitation. Functional training addresses both sensory and motor functions with the aim of retraining and restoring flexibility. However, functional training addressing only the actual benefits in ROM or muscle strength is suggested as being too narrow a focus in occupational therapy (Fisher, 1998). Functional training should also be evaluated from the perspective of impact on ADL (Schkade & Schultz, 1992). As there is no cure for MD, it is important to investigate the effects of hand training in these patients, as there is limited knowledge about whether training can interfere with the disease progression.

1.3.4 Hand function in WDM and DM1 patients

Persons affected with WDM demonstrate muscle weakness and wasting primarily in the extensor muscles of wrist and hands, but the interossei, lumbrical and thenar and hypothenar muscles are also affected. The initial symptoms are clumsiness in precise hand movements such as buttoning, handling needles or typing (von Tell, 2004). The

WDM patients have difficulties extending their fingers prior to doing an action like grasping a glass of water and buttoning. This may be one of the reasons that patients with WDM exhibit problems in ADL even though grip strength usually is unaffected. Of course WDM patients' problems in ADL also depend on the amount of weakness and atrophy in the thenar muscles, whose function is controlling the movements of the thumb.

DM1 patients initially demonstrate muscle weakness and wasting of wrist and finger flexors, which leads, for example, to difficulties in grasping utensils and carrying grocery bags. Contractures are common as the diseases progress in the MCP, PIP and DIP joints, making the WDM patient unable to extend the fingers and the DM1 patient unable to flex the fingers. Since both diseases limit the hand function, WDM and DM1 patients therefore experiencing problems in their ADL.

1.4 Muscular dystrophies and training

Most published training studies have included patients with different MDs, for example myotonic dystrophy (MD), limb-girdle muscular dystrophy (LGMD), spinal muscular dystrophy (SMA), facioscapulohumeral muscular dystrophy (FSHD) and Charcot Marie Tooth (CMT). The effects of training of lower extremities including hips/knees and/or upper extremities such as the elbows have been studied (Florence & Hagberg, 1984; Taivassalo et al., 1999; Aitkens et al., 1993; Belanger & Noel, 1991, Kilmer et al., 1994; Lindeman et al., 1995; McCartney, 1988, Milner-Brown & Miller, 1988). Most studies evaluated muscle strength training exercises, aerobic exercises or a combination of these. The studies have met the ACSM guidelines regarding an individual and a progressive program. However, considerable variations were seen in the muscles exercised, type of exercise and resistance, number of repetitions and sets. A moderate level of intensity has been used. Only 30% of these studies met the guidelines of at least 10 weeks duration and approximately 50% met the recommendation for regular supervision to optimize compliance and safety (van der Kooi et al., 2005; Cub et al., 2007). The pathophysiology of the different MDs is markedly different, which means that each MD needs to be studied separately with regard to training and other interventions. Furthermore, there is a marked variation in the designs and methods used for the few published studies of training in MD (Lindeman et al., 1995, Ansved, 2001). Therefore, to date little is known regarding the effects of training in MD patients and the published data shows conflicting results.

1.4.1 DM1 and aerobic training and muscle strength training

One aerobic training study (walking) has been performed on myotonic dystrophy patients (n=7), but the study also included patients with other MDs (Wright et al, 1996) and one aerobic training study (cycle ergometer) including 17 DM1 patients has also been performed (Ørngren et al., 2005). The few existing studies on the effects of muscle strength training involving lower extremities in DM1 patients have yielded partly conflicting results. Lindeman and co-workers (1995) were unable to detect significant alterations in knee torques, fatigability, or in functional abilities after 24 weeks of unsupervised muscle strength training in a study including 33 DM1 patients. However, Tollbäck and associates (1999) reported a significant increase in muscle strength after 12 weeks of continuously supervised high-resistance knee extensor training including nine DM1 patients. No indications of increased deterioration were found in those two studies. Notably, the Lindeman et al. RCT study (1995) included not only DM1 patients but also patients with hereditary motor and sensory neuropathy, i.e. CMT patients. In conclusion, there is insufficient data on the effects of training in patients with MDs (van der Kooi et al., 2005; Cub et al., 2007).

1.4.2 Hand training in WDM and DM1 patients

Besides the feasibility/pilot study (Sandin-Aldehag & Jonsson, 2003) included in this thesis regarding hand training in WDM patients, there has to date been only one previously published article. This was a single-case report of a WDM patient showing increased grip strength and pinch grip after three weeks of moderate-resistance hand training (Erwin et al., 1991). Similarly, other than the two studies (Sandin-Aldehag et al. 2005 & Study IV) included in this thesis on hand training in DM1 patients, no other studies have previously been published concerning the effects of hand training in these patients. However, the study by Aitkens et al. (1993) which is a progressive unilateral muscle strength training study of patients with mixed NMDs (n=12 DM patients) did also include some hand training exercises (hand grip).

1.5 Occupation and Activities of Daily Living (ADL)

1.5.1 Terminology and definition

Participating in everyday occupations is a basic human need, and an important determinant of health and well-being (Rudman et al. 1997; Wilcock, 1998). Occupation is the domain of concern and the therapeutic medium of occupational therapy (Townsend, 2002). Occupation and activity are two core concepts in occupational therapy. Some authors use the terms interchangeably, while others highlight the distinctions between them (Golledge, 1998). The Swedish word for "activity" is used interchangeably for both concepts (http://www.fsa.akademikerhuset.se/etisk kod (2005)). Trombly (1995) equated occupation and activity with purposeful activity, and defines occupation as *"the ordinary and meaningful things people do every day"* (p.237). Fisher (2003 a) defines occupation similarly as *"meaningful doing"* (p.1).

ADL are activities that people perform to take care of themselves and are usually described/classified in two categories: Personal Activities of Daily Living (P-ADL) and Instrumental Activities of Daily Living (I-ADL). P-ADL may comprise toileting, dressing, eating, grooming, ambulating and bathing. I-ADL may comprise communication, shopping, cooking, housekeeping, laundry and transportation (Sonn & Åsberg, 1991; Sonn et al, 1999; Törnquist, 1995). ADL refer to occupation and involves groups of activities and tasks of everyday life, which are named, organized, and given value and meaning by individuals and a culture (Townsend, 2002).

In the CMOP, occupation refers to groups of everyday activities in which people engage over their lifetimes. Occupation and/or activities mean therefore everything that people do to occupy themselves, including looking after themselves (self-care), enjoying life (leisure), and contributing to the social and economic fabric of their communities (productivity) (Townsend, 2002; Townsend & Polatojka, 2007). From the view of CMOP, P-ADL corresponds to the area of self-care, and I-ADL can be included in the area of productivity (Gitlin, 2001).

Occupational performance is viewed by Fisher (2003 a) as *"a meaningful sequence of actions in which the person enacts and completes a specified task that is relevant to his or her culture and daily life role"* (p.24). In this thesis ADL is used as a concept covering occupational performance in the different areas of occupation.

1.5.2 Occupational performance and ADL in MD patients

The complexity and dynamics of ADL are emphasized when life has changed due to a chronic illness (Persson, 2001).

The consequences of a chronic disease are determined by several factors, such as the severity of the disease, its impact on ADL, and the way in which the patient deals with his or her illness (Bergh et al,. 1997). Ahlström (1994) describes in her dissertation that persons with MD encounter a variety of illness-related problems in their ADL and that they find these problems hard to deal with. In Nätterlund's dissertation (2001) similar descriptions are made, i.e. that muscular weakness affects many daily life activities but also that some persons have succeeded in adapting to them in their everyday lives. Her explanation for this is that the time period during which persons have been living with their illness has made adjustments possible to the slow deterioration of their activities. Another explanation may be that limitations in ADL become more acceptable for the person with MD, as the slow progressive nature of the deterioration gives them time to mentally adapt to their muscular weakness. However, the capacity to perform ADL is essential for a person to maintain his or her roles in the family, at work, and in society as a whole (Kiehlhofner, 2008).

As there is no cure for MD, it is important to give continual support and care, assisting the affected persons to manage their ADL and find meaningful occupations (Wilcock, 1993). Occupational performance and the ability to perform ADL may be evaluated for a variety of purposes. Therefore, the assessment approach may also vary, comprising observation, interview and self-assessments (Ottenbacher & Christiansen, 1997). In this thesis occupational performance and ADL have been evaluated by using both quantitative and qualitative assessments including the ADL taxonomy (Törnkvist, 1995), Canadian Occupational Performance Measure (COPM) (Townsend, 2002) and Assessment of Motor and Process Skills (AMPS) (Fisher, 2003 a & b) (see 3.3 Hand function testing instruments and ADL instruments).

A WDM patient who is having difficulties buttoning her shirt and a DM1 patient who is having difficulty using and handling a bread knife.

1.6 Life satisfaction

In the literature there is a confusion between the concept of life satisfaction and the concept of quality of life and thus these terms are used interchangeably (Melin, 2003). Overall life satisfaction is considered to be synonymous with degree of happiness (Veenhoven, 1984). Life satisfaction is seen as a subjective aspect of how people perceive their lives. On the other hand, quality of life, though defined in various ways, has a much broader focus and also incorporates both objective views such as economy and housing, and a subjective perspective on life (Meeberg, 1993). In Study I, a self-rated life satisfaction checklist was used before and after hand training. It was a modified version of the Life Satisfaction Checklist (LiSat9) (Fugle-Myer et al, 1991: Bränholm, et al., 1996) and it was used to compare the impact of the decreased hand function on life satisfaction before and after the training period. The modified checklist included self-care, housing, work and leisure, but excluded economic and sexual factors. However, this type of assessment was shown to be too general and unspecific to be able to measure changes of specific hand training and was therefore only assessed in Study I.

1.7 Myotonia in DM1 patients

Myotonia is one of the hallmarks of DM1 and is characterized by delayed relaxation of the muscles after voluntary contraction or electrical stimulation. It is present in the hands, facial muscles, tongue and other bulbar muscles, causing problems when talking, chewing and swallowing. Myotonia is caused by abnormal muscle fibre membrane electrical activity, which can be seen by electromyography (EMG) as a repetitive muscle-fibre discharge that waxes and wanes in frequency and amplitude, giving a characteristic sound on the audio monitor (Machuca-Tzili et al., 2005). Myotonia is best examined in the hand muscles where, following a forceful grip, there is a delayed ability to relax the grip. A firm tap to the thenar eminence with a patellar/reflex hammer elicits the characteristic sequence of movements as the thumb is opposed towards the little finger, and remains in that position for several seconds, after which it slowly returns to the initial position. The myotonia is aggravated by cold. It can be elicited in almost every symptomatic adult patient, but is also frequently found in presymptomatic individuals. Repeated contractions and relaxation may diminish the myotonia and is called “the warm-up phenomenon” (Harper, 2001; Machuca-Tzili et al., 2005). Self-rated myotonia before and after hand training was measured in Study II, but not in Study IV.

2. AIMS OF THE THESIS

2.1 General aim:

To study and gain knowledge of the effects of hand training on both functional capacity such as hand function and ADL in patients with hand weakness due to a muscular dystrophy (WDM or DM1).

2.2 Specific aims:

- To evaluate positive and/or negative effects on hand function and on ADL after a three-month hand training regime in WDM patients (Study I).
- To evaluate positive and/or negative effects on hand function and on ADL after a three-month hand training regime in DM1 patients (Studies II & IV).
- To evaluate reliability of the functional instruments used to measure functional capacity/hand function in WDM and DM1 patients in Studies I, II and IV (Study III).

3. PATIENTS AND METHODS

3.1 Patients

The studies were performed at the Division of Neurology, Department of Occupational Therapy, Karolinska University Hospital. The patients included in the various studies are presented in Table I. The patients who were asked to participate in the studies were recruited from the outpatient clinic, Division of Neurology, at the Karolinska University Hospital and Neuroenheten at Läkarhuset Odenplan. All together, the studies included 68 patients with either WDM (n=23; 13 women and 10 men) or DM1 (n=45; 25 women and 20 men), of which seven WDM patients participated in the feasibility (pilot) study (Study I) and in the reliability study (Study III) and eleven DM1 patients in the reliability study (Study III) and the RCT (Study IV). None of the DM1 patient participated in both interventional studies (Studies II & IV) (see Table I). Inclusion criteria for participating in the studies (Studies I-IV) were that patients were diagnosed with either WDM or DM1. Additional inclusion criteria for the interventional studies (Studies I, II & IV) were that patients achieved a score of at least three out of five in Manual Muscle Testing (MMT; 0-5-scale) (Hishop & Montgomery, 1995) in wrist and hand muscles (flexors and, respectively, extensors) and also that they were able to handle the instruments used in Study III. The mean age of the DM1 patients was 52.0 years in Study II, 41.3 years in Study III, and 45.4 years in Study IV. The mean age of the WDM patients was 62.5 years in Study I and 60.6 years in Study III. The response rate for participation in Study I was 87.5% and 100% in Study II. The response rate for participation in the reliability study (Study III) was 100% for the WDM patients and 89% for the DM1 patients. The response rate for participation in the longitudinal RCT (Study IV) was 40.7%. Withdrawal from participation, i.e. drop-outs, included two WDM patients in Study I and ten DM1 patients in Study IV, seven patients in the first hand training group (T-C group) and three patients in the second hand training group (C-T group).

Table I. Demographic data of the patients who participated in the four studies.

Study	Diagnosis	Number of patients	Drop-outs	Gender (men/women)	Mean age (range)
I	WDM	14	2	7m/7w	62.5 (39-83)
II	DM1	5	0	2m/3w	52.0 (28-67)
III	WDM/DM1	16/16	0	6m/10w vs. 8m/8w	60.6 (40-78) vs. 41.3 (18-59)
IV	DM1	35	10	14m/21w	45.4 (26-69)

3.2 Study designs, procedures and data analyses

An overview of the study designs, study contexts, methods of data collection and data analysis is shown in Table II.

3.2.1 Study designs

This thesis employs quantitative methods only. ***Study I*** is a feasibility/pilot study on WDM and ***Study II*** is a changing-criterion single-case study (Franklin et al., 1997) on five DM1 patients, whereas ***Study IV*** is a longitudinal RCT study, a follow-up of Study II. However, all three (Studies I, II & IV) are interventional studies with pre- and post-evaluation after three months of hand training including self-training and guided training by an Occupational Therapist (OT). Study IV has a crossover design with one-year follow-up, i.e. the DM1 patients were divided into two groups stratified for grip force. One group received 12 weeks of training; the other served as control. After a wash-out period of 12 weeks the control group received training for 12 weeks and the previous hand-trained group became the control group.

Study III is a reliability study of the two patient groups including test-retest evaluation. Inter-rater reliability was also tested in the DM1 patients (Study III).

Table II. Overview of the four studies: Designs, study contexts, methods of data collection and data analysis.

	Study I	Study II	Study III	Study IV
Study design	Feasibility/pilot	Single-case	Reliability	RCT with crossover
Study context	Division of Neurology, Department of OT, Karolinska Univ. Hospital and in patient's home	Division of Neurology, Department of OT, Karolinska Univ. Hospital and in patient's home	Division of Neurology, Department of OT, Karolinska Univ. Hospital	Division of Neurology, Department of OT, Karolinska Univ. Hospital and in patient's home
Data collection	One pre- and one post-training test with 12 weeks of hand training	Nine pre-training and nine post-training tests with 12 weeks of hand training	Test-retest in two sessions with three trials per session. Inter-rater (DM1) at one occasion with three trials per session	Four test sessions (pre1-post1, pre2-post2) during one year
Data analysis	Descriptive statistics, Wilcoxons Signed – and Matched pair test	Descriptive statistics and Paired t-test	Descriptive statistics, RC and ICC	Descriptive statistics, Repeated measures ANOVA, McNemars test, Spearman rank order correlation

3.2.2 Study procedures

In ***Study I***, pre- and post-training tests were performed in one session each.

In ***Study II***, pre- and post-training tests were performed for a total of nine times each. The pre- and post-training tests were performed three times a week (every other day), one week for the pre- and one for post-training test. Each day included three measurements, three times each, i.e. one in the morning, one at lunchtime and one in the afternoon, approximately two to three hours apart.

In ***Study III***, for test-retest analyses, there were three trials (called one session), and the WDM and DM1 patients were tested on two consecutive weeks, on the same day of the week and the same time of day. During the second week the DM1 patients were tested before (n=8) or after (n=8) retest for inter-rater reliability. A coin was tossed for which hand would be tested first, and for each trial for which test instrument to start with; this randomness should have minimized the systematic errors. However, the Purdue Pegboard and GAT were always tested before the muscle force assessments, i.e. the Grippit® and the hand-held Myometer (Microfet2™), to avoid fatigue. The DM1 patients rested for one hour between the tests (i.e. between the retest and the inter-rater testing).

In ***Study IV***, the DM1 patients were tested four times during one year.

3.2.3 Data analyses

Non-parametric and parametric methods have been used to analyse data. Statistical power calculations were performed for Studies III and IV only. For Study III, statistical calculation revealed that if six pairs of WDM and DM1 patients were to be enrolled in the study, the study would have a power of 89.9% to detect a clinical relevant difference/yield a statistically significant result. For Study IV, statistical power calculation revealed that if 17 pairs of DM1 patients were to be enrolled in the study, the study would have a power of 89.9% to yield a statistically significant result. Both were based on the Grippit®, mean value of 20N difference and the criterion for significance was set at 0.05.

In ***Study I***, the hand function testing instrument was analysed using the Wilcoxon Signed test. The Wilcoxon Matched Pair test was used to analyse the pre- and post-training results in ADL comparing changes in the eleven areas of activities out of twelve (excluding ambulation) from the ADL taxonomy.

In ***Study II***, with the changing-criterion single-case design of five DM1 patients, descriptive data from a single individual representing repetitive measures are presented in figures with regard to changes in levels or trend. Paired t-test was used for comparisons of mean values of pre- and post-training tests of the five patients who participated (Study II).

In ***Study IV***, data was analysed using the ANOVA repeated measures design, i.e. General Linear Method (GLM) for changes within each of the two training periods, with treatment and order of treatment as fixed factors in the model. The interaction term for treatment and order was also included. The intention-to-treat (ITT) population was the primary analysis population in Study IV, which consisted of all patients randomised to one of the two intervention arms. Missing data was replaced using the last-observation-carried-forward (LOCF) method. The complete cases (CC) population was used as the secondary analysis to perform a sensitivity analysis, and consisted of all patients with complete measurements at all four test sessions. Additionally, for the ADL instruments, the McNemar test was used to analyse the proportion of patients with clinically meaningful changes, i.e. those patients who

fulfilled the response criteria for the AMPS (0.5 logits) (Fisher, 2003 a & b) and the COPM (2 points) (Townsend, 2002). Correlation between reported training (training compliance) and the grip force as measured by Grippit®, mean value, was analysed with Spearman rank order correlation. In Study IV, data for each individual are described with regard to the repeatability coefficient (see below) of each hand function testing instrument as derived from the previous reliability study (Study III).
In ***Study III***, mean and standard deviations for the intra-rater (test-retest) assessments of the three trials per session (total of two sessions) were evaluated using the Repeatability Coefficient (repeatability/RC) and the intra-class correlation coefficient, ICC (the intra-examiner reliability) (Bland & Altman 1996 a & 1996 b). The calculations were made according to the formula: R=mSSB-SST/ (m-1) SST, where the SST is the total sum of squares, the SSB is the sum of squares between the subjects, and m is the number of measurements per subject. The inter-rater reliability was also evaluated using the intra-class correlation coefficient (ICC) (Bland & Altman 1996 a & 1996 b). For the ICC the values range from 0, indicating no agreement, to 1, indicating complete agreement in repeated measurements (Bland & Altman 1996 a; 1996 b). ICCs were interpreted according to established criteria for judgement: ≤ 0.20 poor, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-0.80 good, 0.81-1.00 very good (Altman, 1991). Results with p-values ≤ 0.05 were considered significant throughout the studies.

3.3 Hand function testing instruments and ADL instruments

An overview of the hand function testing instruments, occupational performance and ADL instruments that were used in this thesis are shown in Table III. Hand and wrist function was measured with the Grippit® (Studies I-IV), the hand-held Myometer (Microfet2™) (Studies II-IV), the Purdue Pegboard (Studies II-IV), the Grip Ability Test (GAT) (Studies III-IV), finger goniometer (Study I) and Manual Muscle Testing (MMT, 0-5-scale) (Study I). MMT also served as inclusion criteria in the three interventional studies (Studies I, II & IV). As mentioned above, a modified version of the Life Satisfaction Checklist (LiSat9), pre- and post-training, was used only in Study I and self-rated myotonia was used only in Study II.

Manual Muscle Testing (MMT; 0-5 scale) was used to evaluate muscle strength of WDM patients as an outcome measure in Study I only, but served as a inclusion criteria in the three interventional studies (Studies I, II & IV). Ratings for a MMT are recorded as numerical scores ranging from zero (0= no activity, i.e. muscle is completely quiescent on palpation or visual inspection) to five (5= normal activity, i.e. maximum resistance and full ROM). This test is based on motions (ROM) and strength rather than on strength of individual muscles and therefore represents the performance of all muscles in a motion (Hishop & Montgomery, 1995).

A ***Standard finger goniometer*** was used to evaluate isolated active extension ROM of each joint of the fingers. Changes of less than five degrees were not analysed (Bear-Lehman & Colon-Abrue, 1989). The goniometer was used in Study I.

The ***Hand-held Myometer*** (Newton; N) (Microfet2™, Hoggan Health Industries, Utah, USA) was used to measure muscle force of wrist extensors and flexors, and, respectively, finger extensors and flexors (excluding thumb). Break-test was used and three maximum contractions for each muscle group were tested. For "break-test" the patient exerts a maximum force against the hand-held Myometer and the examiner applies just enough resistance to overcome the force exerted by the patient (Beverly et al., 2000). The Myometer was used in Studies II-IV.

The ***Grippit®*** instrument (Newton; N) (AB Detector, Göteborg, Sweden) was used to measure maximum grip force and pinch grip (tip position) for a total of 10 seconds and the maximum, mean and final values, i.e. the value at 10 seconds, were registered. The Grippit® is an electronic instrument that measures isometric grip and pinch force from 0 to 999 Newtons with automatic registrations every half second for 10 seconds (Wallström & Nordenskiöld, 2001). The Grippit® instrument was used in all studies (I-IV).

The ***Purdue Pegboard Model 32020*** (Lafayette Instrument Co.®, Lafayette, IN, USA) was used to measure fine motor control (precision and speed) of the right and left hand by counting the number of pegs placed on the Pegboard in 30 seconds (Buddenberg & Davis, 2001). The Pegboard was used in Studies II-IV.

The ***Grip Ability Test (GAT) –*** GAT was developed to evaluate hand function on the disability level. The GAT is a disease-specific test for clinical evaluation of hand function in patients with rheumatoid arthritis (RA), and is a modified version of the Sollerman Grip Function test (GFT) (Sollerman & Ejeskär, 1995). The test consists of three practical tasks including putting on a flexigrip stocking over the non-dominant hand (simulating putting on a glove), putting a paper clip on an envelope and finally pouring water into a cup from a one-litre plastic jug. The GAT score is noted in weighted seconds and a high score indicates decreased hand function. A GAT score below 20 seconds in RA patients is considered normal (Dellhag, 2000). However, each practical task was assessed bilaterally and the time it took to perform each task was registered. It was assessed in Studies III and IV.

The ***Assessment of Motor and Process Skills (AMPS).*** The AMPS is an ADL assessment based on the level of skill displayed during the performance of a familiar, culturally relevant and self-chosen ADL task. When a patient performs an AMPS ADL task, the OT observes and rates the performance on the basis of efficiency, safety, level of effort and independence in performing the task in 16 ADL motor skills items (such as Walks, Reaches, Manipulates and Grips) and 20 ADL process skill items (such as Paces, Inquires, Initiates and Restores). Each motor and process skill item is graded on a 4-point scale, where 4= competent and 1= markedly deficient. The AMPS has a test battery of 83 tasks; 74 I-ADL tasks and, respectively, nine P-ADL tasks that allow the patient to perform an ADL task that is meaningful and relevant to him or her, and also specifically chosen by the patient. In the AMPS manual, Volume 1, (Fisher, 2003 a; p. 146) it is stated that an improvement of at least 0.5 logits between Test 1 and Test 2 in the graphic report on either of the AMPS motor or process ability scale indicates that one can confidently and objectively state that a patient's ADL motor and process ability has changed to a degree that has clinical and statistical meaning (i.e. improved ADL performance). The AMPS was assessed in Study IV only. The AMPS evaluations in Study IV comprised ten I-ADL tasks only, due to the design of the study. The ten I-ADL tasks that were used had different challenges (Task hierarchy) and depending on the patient's performance and the result of the AMPS interview the tasks included, starting from "easier than average" e.g. hand-washing dishes (J-2); folding a basket of laundry (L-1), "average tasks" e.g. ironing a shirt (board already set up L-5; setting up the ironing board L-4); vacuuming (moving no furniture J-3; moving light furniture J-4); brewing coffee or tea and serving biscuits at a table (G-1); setting a table for four persons (M-2), "harder than average" e.g. ironing multiple garments and putting them away (L-6); making fresh fruit salad (H-2) (Fisher, 2003 b).

The ***Canadian Occupational Performance Measure (COPM).*** COPM is a semi-structured interview instrument used to assess occupational performance and the patient’s satisfaction with his/her performance in three areas – self-care, productivity and leisure. The patient identified self-defined important and difficult occupational problems within these areas, and rated the importance of each problem. The five most important self-rated problems were selected and rated on a 1-10 scale regarding both Performance and Satisfaction, for which 1= not able to perform/not satisfied at all, and 10= performed extremely well/extremely satisfied. A difference in either Performance or Satisfaction of two points between Test 1 and Test 2 is considered a clinically meaningful change (Townsend, 2002). The COPM was used in Studies II and IV.

Self-rated Life Satisfaction, a modified version of the Life Satisfaction Checklist (LiSat9) (Fugle-Myer et al., 1991; Bränholm et al., 1996) was used to compare the impact of decreased hand function on life satisfaction before and after the training period. The modified checklist included self-care, housing, work and leisure but excluded economic and sexual factors. It was used in Study I.

Self-rated Myotonia. The patients rated the degree of myotonia of their hands during rest and during activities by a 1-10 Visual Analog Scale (VAS), for which 1= no myotonia, 10= maximum myotonia. It was assessed in Study II.

Table III. Methods of hand function testing instruments used in the four studies.

Instruments	**Instrument characteristics**	**Study**
Grippit®	Grip-/pinch force measured in Newtons (N)	I-IV
Grip Ability Test (GAT)	Three functional grips, measured in weighted seconds	III-IV
Myometer (Microfet2™)	Force of wrist and finger extensors and flexors measured in Newtons (N)	II-IV
Purdue Pegboard	Number of pegs in 30 seconds	II-IV
MMT	Manual Muscle Testing, 0-5-scale	I *
Finger goniometer	Active finger extension in MCP, PIP & DIP	I
ADL taxonomy	Semi-structured interview about patients experiencing problems in ADL	I
AMPS	ADL observations in Motor and Process skills, score 1-4	IV
COPM	Semi-structured interview yielding information about self-rated occupational performance and satisfaction, score 1-10	II & IV
Life satisfaction checklist (modified version of LiSat9)	Self-rated, score 1-6	I
Myotonia	Self-rated, score 1-10 during rest/activity	II

* also served as inclusion criteria

3.4 Hand training with resistance putty

The interventional studies (I, II & IV) included specific hand training with resistance putties, either De Royal (Medi Royal/De Royal, Knoxville, Tennessee, USA) or Theraputty™ (North Coast Medical, Morgan Hill, California, USA). The training programs included muscle strength training in mass (1-2-3 sets of 10 repetitions or 1-2-3 sets of 15 repetitions) including wrist, hand and finger flexion-extension, isolated (1-2-3 sets of 3 repetitions or 1-2-3 sets of 5 repetitions) finger flexion-extension, abduction-adduction and thumb opposition (see hand training program regime on next page). The patients increased by one set of repetitions every fourth week, starting from one set. The choice of which resistance putty was to be used for each patient was based on their initial assessments in grip force measured with the Grippit® and based on their ability to squeeze into the resistance putty by demonstrating full finger flexion in all repetitions without experiencing exhaustion. In Study IV, for example, five different resistance putties were used: red (medium), a mixture of ½ red/ ½ beige, beige (x-light), a mixture of ½ beige/ ½ white and white (super-soft) and to use white putty the patient needed to demonstrate grip force ≤50 Newton (N), a mixture of ½ beige/ ½ white; ≥51-100 N, beige; ≥101-150 N, mixture of ½ red/ ½ beige; ≥151-200 N, red; ≥201 N.

In all three interventional studies (Studies I, II & IV) the patients were instructed to record all training sessions in a training diary, writing H for home exercises and C for training at the clinic guided by the OT. The OT also recorded each patient’s weekly training in a separate diary to assess the compliance of the hand training program.

Hand training program

- muscle strength training with resistance putty, 3 times/week. Mass movements: 1-3 sets of 10-15 repetitions, isolated movements 1-3 sets of 3-5 repetitions.


Mass wrist extension


Mass wrist flexion


Mass finger flexion


Mass finger extension


Isolated finger flexion


Isolated finger extension


Thumb flexion


Thumb extension


Finger adduction


Finger abduktion


Finger opposition


Stretching of extensor muscles


Stretching of flexor muscles

4. ETHICAL APPROVAL

The four studies in this thesis have been examined and approved by the local ethics committee of the Karolinska Institute, Stockholm, Sweden. [Study I; Dnr 00-067, Study II; Dnr 01-441, Studies III-IV; Dnr 105-31/3].

5. RESULTS

5.1 Effects of hand training in WDM (Study I)

The feasibility/pilot study included three months of specific hand training in WDM patients (n=14), one session guided by an OT and two sessions of self-training per week. The study indicated an improved hand function as judged from statistical significant improvements on group level in: (1) right finger extension (p =0.01) assessed with MMT 0-5 scale; (2) the peak value (in later studies called maximum value) for right and left pinch grip bilaterally (p =0.04); (3) the value after 10 seconds in right hand pinch grip (p =0.04) measured with the Grippit®; in (4) MCP joint extension (p =0.04) of the right index finger; in (5) PIP joint extension (p =0.02) of the right index finger measured with the standard finger goniometer. The patients reported that problems in P- and I-ADL performance were significantly reduced after the period of training (p =0.01). Individual data shows that several patients rated an increased level of satisfaction in self care (n=6), housing (n=4), work (n=1) and leisure (n=5) assessed by a modified version of the Life Satisfaction Checklist (LiSat9), but the results did not reach statistical significance (Sandin-Aldehag & Jonsson, 2003).

5.2 Effects of hand training in DM1 (Studies II, IV)

5.2.1 Changing-criterion single-case study (Study II)

In the five DM1 patients studied, three months of specific hand training three times a week indicated an improved hand function as judged from significant increases in muscle force measured with the Myometer (Microfet2™) of wrist extensor force (right: p =0.0002; left: p =0.0004) and flexor force (right: p =0.047; left: p =0.027), finger extensor force (right: p =0.0071) and flexor force (right: p =0.0004; left: p =0.0003). The mean rating of Performance in occupational performance assessed with the COPM increased by 1.7 (range 0.4-3.8), whereas the mean rating of Satisfaction increased by 2.7 (range 0-6.3), i.e. increased Satisfaction is to be considered a clinically meaningful change after training (≥ 2 points) (Sandin-Aldehag et al., 2005).

5.2.2 RCT with one-year follow-up (Study IV)

Three months of specific hand training in 35 DM1 patients, guided once by an OT and twice per week of self-training, indicated an improved hand function as judged from significant improvements in ITT and CC analyses of hand function testing instruments on group level. This was shown for left hand finger flexor force (ITT; p =0.01) measured with the hand-held Myometer. For grip force, mean value, a statistically significant increase was shown (ITT; p =0.0045) in the left hand and for the 10-second value in the right hand (CC; p =0.04) measured with the Grippit®. Pinch grip, maximum value, in both the right hand (CC; p =0.04) and in the left hand (ITT; p =0.0048, CC; p =0.04) increased as measured with the Grippit®. A statistically significant increase was also shown in the right hand for both mean (CC; p =0.03) and the 10 second value (CC; p =0.02) for the pinch grip measured with the Grippit®. However, when comparing mean values on group level, the above changes cannot be interpreted as clinically meaningful changes, as the changes of the mean values on each variable are too small (not shown).

In summary, on an individual level, two patients demonstrated improved hand function as judged from the repeatability coefficient (RC) in eight or more variables out of 13, either in the left or right hand or bilaterally. Four patients demonstrated improved hand function as judged from the RC in four to six variables out of 13, either in the left or right hand or bilaterally. Ten patients demonstrated improved hand function as judged from the RC in two to three variables out of 13, either in the left or right hand or bilaterally (not shown). The patients' improved hand function correlates well with their training compliance in all but one patient, i.e. the patients with the highest training compliance also showed the best improvements of hand function (not shown). Three patients also showed a decrease in three variables in the right or left hand but this was not judged to be a result of training, but rather a progression of the disease, due to the patients not meeting the training compliance.

ITT and CC analyses on group level showed a statistically significant increase for the AMPS in ADL motor ability (ITT; p =0.0007, CC; p =0.0045) and in ADL process ability (ITT; p =0.002).

A statistically significant increase was also seen for the COPM in Performance (ITT; p =0.047, CC; p =0.05) and in Satisfaction (ITT; p =0.027). However, when comparing the AMPS and the COPM mean values on group level, the changes cannot be interpreted as a clinically meaningful change as the changes in the mean values are too small (not shown).

On an individual level, the McNemar test analysis on ITT population for the AMPS fulfilling the response criteria with a difference of at least 0.5 logits shows that seven (20%) of the patients increased in their ADL motor ability (*p* =0.02). No patient showed increased ability in ADL process ability (not shown). The McNemar test analysis on ITT population for the COPM fulfilling the response criteria of at least two points' difference shows that four (11%) of the patients rated an increased ability in both Performance and Satisfaction, but this was not a statistically significant change (not shown).

5.3 Reliability of hand function testing instruments (Study III)

5.3.1 Test-retest in 16 patients with WDM

Reliability for grip force, maximum and, respectively, mean values, in the right hand measured with Grippit® was judged as very good (ICC≥ 0.81). Reliability for the Purdue Pegboard, 10 seconds' value of grip force, pinch grip (all three values) measured with Grippit®, and finger flexor force measured with the hand-held Myometer (Microfet2™) in the right hand was judged as "good" (ICC≥ 0.61). Reliability for GAT, wrist flexor force, wrist extensor force and finger extensor force in right hand measured with the hand-held Myometer (Microfet2™) were judged as "moderate" (ICC≥ 0.41). For the left hand, reliability was judged as "good" (ICC≥ 0.61) in all instruments but pinch grip, maximum and 10-second value with Grippit®, and wrist flexor force measured with the hand-held Myometer (Microfet2™). They all showed moderate reliability (ICC≥ 0.41) (Sandin-Aldehag et al., 2008).

The RC, i.e. the minimal clinical important difference on an individual level for WDM patients, is presented in Table IV.

Table IV. RC for 16 WDM patients of four hand function testing instruments.

Repeatability Coefficient (RC)	Right hand	Left hand
GAT (weighted seconds)	6	6
Purdue Pegboard (pegs/30 seconds)	2	3
Grippit® Grip force max (N)	34	60
Grippit® Grip force mean (N)	47	59
Grippit® Grip force 10s (N)	48	49
Grippit® Pinch grip max (N)	13	24
Grippit® Pinch grip mean (N)	13	18
Grippit® Pinch grip 10s (N)	15	18
Myometer wrist ext force (N)	39	42
Myometer wrist flex force (N)	37	43
Myometer finger ext force (N)	8	7
Myometer finger flex force (N)	42	46

5.3.2 Test-retest in 16 patients with DM1

Reliability in the right hand for Grippit® regarding grip force (all three values), as well as finger extensors and flexors measured with the hand-held Myometer (Microfet2™) was judged as "very good" (ICC≥ 0.81). Reliability for the Purdue Pegboard, in pinch grip measured with Grippit® (all three values) and wrist extensors and flexors measured with the hand-held Myometer (Microfet2™) in the right hand was judged as "good" (ICC≥ 0.61). Reliability for the left hand in finger flexor force and extensor force measured with the hand-held Myometer (Microfet2™) was judged as "very good" (ICC≥ 0.81), whereas reliability in the left hand for the Purdue Pegboard, all three values of Grippit® for grip force, and wrist extensor force measured with the hand-held Myometer (Microfet2™) was judged as "good" (ICC≥ 0.61). Reliability for the left hand in pinch grip (all three values) measured with the Grippit® and wrist flexor force measured with the hand-held Myometer (Microfet2™) was judged as "moderate" (ICC≥ 0.41). Reliability in the GAT instrument bilaterally was judged as "fair" (ICC≥ 0.21) (Sandin-Aldehag et al., 2008).

The RC, i.e. the minimal clinical important difference on an individual level for DM1 patients, is presented in Table V.

Table V. RC for 16 DM1 patients of four hand function testing instruments.

Repeatability Coefficient (RC)	Right hand	Left hand
GAT (weighted seconds)	8	6
Purdue Pegboard (pegs/30 seconds)	3	2
Grippit® Grip force max (N)	43	32
Grippit® Grip force mean (N)	24	30
Grippit® Grip force 10s (N)	26	31
Grippit® Pinch grip max (N)	17	22
Grippit® Pinch grip mean (N)	15	19
Grippit® Pinch grip 10s (N)	14	16
Myometer wrist ext force (N)	25	27
Myometer wrist flex force (N)	33	40
Myometer finger ext force (N)	5	7
Myometer finger flex force (N)	11	10

5.3.3 Inter-rater in 16 DM1 patients

Reliability for Grippit®, i.e. grip force (all three values) bilaterally was judged as "very good" (ICC≥ 0.81). Reliability for the Purdue Pegboard in the right hand, the GAT of the left hand, all three measured values of pinch grip bilaterally and in all measurements of the hand-held Myometer (Microfet2™) bilaterally, except wrist flexor force, was judged as "good" (ICC≥ 0.61). Reliability for the Purdue Pegboard of the left hand and the GAT of the right hand was judged as "moderate" (ICC≥ 0.41). Reliability in wrist flexor force bilaterally as measured with the hand-held Myometer (Microfet2™) was judged as "poor" (ICC≤ 0.20).

6. GENERAL DISCUSSION

6.1 Major findings

Persons affected by a disease like muscular dystrophy, for which there is no cure, have a desire for interventions that may delay the progression of the disease. There is a need to maintain physical capacity and independence in ADL as long as possible. One of the reasons why this thesis was initiated was that many of the patients asked about the effects of hand training. As mentioned in the prologue, hand training had previously been offered by OTs with individual follow-ups, but without any validation of the training regimes used. This thesis was thus undertaken with the overall aim to study and gain knowledge about the effects of hand training on both functional capacity such as hand function and ADL in patients with WDM and DM1. The thesis has thus arisen from of the clinical setting and has not been aimed at sorting out the underlying pathophysiological mechanisms behind possible training effects, whether these include neuronal adaptation, changes in the neuromuscular transmission or alterations on the muscle fibre level.

The feasibility/pilot study on WDM (Study I) and the changing-criterion single-case design study on five DM1 patients (Study II) were aimed at showing feasibility, and indicated some statistically significant improvements on the group level, as well as individually improvements with regard to hand function, self-rated ADL and occupational performance. The results of the RCT study (Study IV) on DM1 patients show some statistically significant changes on the group level and clinically meaningful changes on the individual level, both in hand function as judged by the RC from the previous reliability study (Study III), and in self-rated occupational performance and ADL ability. These results confirm that hand training may increase hand function. It is probable that patients start to compensate for the loss of muscle strength and ROM in both hand function and ADL earlier than they need to. This is also discussed in McDonald's (2002) study, where the author states that it is likely that the NMD patients' reduction in functional muscle mass and the associated functional impairments are the result of atrophy from disuse and a sedentary life style, and muscle degeneration due to the disease. The reduction of functional muscle mass leads to further reduction in activity level (McDonald, 2002).

In Study IV, ITT population analyses showed statistically significant changes in three variables and CC population analyses in five variables of hand function instruments. Statistically significant changes for treatment order interaction were found in some of the hand function testing instruments, such as the Grippit® for pinch grip, max and mean value, in the right hand in addition to the statistically significant changes between training and control period. Therefore the results in these variables should be interpreted with caution since treatment order may have affected the results. One explanation for this might be that the T-C group fulfilled their training compliance, whereas the C-T group did not. The reason for this is not clear, but might be due to lack of motivation of the patients or to the time of year (spring vs. fall).

Another interesting finding is that the first group (the T-C group) increased their hand function after both the wash-out period and their control period (post2). It can be speculated that their increase in hand function after training enabled the patients to use their hands more readily in ADL. Another explanation might be that their participation in the study also increased their awareness of their hand function, making them more eager to use their hands in ADL situations. However, this affects the results of the statistical analyses due to the crossover design with the wash-out period, as the T-C group continued to improve during the wash-out and control periods. Nonetheless, this is an interesting finding, considering that DM1 is a disease with a slow continuous progression, which would be expected to have given a decreased hand function if the hand training regime had not been implemented. Accordingly, a decrease in hand function was seen in the C-T group during the control period prior to their training. Even though some statistically significant changes were present, the changes in mean values on the group level of each hand function testing instrument did not correspond to a clinically meaningful change. However, when data from each patient was analysed individually with respect to the RC of each instrument, as derived from the previous reliability study (Study III), several patients exhibited a positive effect with increased hand function.

The results from the three interventional studies (I, II & IV) imply that the training had a broader effect – a carry-over of training effect – since ADL ability increased. The positive effects of hand training on ADL is an interesting result. The end point of any training intervention should ideally be improved function, performance and satisfaction in ADL. The carry-over training effect was also noted in the Purdue Pegboard results (Studies II & IV) showing increased fine motor control in several patients on an individual level, as this test assesses dexterity, i.e. precision and speed – variables that were not specifically exercised in the studies.

There are numerous hand function testing instruments available, but no single instrument covers all aspects of hand function (Jarus et al., 1993). However, the instruments used in this thesis have also been reliability tested in Study III, and three out of four demonstrated high reliability, i.e. the hand-held Myometer (Microfet™), Grippit® and the Purdue Pegboard. They, as well as the GAT, are useful measures of hand function, as they assess wrist force, grip force, pinch grip, fine motor control and three practical tasks. Combined, they constitute a clinically relevant test battery for the evaluation of hand function of patients with conditions like the WDM and DM1 muscular dystrophies. Even though the GAT demonstrated moderate to fair reliability it was still included in Study IV as it, compared to the other instruments, assesses three practical tasks.

6.2 The theoretical perspective of this thesis

In this thesis two theoretical frameworks were used, the ICF (WHO, 2001) and the CMOP (Townsend 2002). With the ICF, the body function was approached in the description of hand function/dysfunction in WDM and DM1 patients. Activities and participation were exemplified in connection with ADL and occupational performance. The CMOP was considered a complementary structure for occupational performance issues, as it focuses on the interactions between the individual and the occupation. In this thesis the interaction between the individual's physical function, i.e. hand function/dysfunction and occupation, was illustrated. The ICF serves well as an inter-professional language, but it is not directly congruent with language concepts and assessments used in occupational therapy (Haglund & Henriksson, 2003; Hemmingsson & Jonsson, 2005).

However, in this thesis the different instruments used originated from occupational therapy concepts, but are also related to the main concepts of body function, activity and participation. The hand function testing instruments used in this thesis relate to ICF body function, whereas the ADL taxonomy (Study I) and the AMPS (Study IV) relate to activity and somewhat to participation. However, some of the motor skills in the AMPS such as gripping and manipulating might also relate to body function. The COPM (Studies II and IV) and the modified version of the Life Satisfaction Checklist (LiSat9) (Study I) are more strictly related to participation. As mentioned and discussed above and below, the hand training regime seemed to have a carry-over training effect on occupational performance and ADL ability and therefore the results of this thesis seem to be targeting all three levels in ICF.

6.3 Methodological considerations

6.3.1 Study sample

The four studies included in this thesis consisted of WDM and DM1 patients with hand function that varied from quite good to poor, which might have affected the statistical results, particularly in the reliability study (Study III). This is always a problem when studying a patient group with variable degrees of muscle weakness and fatigue. On the other hand this makes this thesis more clinically relevant; normal distribution of data was present and parametric analysis was therefore used (Studies III & IV). When interpreting the results, the limited number of patients included in each study should be considered. The low number of participants is, of course, primarily due to the fairly low prevalence of the diseases. However, Studies I, III and IV included all known WDM and DM1 patients in the Stockholm area at that time who fulfilled the inclusion criteria. Study II had a changing-criterion single-case design and included five consecutive case controls.

The high level of acceptance and continuation to participate in the three out of four studies (I-III) indicates that the WDM and DM1 patients are interested and concerned about their hand function. WDM is considered a benign MD compared to DM1 as it “only” affects skeletal muscles and primarily the distal limb muscles. In the RCT study of DM1 patients (Study IV), the proportion of patients who accepted participation was less than 50% and ten out of 35 patients withdrew. The drop-out rate was quite large and since not all patients reached the acceptable level of training compliance (≥75%), the results of Study IV must be interpreted with caution. The reasons for non-participation and withdrawal included family and/or work matters, fatigability and concerns about having to travel back and forth to the clinic during tests and the group training. Other reasons for withdrawal included lack of training motivation, and a few patients reported emotional difficulties with meeting patients at the group training with worse symptoms than they had themselves.

6.3.2 Designs and procedures

Major strengths of this thesis include the training regime used in the three interventional studies (Studies I, II & IV), which followed the ACSM guidelines (1997, 1998, 2002), and the study design in II and IV, i.e. the changing-criterion single-case design and the RCT. None of the three interventional studies indicated any negative/adverse effects. Study IV is also the first RCT in patients with DM1 evaluating the effects of hand training. However, due to the limited number of patients participating in the study and the fairly low prevalence of the disease, a crossover design was used and the patients were also stratified regarding grip force at baseline (pre1) before the randomisation, making the two groups more comparable to each other. The crossover design with the wash-out period not only made comparisons possible between the effects of hand training and no training, but also allowed for studying training effects over a longer time period. However, crossover designs are sensitive to dropouts (Altman, 1991), which primarily affected the C-T group, and not the T-C group in which progressive improvements were also noted after the wash-out

period. The uneven distribution of drop-outs between the two groups makes the interpretation of data more difficult.
Data collections in the four studies were performed by an OT, the author of this thesis. In Study III intra-rater analysis was also performed by a physical therapist. Both have thorough clinical experience and knowledge about WDM and DM1 patients, as well as of each of the instruments tested, as they are used on a regular basis in the clinical work. The examiner was blinded in Study IV only. For Study I especially, the fact that the examiner was not blinded should therefore be considered a limitation.

Another strength in the reliability study (Study III) was the choice to have three trials per session, which was supported by the results of a previous study (Study II), by our clinical experience with these patients and also by the literature for grip strength measurements and dexterity (Gallus et al., 2003; Innes, 1999; Mathiowetz, 1990). This seemed adequate since some practise effects was observed over the three trials and that some patients also demonstrated a practise effect between the sessions, especially for the Purdue Pegboard and the GAT (as seen from descriptive statistics, not shown). The choice of one-week intervals between test-retest and inter-rater reliability was based on the need to avoid changes in the patients' condition due to the progressive nature of their disease, but also on the fact that there were several instruments to be tested. It was therefore not possible to perform the test-retest and inter-rater test on the same day, a fact which could have influenced the results. However, the test-retest was performed on the same day of the week and time of day as the patients are more likely to have the same routines then.

6.3.4 Hand function, muscle strength training and training effects (Studies I, II & IV)

The WDM and DM1 patients in the studies were mostly right-handed. In Study I, the most affected/dysfunctional hand of the WDM patients was the left hand, which also after hand training demonstrated the best training results. This has also been noticed in the author´s clinical work. This trend has not been seen in DM1 patients, neither in these studies (Studies II & IV) nor in the clinical work. One of the inclusion criteria used in Studies I, II and IV, i.e. for the patients to demonstrate at least three out of five in MMT, is an important clinical measure when deciding whether it will be worthwhile for individuals to engage in any form of training. If a patient is unable to demonstrate full hand flexion, due to severe atrophy and weakness, strength/resistance training is unlikely to be beneficial. However, if the patient is demonstrating full ROM and some residual muscle strength, there is still a substantial amount of functioning muscle fibers left and the patient may be a candidate for training (Ansved, 2001; Eagle, 2002). The author of this thesis wants to emphasize that another important issue when deciding if training might be beneficial is the patient's overall life situation, i.e. elements like the kind of occupation, the involvement in other training activities, hobbies, all of which may influence hand function. The patient may already have a high "training" level in which case additional training may instead be deleterious due to the risk of overload.

The above-mentioned reasons for non-participation and withdrawal emphasize the difficulties encountered when performing a training study. It is a challenge to maintain training compliance throughout the study period. Another difficulty is that these patients are suffering from a continuously progressive disease with a number of symptoms like progressive weakness, fatigue, and cognitive defects which in one way or another affect the outcomes. The diseases have fairly low prevalence, and to obtain a reasonable amount of patients the examiner/investigator usually has to include patients who differ regarding age, sex, and symptom severity, distribution of weakness and rate of progression. The potential improvements after training depend on factors like muscle strength and endurance, and the intensity, frequency and nature of the exercise program. This makes comparisons between training studies difficult as the methods and designs usually differ (Ansved, 2001).

Studies I and II included individual training sessions with an OT, as compared with the RCT study, which offered supervised group training only. On the other hand, the group training (Study IV) turned out to be a forum for sharing experiences and thoughts regarding their disease, which the majority of patients considered positive. The training compliances, measured by the training dairy, were high in Studies I and II but for Study IV the adequate training compliance (≥75%) was met only by the first group who received hand training (T-C group).
However, it is highly likely that patients, either WDM or DM1, need continuous supervision and verbal encouragement in order to continue their training. Similar conclusions were made by Tollbäck and associates (1999) in their 12-week study of knee extension training of DM1 patients. Other reasons to have supervised training include being able to follow positive or negative changes in functional capacity and

compliance, as well as being able to increase sets and repetitions in the program during the period of training. Only a few patients have continued with their hand training after completion of the interventional studies, and these are mainly WDM patients.

When comparing the results of each DM1 patient in Study II, it was noted that the patients who were not engaged in other training activities, i.e. had a sedentary life style, showed the best improvement in hand function after training as compared to those with active life styles prior to and during the training period. This suggests that the patients who had been regularly participating in any form of training or in ADL engaging hand muscles prior to the study might be closer to their maximum functional level. However, these patients also improved in hand function and self-rated ADL, although less pronounced. Nonetheless, a general conclusion both from the studies in this thesis and experiences from my clinical work is that the patients who are used to performing training of any kind usually demonstrate higher training compliance and need less verbal encouragement.

6.3.4 Occupational performance and ADL (Studies I, II and IV)

In Studies I and II no objective ADL measure or instrument was used, which possibly makes the results more unreliable, but the results should still be seen as an important observation. In Study IV, however, objective measurements of ADL were obtained, as the AMPS (Fisher, 2003 a & b) was used. Some DM1 patients (Studies II & IV) had difficulties expressing experienced self-rated problems in self-care, productivity and leisure evaluated with the COPM. They reported comparatively few activities as experienced problems even though they demonstrated decreased hand function and ADL ability as observed with the AMPS instrument. An explanation for this might be that they have succeeded in coping with their limitations in their everyday lives and/or that they have become skilled in using compensatory strategies in order to manage ADL competently, despite limitations in hand function. Another explanation might be that they simply were unaware of their functional deficits, possibly due to cognitive deficits. Some patients’ difficulties in expressing ADL problems were also reported by Nätterlund (2001).

In Study IV, for the ADL instruments, statistically significant changes were seen in the AMPS for both ADL motor and ADL process ability and in the COPM for both Performance and Satisfaction (ITT population analysis). However, CC population analyses showed only statistically significant changes in ADL motor ability for the AMPS and Performance in the COPM. The authors did not expect to find any statistically significant changes for the ADL process ability as hand training should not directly effect too many variables of the ADL process ability. Therefore the CC population analyses should, in this case, be considered a more reliable finding. Also, the McNemar test reveals that there were no patients showing, on an individual level, increased ability in ADL process ability. The conflicting results of the ADL instruments may be due to the fact that in the first analyses these were analysed on the group level (ITT/CC) without respect to fulfilling the criteria for a clinically meaningful change as analysed with the McNemar test. Statistically significant changes for treatment order interaction were seen in the AMPS, in ADL motor and in ADL process ability, in ITT population analyses, and in CC population analyses. These results should therefore be interpreted with caution.

Even though the AMPS does not evaluate hand function per se, but rather the quality of performance processes and outcomes, the authors chose to include this ADL assessment as we believe it to be the most used standardized observational tool to assess ADL ability in a variety of disorders. However, since the primary outcome measure for the intervention in this study was grip force, the fact that improvements of such body functions/capacities may not directly lead to improvements in observed ADL ability is not surprising. This is also supported by other studies (Fisher 2003 a).

6.3.5 Reliability of hand function testing instruments (Study III)

A limitation in this thesis is that only reliability (test-retest for WDM and DM1 patients and inter-rater for DM1 patient only) has been examined for the instruments used for WDM and DM1 patients, and not validity. However, validity has previously been tested for e.g. the Grippit® vs. the Jamar dynamometer in healthy subjects (Massy-Westropp et al., 2004) and the GAT vs. HAQ (Health Assessment Questionnaire) in RA patients (Dellhag, 2000).

Optimally, in addition to the ICC and RC analyses, Standard error of measurement (SEM) should have been calculated.

Overall, fine motor control and practical tasks got better scores after the first trial, especially in the left hand (descriptive statistics, not shown). All patients were right-handed and therefore the practice effect in the Purdue Pegboard and the GAT

instruments was seen in their left hands. Highest reliability was consequently seen in the right hand for most of the instruments in both patient groups.
A systematic bias was observed on the second and third Purdue Pegboard scores; they tended to be higher than the first (descriptive statistics, not shown). Clinicians must therefore be cautious when interpreting a better score at a second evaluation. A practise effect may influence the results without reflecting a real improvement. This practise effect was also reported by Desrosiers et al. (1995) and Reddon et al. (1988), but not by Gallus & Mathiowetz, (2003). Again, the author wants to emphasize that one trial is not enough when examining and drawing conclusions from fine motor control and dexterity.

The reliability test for the ***GAT*** ("fair-good") in WDM and DM1 patients showed better reliability in the left hand. This was also seen in the inter-rater reliability test. One concern when doing a complex task like the GAT, which was performed bilaterally, is that the results of the first hand may have an impact on the results of the second hand due to learning effects on factors like fine motor control, coordination and strategy in planning of the performed movement. The Tubigrip stocking subtest/practical task fluctuated the most, which may have affected the reliability of the right hand. The GAT instrument was originally developed for RA patients and for that patient group, the test-retest and inter-rater reliability was found to be high and significant (Dellhag, 2000). This further underscores that each test instrument must be validated for each diagnosis, i.e. for each patient group to be tested.

The test-retest and inter-rater reliability test of ***the Purdue Pegboard*** was "good" in WDM and DM1 patient bilaterally except in inter-rater testing for the left hand ("moderate"). Other reliability studies performed on healthy subjects and on patients with multiple sclerosis support these findings (Desrosiers et al., 1995; Gallus & Mathiowetz, 2003).

The Grippit® instrument for measuring grip force showed the highest test-retest and inter-rater reliability ("very good-good") in both WDM and DM1 patients. One explanation for this is that Grippit® is an electrical instrument with a timed test and that the testing situation is easily reproducible with the use of the forearm support and grip position. Other reliability studies of the Grippit® for measurement of grip force have shown high reliability and precision in patients suffering from stroke (Hammer &

Lindmark, 2003), in healthy subjects (Lagerström & Nordgren, 1998), in rheumatoid arthritis (RA) patients (Nordenskiöld & Grimby, 1993), and in patients with Charcot-Marie-Tooth (Svensson & Häger-Ross, 2006). However, the pinch grip did not show as high reliability as the grip force, the reliability ranging from "fair" to "good" for both patient groups. Explanations for that might be that compared with grip force in which mass movements are tested, pinch grip measures isolated movements that have less muscular endurance. Svensson and Häger-Ross (2006) drew similar conclusions in their study of hand function of Charcot-Marie-Tooth patients. However, in Study IV, only two trials were assessed with the Grippit® on each test occasion (pre1-post1; pre2-post2). This was due to the extensive evaluation including the four hand function testing instruments and the two ADL instruments. Prior to that decision, additional reliability analysis, i.e. ICC and RC was calculated and the values were comparable with those of the three trials as evaluated in Study III.

The hand-held Myometer (Microfet2™) showed "very good to moderate" reliability for test-retest in WDM and DM1 patients. Highest test-retest reliability was seen in DM1 patients, which is an interesting finding due to the extensive symptoms of the DM1 disease as compared to WDM. The same was seen for RC values, i.e. less fluctuations in DM1 compared to WDM. For inter-rater examinations in DM1 patients, "good" reliability was seen in wrist extensors, finger extensors and flexors. "Poor" reliability was shown in wrist flexors, probably due to the fact that the two examiners' placements of the Myometer differed. One placed the hand-held Myometer transducer more distally than the other examiner. Two previous reliability studies have been performed using the hand-held Myometer (Microfet2™). Both of these studies tested hip abduction and in the study performed by Click Fenter et al. (2003) "poor" reliability was shown in comparison with two other hand-held dynamometers, whereas Van Meeteren et al. (1997) presented "very good" reliability with this instrument. The authors of Study III want to emphasize that when muscle force tests are performed with a hand-held Myometer (Microfet2™), the examiner needs to have good knowledge about the instrument and about where to place the transducer for the different muscle groups that are going to be tested. The examiner also needs to have an arm strength that exceeds that of the muscle tested. When testing lower extremities this is a challenge and might therefore be an explanation of previous conflicting reliability results regarding measurements of hip abduction. This is further supported by a dynamometer study performed by Richardson et al. (1998) where measurements of strength were more reliable in the upper than in the lower extremities.

Inter-rater reliability in DM1 patients was higher than test-retest in three of the instruments, in either right and/or left hand. This is likely due to the fact that the inter-rater test was performed during the same day as the retest measurements, whereby an additional practise effect or fatigue (eight patients, i.e. 50%, were tested after inter-rater reliability testing) may have played a role. As mentioned above, evaluation of hand function is complex, and without an accepted gold standard assessment of hand function for individual populations, research studies will need to be reviewed with careful consideration of the reliability and validity of assessment tools for each patient population (Tyler et al., 2005).

6.3.6 Statistical analyses

A major strength of the present thesis was the fact that the results were analysed both on the group level and the individual level. Statistical power analysis was performed for Studies III and IV. There may be some inconsistencies in the thesis's analytical approaches, using different mixtures of parametric and non-parametric statistics. For example, in the changing-criterion single-case design, the study on DM1 patients (Study II) paired t-test was used. Preferably, a non-parametric analysis should have been used because of the uncertainty of the data distribution. On the other hand, post hoc analysis shows that a parametric test would not alter the results. Parametric statistics were used as the only analysis of data in Study III and for the majority of data in Study IV. Data were approximately normally distributed in these studies as the participating patients demonstrated mild to moderately severely impaired hand function.

Another strength in the reliability study (Study III) is that RC was analysed in addition to the ICC analyses. The RC gives the minimal clinical important difference of each hand function testing instrument and can therefore be used clinically to compare hand function pre- and post-training in WDM and DM1 patients. However, the statistically significant results and the clinically meaningful difference on the individual level regarding pinch grip measured with the Grippit® and the GAT need to be interpreted with caution, as the reliability varied from good to moderate (ICC$\leq$0.41) (Study III). The results for finger extensor force in Study IV based on the RC from Study III must also be interpreted with caution, as it turned out, in this study (Study IV), that the majority of the patients improved after training (unlike the cases in the other hand function instruments used in the study) even though several patients didn't meet the acceptable training compliance (≥75%). Furthermore, several patients demonstrated improvements in finger extensor force during the control period and some even before their training periods. Again, this was not seen for the other hand function instrument variables.

In Study IV the intention-to-treat (ITT) analysis population was used according to the guidelines for evaluation of RCT and was the primary analysis population in the study (CONSORT; Altman et al., 2001). Also, as a secondary and sensitivity analysis, the complete cases (CC) analysis population was evaluated for the patients who fulfilled the entire study design and protocol, i.e. observed and tested values of all measurements at all four test occasions during the one-year study period. This made it possible to better understand the real effects on the patients' hand function, occupational performance and ADL ability of those who continued to participate during the whole study period.

6.2.7 Ethical considerations

The four studies in this thesis have been examined and approved by the local ethics committee of the Karolinska Institute, Stockholm, Sweden. Both written and oral information was given to all the patients included in the studies concerning the aim, design and procedure, including time aspects. Informed consent, confidential treatment and presentation of data, either individual or group, have been routine procedures, as has emphasis on voluntary participation that can be terminated at any time during the course of the studies.

The patients' hand function was continously followed during the training periods and they had individually customized resitance putties, which should have limited any possible overexertion of their wrist and hand muscles.

6.2.8 Future studies

Future studies should include multi-centre studies to enable the inclusion of more patients fitting the inclusion criteria and thus increasing the statistical power. Of course it would be preferable to perform a longitudinal RCT hand training study on WDM patients, a follow-up of Study I, to better understand the effects of hand training in these patients. It would be interesting to study and evaluate more functional exercises with the same or comparable effect as muscle strength training with resistance putties to better promote generalization of the training effects on hand function to ADL function.

7. SUMMARY AND CLINICAL APPLICATION

7.1 Summary:

- The three interventional studies (Studies I, II & IV) indicate that three months of hand training in WDM and DM1 patients are safe, with minor but significant improvements in hand function, occupational performance and ADL ability. However, since Study I on WDM patients was a feasibility/pilot study, further research is needed on this patient group to confirm the results.
- The hand-held Myometer (Microfet™), Grippit®, Purdue Pegboard and the Grip Ability Test (GAT) represent useful measures of hand function. They assess wrist force, grip force, pinch grip, fine motor control (dexterity) and three practical tasks. In combination they constitute a clinically relevant test battery for hand function evaluation of patients with WDM and DM1. The statistical analyses show mainly very good to good intra- rater (test-retest) and inter-rater reliability in three out of four instruments tested, i.e. the Purdue Pegboard, Grippit® and the hand-held Myometer (Microfet2™). These instruments are used clinically and, according to the results from Study III, are reliable for evaluating hand function in WDM and DM1 patients.

7.2 Clinical application:

- Among WDM and DM1 patients, contractures are common in the MCP, PIP and DIP joints, which together with the muscle weakness make the WDM patient unable to extend the fingers, and the DM1 patient to flex the fingers. Contractures may be of functional value to some patients, e.g. giving the patient a passive grip due to the contractures, when normal active gripping is absent due to muscular atrophy and weakness. When giving the patient stretching prophylaxis to prevent contractures, one should take this into consideration. However, the contractures can also hamper the patient in ADL. WDM patients should, for example, limit stretching of wrist extensors, but concentrate on the stretching of wrist flexors, as shortened wrist extensor muscles enable the patient to more easily extend and stabilize the wrist. A DM1 patient should focus on the stretching of the finger flexors to avoid contractures in the finger joints that make the patient unable to flex and adequately use his/her fingers.

- Hand training should focus on maintaining and preserving hand function rather than improving hand function. A moderate level of intensity should be used to prevent adverse/side effects. However, before hand training is considered, it is important to investigate the overall life situation, including the kind of occupation, the involvement in other training activities and hobbies, all of which may influence hand function. The patient may already have a high “training” level at which case additional training may instead be deleterious due to overwork and overexerting muscles might accelerate disease progression.
- Hand training in WDM and DM1 patients should be done under the supervision of an experienced therapist who is able to monitor positive and negative effects of hand training, prevent injuries, and to combine muscle strength training exercises with more functional exercises to promote an increase, not only in muscle strength, but also in ADL.

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9. SUMMARY IN SWEDISH – SAMMANFATTNING PÅ SVENSKA

Det finns ett stort behov av interventioner som kanske kan försena sjukdomsförlopp hos människor som är drabbade av en sjukdom såsom muskeldystrofi, som det inte finns någon bot för. Att bibehålla fysisk funktionsförmåga och självständighet i det dagliga livets aktiviteter (ADL) så långt det går hos de drabbade är därför av största vikt. Detta var en av orsakerna till att aktuell avhandling initierades. En annan var att patienterna själva efterfrågade träning och dess påverkan på handfunktion.

Det övergripande syftet med avhandlingen var att studera och nå vetskap om handträning och dess effekter på handfunktion och ADL hos patienter med Welanders distala myopati (WDM) och Dystrofia Myotonica typ 1 (DM1).

Avhandlingen består av fyra delarbeten varav tre av dem är interventionsstudier gällande handträning (delstudie I, II & IV). Delstudie IV är en större kontrollerad randomiserad handträningsstudie som utgör en uppföljning av delstudie II. Delstudie III är en reliabilitetsstudie där fyra bedömningsinstrument av handfunktion utvärderats och bedömts med avseende på deras tillförlitlighet (reliabilitet) och upprepbarhet (repeatability).

De bedömningsinstrument som använts för att bedöma handfunktion är: 1; Grippit® som mäter muskelkraft i helhandsgrepp och pincettgrepp (använts i delstudie I-IV). 2; Grip Ability Test (GAT) som bedömer 3 olika handgrepp i aktivitet (delstudie III-IV). 3; Myometer (Microfet 2™) som använts för muskelkraftsmätning i handled och fingrar (delstudie II-IV). 4; Purdue Pegboard som bedömer snabbhet och precision (finmotorik) (delstudie II-IV). 5; Manuell Muskel Test (0-5-skala) har använts som inklusions kriterie i interventionsstudierna (delstudie I, II & IV), men också som ett resultatmått i delstudie I. En finger goniometer som bedömer aktiv ledrörlighet användes i delstudie I. Självskattad myotoni, dvs. svårigheter att relaxera fingrarnas böjarmuskler (släppa greppet efter t ex. handskakning) användes i delstudie II. För att utvärdera eventuella handträningseffekter på ADL-förmåga användes bedömningsinstrumenten ADL-taxonomin i delstudie I men enbart som semistrukturerad intervju. Självskattningsinstrumentet Canadian Model of Occupational Performance (COPM) användes i delstudie II och IV och Assessment of Motor and Process skills (AMPS) i delstudie IV. Livstillfredsställelse, utvärderades med hjälp av en modifierad version av Livstillfredsställelse Checklistan (LiSat9) men endast i delstudie I.

Fjorton WDM patienter ingick i delstudie I, fem DM1 patienter i delstudie II, 16 WDM och 16 DM1 patienter i delstudie III, samt 35 DM1 patienter i delstudie IV.

Delstudie IIIs resultat påvisade god tillförlitlighet (intra-class correlation coefficient (ICC) $\geq$ 0.61) hos tre av de fyra bedömningsintrumenten som utvärderades, dvs. Grippit®, Myometer (Microfet2™) och Purdue Pegboard, både för inom- (WDM och DM1 patienter) respektive mellanbedömarreliabilitet (enbart DM1 patienter). De tre interventionsstudierna (I, II & IV) inkluderade alla en 3 månadersperiod av handträning med siliconbaserad motståndsmassa. Resultaten från dessa (delstudierna I, II & IV) påvisade små, men positivt signifikanta skillander hos WDM och DM1 patienter efter handträning både avseende handfunktion och ADL.

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