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STRENGTH TRAINING AFTER STROKE: EFFECTS ON MUSCLE FUNCTION, GAIT PERFORMANCE AND PERCEIVED PARTICIPATION

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STRENGTH TRAINING AFTER STROKE:

EFFECTS ON MUSCLE FUNCTION, GAIT PERFORMANCE AND PERCEIVED PARTICIPATION

Ulla-Britt Flansbjer

Thesis 2006

LUND UNIVERSITY

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In memory of my father Erik
Born in Flansbjer 1918

Contents

Abstract

The overall aim of this thesis was to evaluate the effects of strength training on muscle function, gait performance and perceived participation in subjects with chronic mild to moderate post-stroke hemiparesis.

A main impairment after stroke is reduced muscle strength. This post-stroke weakness is a major contributor to mobility limitations, which can prevent the resumption of activities of daily living and have an adverse effect on perceived participation: persons' lived experiences of involvement in their life situation. Improving muscle function is important in stroke rehabilitation, but strengthening exercises have been controversial due to the hypothesized risk of increasing muscle tone.

To be able to evaluate changes following strength training, we need equipment and methods that provide reliable measurements of muscle strength and gait performance and also an increased knowledge about the relationships between muscle strength, gait performance and perceived participation in chronic post-stroke subjects. In the first two studies the reliability of different tests, assessing isokinetic knee muscle strength and gait performance, was evaluated. In the third study the relationships between isokinetic knee muscle strength, gait performance and perceived participation were analysed. The 50 subjects participating in these studies (mean age 58 ±6.4 years, 6-46 months post-stroke) were able to walk independently, and could understand both verbal and written information. The results showed that all measurements for isokinetic knee muscle strength and gait performance were reliable and for each measurement, limits were set to detect real improvements following an intervention. The relationship between knee muscle strength in the paretic knee muscles and gait performance was significant, and gait performance was in turn related to perceived participation. This indicates that improvements in knee muscle strength could have a potential effect on gait performance and perceived participation. To evaluate changes following an intervention, both isokinetic knee muscle strength measurements and gait performance tests are reliable and sensitive enough to detect real (clinical) improvements.

In the fourth study the effects of progressive resistance training (PRT) on knee muscle function, gait performance and perceived participation were evaluated. Twenty-four subjects (mean age 61 ±4.9 years) participated in this single-blinded randomised controlled study (ratio 2:1 training/control). All subjects were more than 6 months post stroke, could understand both verbal and written information, had muscle weakness greater than 15% in the paretic knee muscles (mean isokinetic peak torque at 60°/s) and were able to walk independently. The intervention consisted of PRT for the knee extensor and flexor muscles twice weekly, for ten weeks, at a load about 80% of maximum strength (6-8 reps, in 2 sets). Measurements of knee muscle strength, muscle tone, gait performance and perceived participation were performed before and after the intervention. The results showed that ten weeks of PRT significantly improved knee muscle strength, without any increase in muscle tone. Gait performance improved, with slow walkers at baseline having the best gains. Improvements in gait performance were, furthermore, related to improvements in perceived participation. For the control group there were some improvements in gait performance, but low or no increase in knee muscle strength and perceived participation.

In conclusion, PRT improves knee muscles strength and gait performance, without any negative effects on muscle tone and improvements in gait performance, in turn, positively affects perceived participation. Thus, PRT is an effective form of training in chronic stroke patients that can be used both as physiotherapy treatment for those with residual hemiparesis and as fitness training for those with a minor disability.

List of publications

This thesis is based on the following papers referred to in the text by their respective Roman numerals

I Flansbjer U-B, Holmbäck AM, Downham D, Lexell J. What change in isokinetic knee muscle strength can be detected in men and women after stroke? Clinical Rehabilitation 2005;9:514-522

II Flansbjer U-B, Holmbäck AM, Downham D, Patten C, Lexell J. Reliability of gait performance tests in men and women with hemiparesis after stroke. Journal of Rehabilitation Medicine 2005;37:75-82

III Flansbjer U-B, Downham D, Lexell J. Knee muscle strength, gait performance, and perceived participation after stroke. Archives of Physical Medicine and Rehabilitation 2006;87:974-980

IV Flansbjer U-B, Miller M, Downham D, Lexell J. Progressive resistance training after stroke: Effects on muscle function, gait performance and perceived participation. Manuscript

Papers I-III were reprinted with permission from the publishers.

Abbreviations and definitions

6MW	six minute walk
BMS	the variability between subject mean square
CGS	comfortable gait speed
CI	confidence interval
FGS	fast gait speed
FIM	functional independent measure
ICC	intraclass correlation coefficient
ICF	international classification of functioning, disability and health
ICIDH	international classification of impairments, disabilities and handicaps
LOA	limits of agreement
MAS	modified Ashworth scale
Nm	Newton meter
PRT	progressive resistance training
PT	peak torque
RM	repetition maximum
ROM	range of motion
SCas	stair climb ascend
SCde	stair climb descend
SD	standard deviation
SE	standard error
SEM	standard error of the measurement
SEM%	a percentage value of the standard error of the measurement

SIS	stroke impact scale
SRD	smallest real difference
SRD%	a percentage value of the smallest real difference
TUG	timed “up & go”
WMS	the variability within subject mean square

concentric movement - shortening of the contracting muscle during the movement action

dynamic strength (isotonic strength) - the muscle strength in the mid range of a dynamic movement

eccentric movement – lengthening of the contracting muscle during the movement action

isokinetic strength - muscle performance measured in a dynamometer at a constant velocity with a variable resistance through the movement

muscle strength – the maximal force or torque that can be generated by a muscle or muscle group at a specific velocity

peak torque - the maximum point on the strength curve obtained during a contraction in Newton meter

Background

Stroke

According to the World Health Organization (WHO) stroke is defined as an "acute neurological dysfunction of vascular origin with sudden or at least rapid occurrence of symptoms or signs corresponding to involvement of focal areas of the brain". Stroke is caused by a disruption of the blood supply to the brain, leading to damage of the brain tissue, as a result from either blockage (infarct 85%), a rupture of a blood vessel (intracerebral haemorrhage 10%) or other causes (i.e. subarachnoid haemorrhage 5%). In recent years 15 million people worldwide suffer a stroke annually, and 5 million of these are left permanently disabled (1). In Sweden there are more than 25 000 new incidents per year (2) with a total of about 90 000 persons in Sweden living with a disability due to stroke. The incidents of stroke doubles with each decade for individuals over the age of 60, which makes stroke a problem mainly for the ageing population. In Sweden the median age for having a stroke is 74 years for men and 78 years for women, with more than 20% younger than 65 years old.

There are several risk factors for stroke (3), many similar to those for arteriosclerosis. Many risk factors can be influenced by cardiovascular diseases preventions: for example efficient treatments for heart disease, hypertension and diabetes, and also support changes from an unhealthy lifestyle such as smoking habits, unhealthy diet and physical inactivity. During the last decade the incidence of stroke has declined, however, the prevalence of stroke has increased due to the ageing population. The number of stroke survivors in society today has never been greater. Having a stroke is regarded as an acute condition, comparable with an acute heart attack. It is important with immediate acute care to limit the brain damage (3). Specific stroke units with active managements have resulted in reduced mortality during the first year post stroke, fewer functional restrictions and a less need for institutional living for the stroke patient (4).

Consequences of stroke

In the acute phase after stroke symptoms such as hemiparesis, lack of balance, speech and visual problems and cognitive dysfunction are common. Spontaneous recovery during the first weeks does occur (5) and many patients recover considerably during the first months post-stroke with the peak of neurological recovery by weeks 12 to 13 post-stroke (6-8). Despite this only a small proportion of all stroke patients are completely neurologically and functionally recovered and many stroke patients remain chronically disabled with a need for further rehabilitation for long periods (7, 9).

Motor impairments are the most prevalent of all deficits seen after stroke (10). It has been reported that the hemiparesis after stroke can dramatically reduce the muscle mass available for contraction during physical activity and the weakness in the lower limb affects mobility, especially gait (7, 11-13). In the non-paretic limb there is also a reduction in muscle strength, evident at an early stage following stroke (14, 15). The muscle weakness negatively affects mobility and balance which in turn increases the risk of falling (4, 16). In healthy people immobilisation can lead to a rapid loss of cardiorespiratory fitness, muscular hypotrophy and adverse changes in local muscular metabolism (17, 18). Some clinicians have argued that muscle hypotrophy is not a primary problem post-stroke (19) and have stated: “the need for strengthening muscles is a secondary problem post-stroke as atrophy is rare in cases with spasticity, when the peripheral nerve supply is intact and atrophy usually develops late if at all”. This is now seriously questioned, and there is evidence to support the hypothesis that reduced level of physical activity leads to muscle atrophy also post stroke (20).

Walking is one of the most important domains of the activities and participation components according to the *International Classification of Functioning, Disability and Health* (ICF) (21, 22). A major aim after stroke is to improve muscle function to regain transfer and walking ability (23-26). Even if a majority of persons post stroke (about 80%) regain walking ability, about 60% have an abnormal gait that prevents them walking longer distances at a reasonable speed (27). Walking at a slow speed due to a hemiparesis can expend the same oxygen consumption as healthy people walking approximately twice as fast (28).

Carrying out everyday tasks might require a higher proportion of their maximum capacity leading to increased fatigue and may even result in avoidance of the task. The reduction in walking ability could be one explanation for difficulties in resuming daily activities, work and leisure occupations and thereby encroach upon perceived participation.

Rehabilitation and health – the ICF framework

Rehabilitation is a process delivered by an integrated team which includes the person in need of rehabilitation. “Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (WHO, 1946). In previous frameworks for health, the negative aspects have been emphasized: impairments, disability and handicap (ICIDH) (29). According to the new framework for health from WHO (2001), ICF (21), all domains included have both a positive and a negative aspect. The domains in ICF are divided into three main parts: body structure and function, activity and participation. Furthermore, environmental factors and personal factors are needed to understand the complexity of the rehabilitation process. There is an interaction between the different domains which affects health. An important shift of focus is the change from the term “handicap” as judged from the health professionals’ point of view, as compared with normality in society, to the term “participation”. Participation is defined as persons’ lived experiences of involvement in their life (21). During the acute phase care is focused on body structure and function. In rehabilitation different treatments to improve body function are also used, but the main goals in rehabilitation are set on the level of activity and participation (30). An important aim for scientific research in rehabilitation is to develop efficient treatment strategies to improve body functions that are beneficial for activity and perceived participation.

One question to be answered is: are the different domains related? If there are relationships between function (knee muscular strength), activity (gait performance) and perceived participation post-stroke, then improvements in one domain might influence the others. Muscle strength has been shown to have a moderate to strong correlation to gait velocity post-stroke (31, 32) and studies have investigated the effects of strength training on gait performance, but the results are conflicting (33,

34). As participation is a new term most previous studies have focused on the activity limitations in terms of handicap. Currently we have very limited data demonstrating the effects on perceived participation by increased strength or improved walking ability (33).

Muscle strength training

Muscle strength can be defined as the maximal force that can be generated by a specific muscle or muscle group at a specific velocity (35). To generate sufficient tension in a muscle for the purpose of posture and movement is important for the performance of physical activities and activities of daily living. Muscle strength can decrease due to reductions in muscle mass or by inadequate voluntary activation. This muscular weakness, noted as a clinical sign or a symptom, can be due to factors such as inactivity, aging, disease and/or injury (18, 36-38).

An effective way to improve strength in healthy individuals is progressive resistance training (PRT) (39). Almost 60 years ago the principles for PRT were described by DeLorme and Watkins (40). These principles can be summarised as: i) to perform few repetitions until fatigue (maximal 10), ii) to allow sufficient rest for recovery and iii) to progressively increase the resistance. In other words the muscle must be progressively overloaded to increase muscle strength in a way that does not cause overtraining (41). Adaptations to resistance training include enhanced neural function, increased muscle cross-sectional area, and changes in muscular architecture and metabolites (39, 42, 43). Strength training has traditionally been used in healthy adults to improve fitness and performance in sport (43), and in the last decade to maintain or improve muscular strength in the older population (44-47). Recently, strength training has also been recommended in overall fitness programs to reduce risk of diabetes and cardiovascular disease (43). For post-stoke patients there is now growing evidence that strength training can improve motor function and thereby reduce the risk for secondary complications of inactivity (33, 48).

Physiotherapy after stroke

Physiotherapy in the early 1950's focused on orthopaedic disorders. Thus, the emphasis of physiotherapy within the field of neuro-rehabilitation was strength training of the non-involved muscles, joint mobility, bracing and training with orthotics. Dissatisfaction with the orthopaedic approach for addressing neurophysiological deficits such as spasticity and hypotonus as a result of brain disorders led to the development of treatments aimed at normalizing tonus. In general, the assumptions of the new neurophysiological approach were grounded in interpretations of a reflex-hierarchical model of motor control based on the earlier pioneer of physiological research (49). Physiotherapy treatments aimed at improving physical function after stroke that evolved from the reflex-hierarchical model can be summarised as: Bobath treatment (19), Brunnström model (50) and Proprioceptive neuromuscular facilitation (PNF) (51).

According to the understanding of Bobath (19), motor deficits after stroke were primarily attributed to spastic hypertonus. Strength training of paretic spastic muscles was strictly prohibited, based on the assumption that muscle atrophy was not a contributing factor to post-stroke weakness and that strength training would enhance the spastic resistance from antagonist muscle groups thus impairing function. On the other hand the architects of PNF, Kabat, Knott and Voss (51, 52) advocated the use of repetitive manual resistance to strengthen weak spastic muscles. Furthermore, the weak limbs should overcome the manual resistance which was to be applied in very specific movement patterns. Brunnström (50) documented her observations that spontaneous motor recovery post stroke followed a preset order of control over movement synergies. Brunnström hypothesised that these synergies should be encouraged to hasten recovery of voluntary control. Scientific evidence of the merits of treatments grounded in the neurophysiological approach was inadequately pursued and the treatment modes were spread worldwide through practical courses, single case observations and handbooks for clinical practice. The Bobath understanding of the nature of spasticity and motor deficits post stroke developed into a treatment concept (53) that dominated physiotherapy practice for acute stroke patients into the 1990's (54-56).

In the early 1990's Carr and Shepherd (5) seriously questioned the reasoning and assumptions of the Bobath concept. Using a deductive approach in which they gathered scientific documentation from the fields of neurophysiology, muscle physiology, motor learning, biomechanics and research on the theories of motor control, they concluded that motor deficits post stroke cannot solely be attributed to pathological hypertonus. They proposed that the physiotherapist must facilitate a relearning process whereby the patient, through cognition and practice, regains an improved motor control of meaningful activities. They also deducted that inherent muscle factors such as muscle fibre shortening, stiffening and hypotrophy due to a lower activity level post stroke contribute to the weakness.

Most physiotherapy treatment after stroke has been based on clinical knowledge. Today physiotherapy treatment in the acute phase is mainly addressing the ability to regain motor control and mobility and to prescribe appropriate aids. The content of physiotherapy treatments from four different countries in Europe has been compared (26). In all countries a common content of physiotherapy treatments were the training of selective movements, but also exercises and balance training in sitting and standing and ambulatory exercises.

In the last decade there is a growing demand in evidence-based medicine among medical professionals and an awareness of the importance of using beneficial treatments in rehabilitation. In several reviews the importance of good methodological quality of trials has been emphasized, (57, 58) and the study designs have been evaluated from different criteria such as: diagnosis, randomization, baseline comparison of groups, blindness of recipients and outcome assessors, reliability of outcome measurements, report of methods, loss to follow up and other potential confounders. Several reviews following these quality guidelines have addressed physiotherapy treatments after stroke (33, 34, 59-61). Many trials have considered global approaches, rather than evidence for individual treatments. A study (59) comparing the effects from different treatment approaches after stroke, concluded that there was no evidence that any approach was clearly better than any other to improve leg strength or walking speed post-stroke. A study addressing the effect of physical fitness training post stroke (60) concluded that

available data are too incomplete to guide clinical practice about fitness training after stroke.

Strength training after stroke

One of the main impairments after stroke is muscle weakness (34, 62, 63). Recent findings have shown that this post-stroke weakness is probably not due to resistance in spastic antagonists but to low force generation by the agonist muscle (64) and also mechanical changes in muscle or other soft tissue (65). There is today growing evidence that this muscle weakness is a primary source of motor impairment post-stroke and that strength training can reduce musculoskeletal impairment post-stroke (33, 66) with no increase in hypertonus, antagonist resistance during voluntary movements, or decreased movement quality (66-72). The recommendations for stroke rehabilitation from the American Heart Association 2004 (73) and Physiotherapy Concise Guide for stroke in the United Kingdom (67) now include strength training. The American Heart association concludes that there are no accepted guidelines for determining when and how to initiate resistance training after stroke, but recommend 10 to 15 repetitions with 1-3 sets 2-3 days/week. This is similar to the recommendations for post-myocardial infarction patients and for healthy elderly individuals (43, 44). In a recent study by Andersen et al. (74) the importance of using appropriate training load to reach higher neuromuscular activation, than in more functional exercises, are highlighted. For healthy elderly, PRT with resistance loads of 80% of maximal strength or more has been used successfully (44, 46). Resistance training appears to be a safe and potentially beneficial form of exercise for the great majority of the population, even including categories of patients with neuromuscular disorders (75).

An important issue is the generalization of the positive effect of PRT in healthy young and old subjects to a population of post stroke patients, and possible adverse effects of using PRT after stroke. Even if the brain damage causes the weakness after stroke, it is evident that for some individuals there are components of muscular hypotrophy (20, 76-79). Many stroke patients have had some time of immobilization in the acute phase affecting strength in both lower limbs (14, 15). Signs of inactivity in stroke patients have been shown to be due to both dysfunction and by

disuse (62, 80). Therefore PRT could have potential effects on both the neuromuscular activation pattern and on the skeletal muscle structure, similar to the effects in healthy persons. Recently the effects of PRT in chronic post-stroke subjects have been evaluated (69-72, 81-85). These studies have shown positive outcomes on muscular strength but only a few have been randomized controlled studies (71, 72, 83, 84). In the new Swedish National Guidelines for Stroke Care (Swedish National Board of Health and Welfare) (3), physical activity training to improve mobility is recommended but no recommendations for strength training are given.

Independent walking is the ultimate goal for many post-stroke patients (23) and is one of the important domains of activities and participation in ICF core set for stroke (86). Despite that post-stroke weakness negatively affects gait performance, little is known about the type of training that would be most beneficial for stroke patients. Saunders et al. (60) reported that the available outcome data suggested that cardio-respiratory training improves walking ability (mobility). The effects of physiotherapy treatments on functional outcomes have also been addressed in a recent review by van Peppen et al. (87). Strong evidence was found in favour of task-oriented exercise training, to restore gait performance and for strengthening the lower limb. However in the new guidelines for stroke from the Swedish National Board of Health and Welfare (3) it is concluded that there is low evidence that one treatment mode is more beneficial than another in training of motor ability.

Outcome measurements

In rehabilitation it is important to be able to evaluate the effects from a treatment. When choosing a measurement tool it is important that this is valid and reliable and that the measurement tools used address the different aspects of health (21). For example, even if the primary effect of strength training is that it really affects muscle strength, it is important that an improved strength positively affects also activity and participation.

Measurements of muscle strength in the lower limb often include the knee muscles. After stroke there are indications that knee muscle

strength is an important muscle for mobility (88). Strength measurements from different joints in the lower limb post-stroke are furthermore significantly correlated indicating that weakness in one muscle group, will reflect weakness in other muscle groups of the lower limb (89).

There are several methods to assess muscle strength post stroke (90). Previously the most commonly used measurement for muscle strength has been the 0-5 ordinal scale (Medical Research Council grades (63)). This method does not give completely objective measurements and is most appropriate in subjects with comprehensively reduced muscle strength. For subjects able to perform an isolated movement against gravity, other quantifiable tools could be used (91, 92). The most common form of dynamic strength measurement is the 1-repetition maximum (1RM), the greatest resistance that could be moved through the full range of motion in a controlled manner. Multiple RM can also be used as a measure of strength, e.g. the 6RM, that is the load that can be repeated 6 times but not more (43). Isometric and isokinetic strength can also be measured using a dynamometer at different velocities and modes i.e., concentric or eccentric.

Spasticity, one component of the upper motor syndrome, is described as a velocity dependent resistance to passive movement. Today there is evidence to demonstrate that muscle tone is not only dependent of the upper motor syndrome, but involves changes in the passive mechanical properties of the muscle-tendon complex (34, 93). To test muscle tone different scales have been used (94, 95), biomechanical techniques such as the pendulum test (96), and the relationship between muscle EMG and reflex activity (97). In the clinic the most commonly used measurement of muscle tone is the Modified Ashworth scale (MAS) (95) measuring resistance to passive movement. However, resistance to passive movement is not only offered by hypertonus in spastic muscles (98).

There are several instruments for assessing gait performance (90, 99-101). If the overall gait performance is to be evaluated, gait speed has shown to be an excellent outcome measurement (102), and gait speed is an important variable when evaluating asymmetry in gait (103). The most commonly used gait performance tests assess fast and comfortable

gait speed (90), but also endurance like the 6- or 12-minutes walk are often used in the clinic (104, 105). One gait measurement that includes more complex movements is the Timed "Up & Go" test (TUG) (106) and tests of stair climbing performance commonly used as functional measurements tools (107, 108). A more analytic assessment of gait that involves observations of changes in symmetry and joint movements of the lower limb before and after an intervention have been used (103, 109).

Evaluations of the domain of participation are relatively new to the literature. Previous evaluations of handicap and quality of life have contained various global outcome measurements such as the Human Activity Profile (69), Physical Scale for the Elderly (85) or Late-life Function and Disability Instrument (84). These measurements include some aspects of participation but none fully cover the new approach in the ICF domain (21). A new stroke specific outcome measurement tool – the Stroke Impact Scale (SIS) (110, 111) – has been developed to describe the consequences of stroke. This scale evaluates several domains that are affected by stroke and includes the domain of participation. As the participation domain can be analysed separately it can be used to assess changes following an intervention.

Reliability

Reliability refers to the reproducibility or repeatability of values of a test, in repeated trials on the same individuals (112). To evaluate the effects on a patient following an intervention, reliable measurement tools – both equipment and methods – are needed. Reliability is a broad concept that incorporates the agreement between measurements, the presence of systematic changes in the mean and the size of the measurement error (113). To be reliable a measurement has to be stable over time and sensitive enough to detect a clinically important change. An important aspect is the calculation of limits for the range of 'measurement noise': measurements either for a group of individuals or for a single individual outside these limits would indicate the possibility of, for example, a clinical (possibly important) change after intervention.

The most common approach to assess reliability is to measure a group of subjects, comparable with those for whom the intervention is intended, on two test sessions (a test-retest study) (114, 115). Reliability can be determined for both continuous data and ordinal data by using different statistical methods (116). In recent years there is general agreement that a comprehensive set of statistics have to be used to evaluate reliability (112, 117-119).

Several measurement tools for isokinetic muscle strength in the lower limb and gait performance have been evaluated for intra-rater reliability in post-stroke subjects (31, 99, 106, 120-129). Even if some of the tests were found to be reliable, the statistical analyses were not sufficiently comprehensive for the calculation of credible limits that would indicate clinically important changes following an intervention.

The most commonly used measurement tools of muscle tone (MAS) have been evaluated for reliability and found to be reliable with the best reliability for mild spasticity and when the test-retest was rated by the same assessor (130-132). To evaluate the domain of participation the outcome measurement tool SIS can be used. This scale has been tested and found reliable with low floor and ceiling effects (133, 134).

The rationale for this thesis

More than five years ago, when discussions about the design of these studies started, our main objective was to evaluate the effects of PRT in chronic post-stroke, independent walkers with mild to moderate hemiparesis. Before starting an intervention study, however, the reliability for different outcome measurements for strength and gait performance had to be evaluated. Even if some measurements had been analysed for reliability the analyses were insufficient and had not included calculations for measurement error for post-stroke subjects (99, 106, 109, 121-128, 135, 136). Also, the relationship between knee muscle strength and walking ability had been investigated in several previous studies but the results were not clear (31, 32, 88, 96, 137-140).

As the term participation had recently replaced the term handicap in the ICF (21) there was very limited knowledge of the relation between participation and other components in the ICF. Therefore, the

relationships between the different outcome measurements had to be analysed: how much of the variance in gait performance could be explained by knee muscle strength, and how much of perceived participation could be explained by gait performance? This would provide an estimate of the extent by which an increase in knee muscle strength might improve activity and participation.

With this background a general aim and a set of specific aims were developed.

Objectives

General aim

The overall aim of this thesis was to evaluate the effects of progressive resistance training (PRT) on muscle function, gait performance and perceived participation in subjects with mild to moderate chronic post-stroke hemiparesis.

Specific aims

- Can knee muscle strength and gait performance be reliably measured?
- How large must a change be to assure a real clinical change after an intervention, for knee muscle strength and gait performance, for a group of individuals and for a single person?
- Are there any relationships between knee muscle strength and gait performance and between gait performance and perceived participation, indicating possible gains if muscle strength is increased?
- Can PRT improve knee muscle strength in subjects with mild to moderate hemiparesis after stroke and are there any adverse effects?
- If PRT improves knee muscle strength does this improvement have an effect on gait performance and perceived participation?

Design of the studies

The design of the four papers in this thesis are summarised in Table 1.

Table 1. The design of the four papers

Paper	Design	Outcome measurements	Statistical evaluations
Paper I	An intra-rater test-retest reliability study	Knee muscle strength: isokinetic concentric extension and flexion at 60º/s and 120º/s, and eccentric extension at 60º/s	The intraclass correlation coefficient ($ICC_{2,1}$), the Bland & Altman analyses, the standard error of measurement (SEM and SEM%) and the smallest real difference (SRD and SRD%)
Paper II	An intra-rater test-retest reliability study	Gait performance tests: TUG, CGS, FGS, SCas, SCde	The intraclass correlation coefficient ($ICC_{2,1}$), Pearson's correlation coefficient, the Bland & Altman analyses, the standard error of measurement (SEM and SEM%) and the smallest real difference (SRD and SRD%)
Paper III	Descriptive analysis	Knee muscle strength: isokinetic, concentric at 60º/s. Gait performance tests: TUG, CGS, FGS, SCas, SCde and 6MW. SIS participation	T-test for independent groups, stepwise multiple regression analyses, Pearson's correlation coefficient, Q-Q plots and Kolmogorov-Smirnov tests
Paper IV	A single-blind, randomised controlled intervention study	Knee muscle strength: dynamic and isokinetic, concentric at 60º/s knee. Spasticity by MAS. Gait performance tests: TUG, FGS and 6MW. SIS participation.	Fishers exact test, t-test for independent and paired groups, Mann-Whitney U test, Wilcoxon's sign rank test, Pearson's correlation coefficient, Kolmogorov-Smirnov test

Reliability

The first two objectives were covered in papers I and II using an intra-rater test-retest design. The same physiotherapist supervised the sessions which were one week apart.

The intraclass correlation coefficient ($ICC_{2,1}$) and Pearson's r were calculated (141). The 'Bland & Altman analyses' were applied to identify, and to evaluate, systematic changes in the mean and the 'Bland & Altman graphs' were formed to visualize the variations in the differences of the measurements about zero (114, 115). The limits for the measurement error were calculated, the SEM% and the SRD%, which are to be used to indicate when the results from repeated measurements lie outside the range for measurement noise for a group or for a single individual, respectively (116, 142).

Relationships between different domains of health

The third objective, reported in paper III, was addressed by identifying firstly the relationships between knee muscle strength and gait performance, and secondly the relationships between gait performance and perceived participation. To determine these relations and the possible influence of other factors not related to knee muscle strength (sex, age, time since stroke onset and side of weakness) stepwise multiple regression analyses were performed (116).

Effects of progressive resistance training

The fourth and fifth objectives were investigated in paper IV, using a single-blinded randomized controlled trial design (stratified by sex, ratio training/control 2:1). The effects from 10 weeks of PRT (6-8 repetitions, equivalent to a load of approximately 80% of 1RM, 2 sets, twice weekly) of the knee extensor and flexor muscles were evaluated by comparing the results from the outcome measurements before and after for dynamic (isotonic) and isokinetic concentric knee muscle strength, muscle tone, gait performance and perceived participation.

Subjects

A summary of the characteristics of the subjects in the four papers are presented in Table 2.

Paper I-III

The inclusion criteria were: i) a minimum of 6 months and a maximum of 48 months post-stroke (only cortical/subcortical); ii) residual hemiparesis at discharge from interdisciplinary rehabilitation services; iii) at the time of the study no medication, cognitive dysfunction, neglect, visual deficit, depression, or other physical or mental diseases that could impact upon knee muscle strength, gait performance or perceived participation; iv) able to understand both verbal and written information; and v) able to walk without supervision at least 300 m with or without a unilateral assistive device.

All subjects in paper I-III had been treated in the Department of Rehabilitation Lund University hospital during the period 2000-2002. A total of 59 potential subjects were identified. From these, 50 subjects (38 men and 12 women) met the inclusion criteria and gave informed consent to participate in the studies. The sex ratio reflects the number of men and women admitted to the Comprehensive Integrated Rehabilitation Unit during the period 2000-2002 (122 men and 48 women).

Paper IV

The inclusion criteria used in paper I-III were slightly modified. To assure that all subjects had a post-stroke weakness the minor level for weakness was set at 15% reduction of strength (isokinetic mean peak torque at 60°/s) as smaller strength differences could be attributed to the measurement error (143). Subjects able to walk at least 200 m were also accepted. All subjects for paper IV were recruited from the two University hospitals in the south of Sweden. From 133 potential subjects, 25 subjects were interested in participating and met the inclusion criteria (22 % of the potential subjects for the women and 17% for the men). There was one drop-out in the training group, not due to PRT.

The flow chart and test steps for paper IV are illustrated in Figure 1.

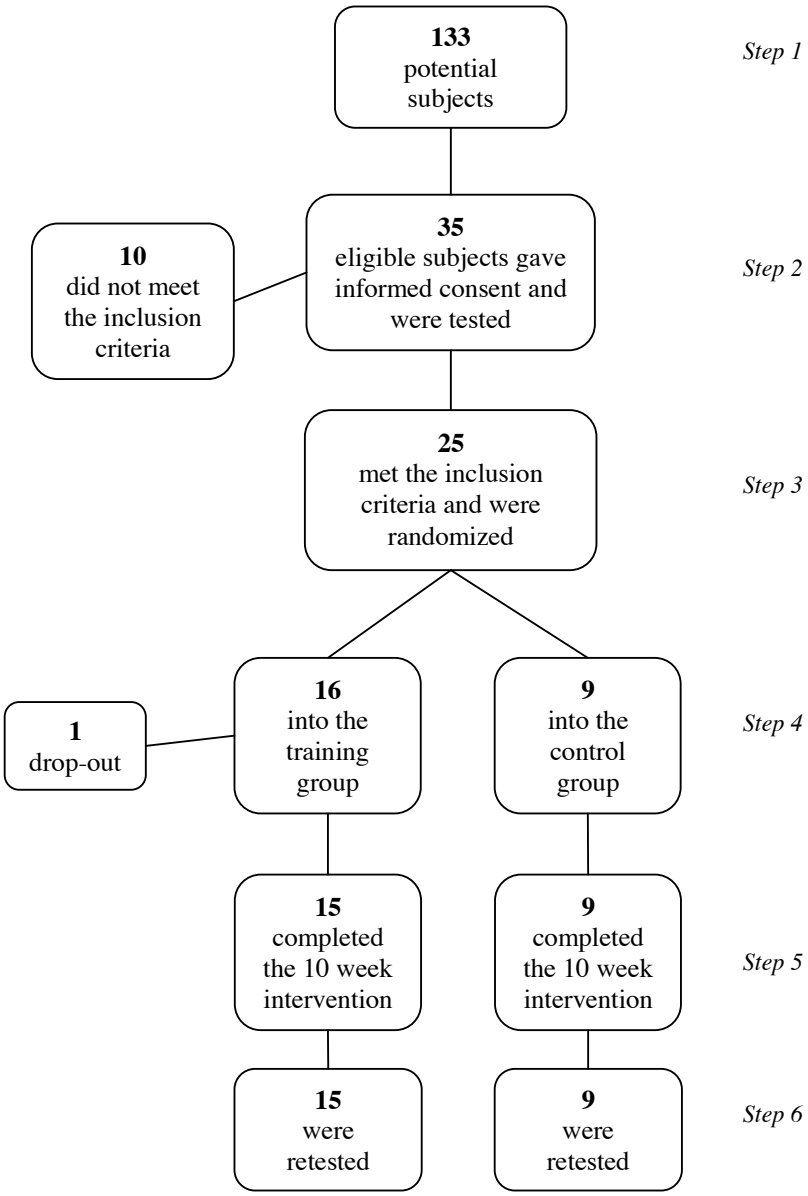

Figure 1. *Study flow chart.*

- *Step 1:* From the 133 potential subjects contacted (84 men and 49 women, mean age 62 (44-70) years), 78 did not meet the inclusion criteria (43 too strong, 13 too weak, 22 medical reasons) and 20 were not interested.
- *Step 2:* The remaining 35 subjects gave informed consent and were tested for muscle tone, gait performance, perceived participation and isokinetic knee muscle strength. From these subjects, 10 did not meet the inclusion criteria (4 too strong, 1 too weak, 5 medical reasons)
- *Step 3:* The 25 subjects that fulfilled the inclusion criteria were stratified by sex, and randomized into either a training group (n=16) or a control group (n=9)
- *Step 4:* Dynamic strength was tested before the start of the intervention.
- *Step 5:* The training group participated in 10 weeks of PRT (in this group there was one drop-out) and the control group continued their usual activities and training at home. During the last two weeks of the intervention the dynamic strength was retested.
- *Step 6:* The measurements for isokinetic strength, muscle tone, gait performance and perceived participation were repeated directly after the ten weeks intervention.

Table 2. Summary of the characteristics of the subjects in paper I-IV

	Numbers (men/ women)	Mean age (years)	Time since stroke (months)	Subjects with infarct (n)	Subjects using walking aid (n)	Subjects with left side paresis (n)
Paper I-III	50 (38/12)	58 ±6 (46-72)	17 ±9 (6-46)	37 (74%)	11 (22%)	30 (60%)
Paper IV	24 (14/10)	61 ±5 (53-70)	19 ±9 (7-48)	18 (75%)	7 (29%)	15 (62%)

Outcome measurements

Isokinetic strength

Isokinetic strength measurements were performed on a Biodex dynamometer (Figure 2). In papers I and III the Biodex Multi-Joint System II with the Biodex Advantage software version 4.0 was used, and in Paper IV the Biodex® Multi-Joint System 3 PRO dynamometer was used. There were no changes in performing the tests the differences between the two systems were in the developed software. The same test protocol, instructions and warm-up was used in the test session to ensure similar conditions for the different measurements. Before testing each day the equipment was calibrated. The subjects were positioned in the seat, with back support and hip flexion 85°. The subjects were

Figure 2. *Isokinetic knee muscle strength measurement, performed in a Biodex dynamometer.*

firmly stabilized with straps across the shoulders, waist and thigh. The ankle cuff of the lever arm was strapped 3 cm proximal to the malleoli of the tested limb. Before each measurement the full range of motion (ROM) was set. To account for the influence of the gravity effect torque on the data, each subject's lower limb was weighed and the Biodex software corrected the data, and the subject's knee joint was adjusted to the movement axis of the dynamometer.

After a structured warm-up, each subject performed different sets of maximal isokinetic contractions starting with concentric extension and flexion, and if eccentric extension was measured (paper I) it was the final test. There was a minimum of 2 minutes rest between each measurement. For each mode the testing started with the non-paretic lower limb, followed by the paretic lower limb. The best muscle contraction for extension and for flexion, for each mode and velocity, was recorded as the peak torque. Throughout the tests, subjects sat with folded arms and were verbally encouraged to push and to pull as hard and as fast as possible.

In the reliability study (paper I) different modes and velocities were used according to recommendations from Dvir 1995 (92), to find the most appropriate isokinetic measurements for evaluation of the PRT intervention. The measurements tested in paper I were: isokinetic concentric knee extension and flexion movements at two velocities (60°/s and at 120°/s) followed by eccentric knee extension at 60°/s. Even if all strength measurements were found to be highly reliable there were difficulties for some subjects to performe at higher velocities (120°/s) and in the eccentric mode. The isokinetic concentric knee extension and flexion movement at 60°/s were therefore chosen as the outcome measurements of isokinetic strength in papers III and IV.

Dynamic strength

In paper IV, dynamic strength was used as an additional measure of knee muscle strength. The measurements of dynamic strength were performed at a separate test-session before the intervention. A pneumatic resistance exercise machine (HUR; see Figure 3) (144), giving resistance on both the concentric and eccentric movements was used.

For knee extension and knee flexion, the range of motion and the maximal load were determined for each subject, in their paretic and non-paretic lower limbs. The load that could be moved through a comfortable range of motion six times but not more than eight times was considered equivalent to 80% of the maximum load. Each value was used to set the training load and as the baseline value in the evaluation of the intervention. Even if dynamic strength traditionally is assessed with the 1RM, the greatest resistance that can be moved through the full range of motion, multiple RMs – for example, 4RM or 8RM – have been used as a measure of muscular strength. This allows an integrated evaluation in the training program and the true 1RM need not be estimated (43). The values from the multiple RM, calculated in Newton meters (Nm), were used to evaluate dynamic muscle strength and to set the training load at the start of the PRT.

Figure 3. *Dynamic strength measurement performed in a pneumatic resistance exercise machine.*

Muscle tone

To assess muscle tone the modified Ashworth scale (MAS) was used (94, 95). The MAS is a 6-point rating scale, ranging from 0 (no increase in tone, both low and normal tone) to 5 (the limb is rigid in flexion or extension). The subject was lying in a supine position without shoes and the paretic lower limb was moved passively and quickly, 3-4 times in succession. The tested muscle groups were: hip adductors, hip extensors and flexors, knee extensors and flexors and ankle dorsiflexors and plantar flexors. As only the paretic lower limb was tested, the maximum score was 35. The outcomes from the MAS were used as a pre-test assessment to characterize the subjects in paper I-II and in paper IV

before and after the intervention to evaluate any effect from PRT on muscle tone.

Gait performance

In paper II the reliability of several gait performance tests was assessed. All these tests have been used in healthy elderly subjects (145, 146) and for the assessment of gait performance after stroke (90, 99-101). However, many tests are fairly extensive, time consuming or require sophisticated laboratory equipment. The six gait performance tests evaluated in paper II were selected because they were easy to administer and meaningful to the patients. As these tests cover different aspects of gait performance, such as velocity, endurance and the complexity of gait, they provide a comprehensive picture of walking capacity after stroke. A more analytic assessment of gait performance might have been useful to assess changes in gait pattern which might to some extent explain changes in gait speed.

All tests followed a structured protocol to assure that the same verbal command and rest time between the different tests were used, at the different test sessions. All subjects wore comfortable shoes and were, if needed, allowed to use their ankle-foot orthosis and assistive device. No verbal encouragement was given during these tests. A digital stopwatch with an accuracy of one decimal figure in units of 1 sec was used to measure time.

Figure 4. *TUG, one of the gait performance tests.*

TUG is a test commonly used in frail elderly and post-stroke patients (106). We used the original design and instructed the subjects to walk at a comfortable speed, 'like fetching something in your kitchen' (Figure 4). The TUG is a complex gait

measurement including both the ability to raise and sit down from a chair, walking 3 m and turning around. The subjects made a pre-trial to become familiar with the test and then performed the TUG twice, with one minute between each trial. The mean time in seconds from these two trials was used in the analysis.

For gait velocity both comfortable gait speed (CGS) and fast gait speed (FGS) were tested. A 14 m distance was marked and the time taken to walk the middle 10 m was recorded. These tests were each done three times, with 30 seconds between. The mean time was calculated for each of the two tests, and used in the analyses. The velocity in metres per second was calculated to make it easier to compare with results from other studies.

The ability to climb stairs, both ascend (SCas) and descend (SCde) was measured by using an ordinary stair with 12 steps (each step was 15 cm high). The subjects performed both ascend and descend stair climb two times, with 30 seconds in between. The mean time was calculated and used in the analyses.

To evaluate the aspect of endurance in gait performance the 6-minute walk test (6MW) was used. The test was conducted in a corridor in a quiet part of the hospital. There were two marks on the floor with 30 m in between. The subjects were instructed to walk the 30 m and after passing either mark they were told to return and walk back. They were instructed 'to walk as far as possible during six minutes' and they were allowed to rest and then to continue walking, if there was any time left. This test was done once and the distance was recorded to the nearest meter.

The gait performance tests started with the 'comfortable speed' tests such as TUG and CGS and ended with the endurance test (6MW). The resting time between trials and tests (varying from 30 seconds to 5 minutes) was regarded long enough for recovery.

In paper III the results from all these 6 gait performance tests were related to concentric knee muscle strength and to perceived participation. In paper IV only three of the tests were used (TUG, FGS and 6MW). They were chosen as they were reliable, sensitive to changes, significantly related to paretic knee muscle strength and participation,

and covered different aspects of gait performance. As the subject should perform both gait performance tests and isokinetic strength measurements in the same test session three gait performance tests were regarded as sufficient.

Perceived participation

In papers III and IV perceived participation was assessed by Stroke Impact Scale 3.0 (SIS; Swedish version) (111). SIS is a self-report questionnaire that assesses eight aspects of the impact of stroke on an individual's self-perceived health with one domain addressing perceived participation. SIS is administered by a medical professional in an interview (Figure 5). All items are scored on a 5-grade scale from 5 (limited none of the time) to 1 (limited all of the time). The mean for each domain is calculated and can be analysed separately. SIS has been shown to be both valid and reliable (111, 133, 147).

As the relationship between gait performance and perceived participation was of specific interest, only the data from the SIS Participation domain were used. SIS Participation addresses the impact of stroke on: work; social activities; quiet recreations; active recreations; role as a family member; religious activities; life control; and ability to help others. For each subject, the mean score of these eight items was calculated as a composite score and converted into a percentage value which yields a value lying in the range 0 to 100, according to Duncan et al. (110). High values represent no or low restriction in participation whereas low values indicate more restricted participation.

Figure 5. *The SIS interview.*

Statistics

All calculations were performed using the SPSS 11.0 Software for Windows. Significance levels exceeding 0.05 were considered statistically not significant.

Reliability statistics

Several statistical methods are required to fully assess the reliability of a measurement tool (118). This includes assessments of retest correlation coefficients, changes in the mean, measurements variability and limits for clinically important changes following an intervention. In paper I and II a comprehensive set of reliability statistics was performed. Firstly the agreement between two measurements was addressed by calculating the intraclass correlation coefficient (ICC) (141). The $ICC_{2,1}$ was used as this form is applicable when all subjects are tested twice by the same rater.

The possibility of systematic changes in the mean was assessed with the 'Bland & Altman analyses' (114, 115). These calculations include the changes in the mean of a measurement ($\bar{d}$ = the mean difference between the two test sessions) and the standard deviation of the $\bar{d}$, used to calculate the 95% confidence interval (CI) of the $\bar{d}$. If zero is within this interval there is no systematic bias. The difference between test sessions 2 and 1 (2 minus 1) was plotted against the mean of the two test sessions for each subject: these are commonly called the 'Bland & Altman graphs'. These graphs illustrate systematic variations around the zero line, heteroscedasticity – a wider spread when the mean values are larger or lower – and possible outliers. The possibility of heteroscedasticity was addressed by forming the Pearson's correlation coefficient of the absolute differences between test sessions 2 and 1 and the means of the two test sessions (116).

To ascertain whether or not the measurements were sufficiently sensitive to detect change after an intervention the limits for the measurement error were calculated. The measurement error indicates when the results from a repeated measurement are outside the measurements noise for a group respectively for a single individual. The SEM (116) is calculated as the square root of the within subject mean square error from the analysis of variance. A percentage value, independent of the units of

measurements can be calculated by dividing the SEM by the mean of all measurements and multiply by 100, giving the percentage value which is more easily interpreted. This SEM% indicates the typical variation for a group of subjects and can be used to interpret the results after an intervention. A way of evaluate clinically important change for an individual is to calculate the SRD (1.96 x SEM x√2), introduced by Beckerman et al. (142). As for the SEM the SRD can be divided by the mean of the measurements and multiplied with 100, to give a percentage value SRD% (118) indicating a 'typical variation' for a single individual.

Statistical evaluation

Different statistical methods were used in papers III and IV (116). The independent sample t-test, the Fishers exact test and the Mann-Whitney U-test were appropriate for comparing groups. When the same group was assessed twice, repeated measurements were compared using the paired t-test and Wilcoxon's sign rank test. Correlations between different variables were illustrated by forming scatter-plots and tested with the Pearson's correlation coefficients (r). To determine relationships between different independent factors, stepwise multiple regression analyses were performed. Normality was addressed in scatter-plots, in Q-Q plots and One-Sample Kolmogorov-Smirnov tests.

Ethical considerations

The subjects in paper I to III were selected from the databases of the Department of Rehabilitation, Lund University Hospital. In paper IV potential subjects were selected from the databases from two university hospitals in the south of Sweden. All subjects were first contacted by a professional from their own clinic. The purposes of the studies were described, and those subjects expressing an interest in participating were given further information both verbal and written about the test procedures and for paper IV the training procedures. Before the first test session, all subjects completed a questionnaire giving demographic and medical information, gave written informed consent and were medically checked by the responsible physician. All subjects were informed about their right to leave the study at any time without giving any reason.

In paper IV all subjects were at the first test session again informed about the randomization procedure, and that they might not be randomized to the strength training group. All subjects participating in the study were interested in strength training, expressing an expectation that the training should improve their muscular strength. Some subjects randomized to the control group expressed disappointment, although they were aware of the randomization process. All subjects in the control group were encouraged to continue their training at home, received advice about suitable forms of physical activities and were informed that all activities except PRT could be performed during the intervention. During the intervention the subjects in the control group were all contacted by phone 2-3 times and they came back twice to test dynamic strength and for an interview about their home training activities and treatments during the intervention.

The risk of increased tonus or any injury due to PRT was considered. Even if post-stroke subjects previously have been advised not to participate in PRT due to the risk of increase muscle tonus there were several new studies indicating that muscle tone does not increase due to PRT (66-72). There are also recent findings that spasticity is present in a minority of hemiparetic post-stroke subject and rare in those with mild to moderate disability (148). Mechanical changes in muscle or other soft tissue can also influence the resistance to passive movement (65). Because of these factors, strict recommendations for warm up for all the testing and training protocols were followed (43). During the PRT the resistance for each subject was gradually increased: the subjects did a larger number of repetitions at each training session and the resistance was increased every second week. After each training session the trained muscles were also stretched using a static technique, recommended as being an effective technique to promote the maintenance of flexibility with low risk of injury (43).

The studies were approved by the Ethics Research Committee of Lund University, Lund, Sweden (LU 234-01 and Dnr H4 163/2005).

Results and discussion

In Table 3 a summary of the results from the first test-session for all subjects in paper I-III and paper IV are presented

Table 3. Summary of the measurements from the first test sessions

	Paper I –III (n=50)			**Paper IV** (n=24)		
Test	Mean	SD	Range	Mean	SD	Range
Knee muscle strength; isokinetic, concentric (Nm)						
Extension at 60°/s						
Non-paretic	131.2	42.5	60-239	119.4	38.6	64-203
Paretic	86.9	40.3	8-193	62.1	32.1	22-144
Flexion at 60°/s						
Non-paretic	68.6	27.0	13-141	54.7	21.3	25-114
Paretic	41.2	25.1	8-109	15.6	17.5	0-59
Gait performance						
Timed Up & Go (s)	14.3	5.2	7.5-25.7	28.0	14.1	10.9-55.3
Fast Gait Speed (m/s)	1.34	0.5	0.5-2.2	0.81	0.46	0.2-1.6
6-Minute Walk (m)	384	132	122-606	230	133	60-434
Participation						
SIS participation	76.2	18.4	34-100	56.8	20.5	25-97

Reliability

The results showed that in chronic post-stroke subjects with mild to moderate weakness isokinetic knee muscle strength and gait performance can be reliably measured. The tests can be used to detect changes following an intervention for a group. The data for all the gait performance tests are highly related and appear sensitive enough to detect changes in an individual subject. However, for the isokinetic dynamometry only the extension measurements are sensitive enough to detect individual changes. The reliability results of paper I-II are summarised in Table 4 and Table 5.

Three main factors influence the reliability of a test: the tested subject, the sample size and the test protocol. The subjects included in these studies had all recovered well after their stroke but were still restricted by their hemiparesis. The results from these studies are therefore primarily representative for fairly active post-stroke individuals. A reliability study is influenced by the sample size of the group tested. It has been recommended that in test re-test studies the sample size should be at least 30 and preferably 50 (112, 149). As a general principle the larger the sample size of test re-test reliability studies the more compelling is the argument for extrapolating the measurement tool to a given population. The test protocol can also have several sources of error. These have to be recognised and their effects reduced to optimize reliability. In these studies all tests and test protocols were strictly standardised and the protocols were carefully followed.

Even if all isokinetic strength measurements were reliable and can be used to detect changes that indicate a real improvement for a group, there are some restrictions. Two subjects were not able to perform concentric knee flexion at higher velocity and six could not perform the eccentric knee extension measurements. This means that concentric measurements at lower velocities might be preferred as an outcome measurement of isokinetic knee muscle strength. Furthermore, the measurements of flexion movements might be insufficiently sensitive to allow the detection of changes for an individual subject. For the gait performance all tests were reliable with the best sensitivity for identifying changes for FGS and 6MW. This indicates the usefulness of

the gait performance tests, as they can be used to evaluate changes for both a group and an individual subject after intervention.

Table 4. Isokinetic knee muscle strength; Nm (n=50)

Test	ICC $_{2,1}$	SEM%	SRD%
Concentric knee muscle strength			
Extension at 60°/s			
Non-paretic	0.92	9	26
Paretic	0.94	12	33
Flexion at 60°/s			
Non-paretic	0.89	14	39
Paretic	0.92	17	48
Extension at 120°/s			
Non-paretic	0.93	10	27
Paretic [a]	0.95	11	31
Flexion at 120°/s			
Non-paretic	0.89	9	42
Paretic [a]	0.93	6	55
Eccentric knee muscle strength			
Extension at 60°/s			
Non-paretic [b]	0.96	8	22
Paretic [b]	0.95	9	25

[a] n=48; [b] n=44;
ICC Intraclass Correlation Coefficient; SEM Standard Error of the Measurement; SRD Smallest Real Difference.

Table 5. Gait performance tests (n=50)

Test	ICC $_{2,1}$	SEM%	SRD%
Gait performance			
Timed Up & Go (s)	0.96	8	23
Gait Speed (m/s)			
Comfortable	0.94	8	22
Fast	0.97	6	16
Stair Climbing (s)			
Ascend	0.98	7	18
Descend	0.98	8	23
6-Minute Walk (m)	0.99	5	13

ICC Intraclass Correlation Coefficient; SEM Standard Error of the Measurement; SRD Smallest Real Difference.

Relationships between different domains of health

The results from paper III showed that all correlations between isokinetic concentric knee muscle strength in the paretic limb and gait performance were significantly related ($p<.01$), with no significant correlations between gait performance and knee muscle strength in the non-paretic limb (Table 6). Knee muscle strength in the paretic limb explained up to 50% of the variance in gait performance, with very similar values for knee extension and knee flexion strength. When knee muscle strength in the paretic and non-paretic lower limbs was combined, strength in the non-paretic limb contributed up to 11% (eight of the twelve analyses), but together they explained at most 51% of variance in gait performance.

In this study gait performance and perceived participation was found to be significantly related post-stroke and gait performance could explain up to 40% of the variance in perceived participation (Figure 6). There were only small differences between the results for the different gait performance

Table 6. Correlation between the gait performance tests and the isokinetic knee muscle strength measurements (r), and the results from the linear regression analyses (R^2)

	TUG	CGF	FGS	SCas	SCde	6MW
Extension 60°/s						
Paretic	-0.65**	0.61**	0.67**	-0.58**	-0.61**	0.70**
Non-paretic	-0.14	0.12	0.19	-0.07	-0.13	0.26
Paretic (R^2)	0.42	0.37	0.44	0.34	0.38	0.49
Paretic and non-paretic (R^2)	0.51	0.46	0.50	0.45	0.46	-
Flexion 60°/s						
Paretic (r)	-0.64**	0.61**	0.65**	-0.61**	-0.61**	0.71**
Non-paretic (r)	-0.15	0.09	0.15	-0.06	-0.10	0.25
Paretic (R^2)	0.42	0.37	0.42	0.37	0.37	0.50
Paretic and non-paretic (R^2)	-	0.42	-	0.44	0.42	-

** $p<0.01$

TUG, Timed-up-and-Go; CGS, Comfortable Gait Speed; FGS, Fast Gait Speed; SCas Stair Climbing ascent; SCde, Stair Climbing descent; 6MW, 6-Minutes Walk.

tests: even though they measure different aspects of walking ability, the six gait performance tests are strongly related. When other independent variables (sex, age, time since stroke onset, type of stroke and side of weakness) were added in the multiple regression analyses, increasing age contributed, although to a small degree, to the explanation of both gait performance and SIS Participation.

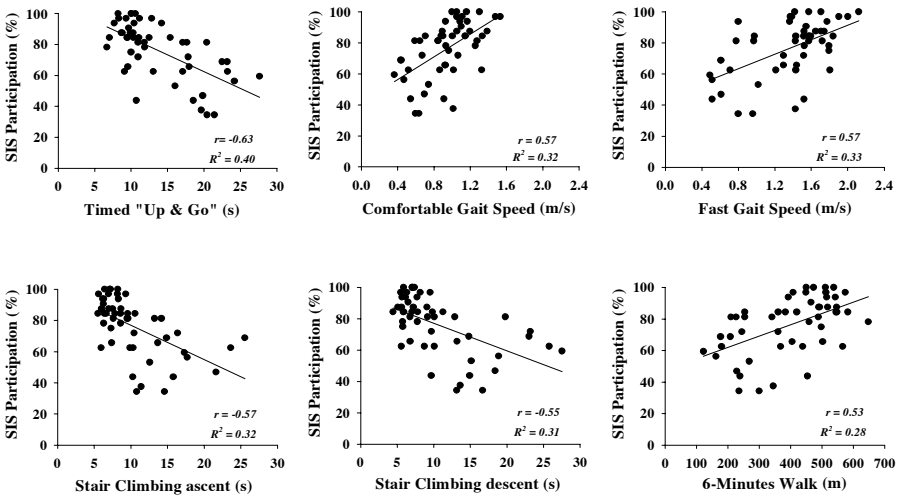

Figure 6. *The relation between SIS participation and gait performance. A better gait performance corresponded to higher SIS values (p<0.01)*

Our results confirm the general contention that knee muscle strength is positively related to walking ability after stroke. The lack of relationship between knee muscle strength in the non-paretic lower limb and gait performance indicates that strength in the non-affected lower limb post-stroke is much less important for the walking ability than strength of the affected lower limb. The measurements of knee muscle strength and the assessments of gait performance used in this study were highly reliable and the sample size was, in our opinion, large enough for the conclusions drawn.

Gait performance and perceived participation post-stroke was found to be significantly related. To measure perceived participation we used SIS. It has been shown to have good internal consistency and validity, to be easy to administer and to cover several important aspects of social functioning. Only four subjects obtained the maximum score of 100 and no subject obtained the minimum score of 0, indicating low floor and ceiling effects for this group of stroke patients.

The results in this study imply that improvements in knee muscle strength following an intervention, such as progressive resistance

training, may partly affect gait performance and gait performance, in turn, may influence perceived participation but to a smaller degree.

Effects of progressive resistance training

The primary aim of paper IV was to assess the effect of PRT in subjects with chronic mild to moderate post-stroke hemiparesis on knee muscle function, dynamic and isokinetic muscle strength, and muscle tone. The second aim was to evaluate if changes in strength affect gait performance and if this in turn impacts on perceived participation.

Dynamic strength measurements and isokinetic concentric measurement at 60°/s, for both paretic and non-paretic knee extension and knee flexion, were significantly related both before and after the intervention ($r=0.76$ to $r=0.87$; $p<0.001$). For the training group, both the dynamic and isokinetic knee muscle strength increased significantly both for the paretic and the non-paretic lower limb after PRT. All percentage differences for isokinetic strength exceeded the SEM% values indicating a real clinical improvement (Table 7). For the control group, only the non-paretic lower limb increased significantly in dynamic strength. For each of the four measurements, the increase in dynamic strength was significantly greater for the training group than for the control group ($p<0.001$). The increase in the isokinetic strength of the non-paretic lower limb was significantly greater for the training group than for the control group ($p=0.049$ for flexion; $p=0.050$ for extension), but there were no significant differences between the two groups for the paretic leg.

There were no negative effects from PRT: that is, there were no injuries and muscle tone was significantly lower after the intervention for both the training group (median 1, 0/7; $p=0.005$) and for the control group (median 1, 0/4; $p=0.017$). For the training group, the ratio between the strength of the flexor and extensor muscles in the paretic lower limb increased after the intervention, for both dynamic and isokinetic knee muscle strength ($p= 0.052$ and $p= 0.016$), indicating that the flexors had improved relatively more than the extensors. The increases in dynamic strength and the baseline values were not related. However, the increases in isokinetic strength for non-paretic extension were related to the

baseline values in the training group and the increases in paretic flexion strength were related to the baseline values in the control group.

Table 7. Changes after PRT for knee muscle strength measurements, gait performance and perceived participation

	Training group (n=15)		Control group (n=9)			Between groups
Test	Diff	Sign	Diff	Sign	***SEM%***	Sign
Dynamic tests						
Extension						
Non-paretic	+44%	p<0.001	+8%	p=0.034		p<0.001
Paretic	+54%	p<0.001	+3%	p=0.482		p<0.001
Flexion						
Non-paretic	+40%	p<0.001	+9%	p=0.003		p<0.001
Paretic	+70%	p<0.001	+5%	p=0.087		p<0.001
Isokinetic tests						
Extension						
Non-paretic	+14%	p=0.008	-1%	p=0.875	***9%***	p=0.045
Paretic	+21%	p=0.003	+0%	p=0.969	***12%***	p=0.304
Flexion						
Non-paretic	+21%	p=0.001	+5%	p=0.309	***14%***	p=0.050
Paretic	+64%	p=0.006	+21%	p=0.066	***17%***	p=0.412
Gait performance						
TUG (s)	+19%	p=0.001	+10%	p=0.001	***8%***	p=0.123
FGS (m/s)	+8%	p=0.044	+9%	p=0.056	***6%***	p=0.421
6MW (m)	+10%	p=0.007	+6%	p=0.054	***5%***	p=0.090
Perceived participation						
SIS (%)	+8%	p=0.205	-6 %	p=0.644		p=0.606

SEM Standard Error of the Measurement

This indicates that those performing less well at baseline improved more. There were no significant differences between men and women in the increase of knee muscle strength.

Furthermore even if dynamic strength measurements have not been evaluated for reliability, these measurements were significantly correlated to the isokinetic knee strength measurements at 60°/s. This indicates that measurements of dynamic strength can be used to assess knee muscle strength in chronic post-stroke subjects. The dynamic strength measurements are easy to perform and more expensive isokinetic dynamometers are not absolutely required.

After PRT the training group improved significantly in all gait performance tests and all percentage differences exceeded the SEM% values (Table 7). The percentage increases in FGS and 6MW were significantly related to their baseline values (Figure 7), but there were no relationship to the percentage improvement in strength. For the control group, there was a significant increase for TUG, but not for FGS or 6MW, but all percentage differences exceeded the SEM% values.

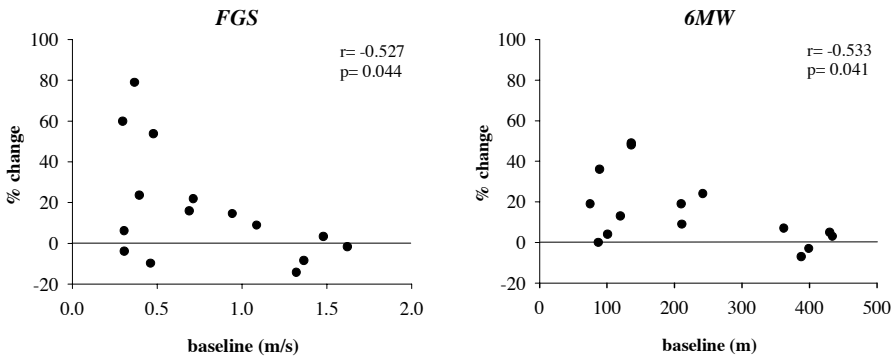

Figure 7. *The relationship between baseline values and percentage changes for fast gait speed (FGS) and six-minute walk (6MW) for subjects in the training group.*

For the training group improvements in perceived participation were significantly correlated to improvements in gait performance for FGS and 6MW (Figure 8).

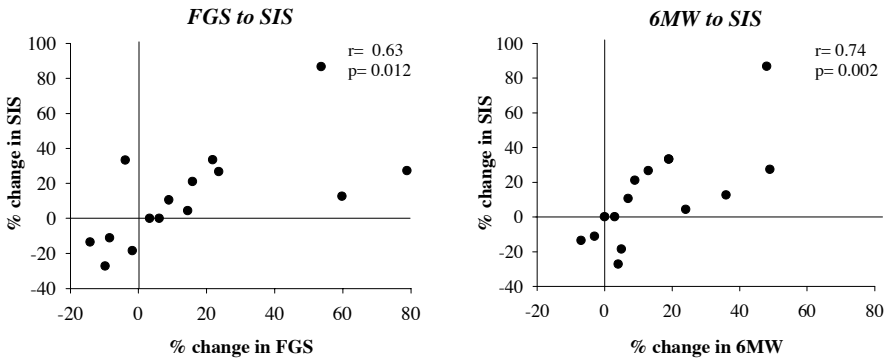

Figure 8*. The relationship between the percentage changes for fast gait speed (FGS) and six-minute walk (6MW) to Stroke Impact Scale (SIS) for the subjects in the training group.*

For the control group there was a significant improvement for TUG but all individual changes was below the SRD% indicating no real improvement for an individual subject (Figure 9). Furthermore for the control group, there were no significant relationships between changes in perceived participation and the gait performance tests.

This suggests that the best effect from PRT is seen in the slower walkers after stroke, compared with those who have regained more of their walking capacity. Similar findings have been reported after a functional exercise program post stroke (150). In older subjects the relationship between muscle strength and functional skills has been described as curvilinear with a threshold where strength is sufficient to perform the activity, and further improvements in strength will not lead to gains in activities (38, 45). During the intervention the subjects in the control group were encouraged to continue their previous functional training at home: five out of nine had supervised training by a physiotherapist during the intervention, which might have contributed to their improvement in gait performance.

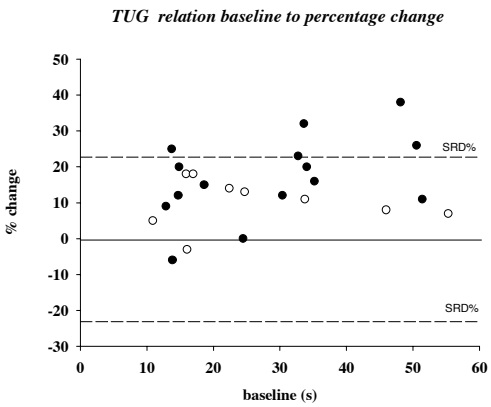

Figure 9. *For TUG the relationship between the baseline value and the percentage change after the PRT intervention are illustrated, filled circles for the training group and open circles for the control group.*

An interesting finding was that, even if there was no significant change in perceived participation at the group level (Table 7), there was a significant relationship between the percentage change in SIS and the increase in FGS and 6MW for the training group. This indicates that those improving most in gait performance perceived improved participation.

General discussion

During the course of this research several interesting questions have arisen: Can one generalise the positive effects of PRT for the population studied to all persons with chronic post-stroke weakness? Can PRT be planned and carried out in different manners? Have the most adequate outcome measurements been applied?

Post-stroke rehabilitation

During the acute stroke care, physiotherapy treatment aims at optimising motor function in order to improve performance of activities of daily living and to enable the patient to reach a higher degree of participation. In the chronic phase after stroke, all aspects of health have to be considered: a treatment should not only improve function but positively impact on activity and participation. Even if function improves, complete recovery in function is rare and more activity oriented goal setting will assist the physiotherapist to choose adequate interventions and to evaluate the outcome. Although rehabilitation process is generally confined to a time scale and achieved goals, further interventions are required. The subject should be encouraged to lead a reasonably active lifestyle to maintain the benefits from the rehabilitation period.

In the acute phase most post-stroke rehabilitation recourses are individually focused. In the later post-stroke rehabilitation phase an efficient way to treat post-stroke subjects could be to create exercise groups, giving individually supervised graded exercises to subjects with similar disability level. Several positive effects could be achieved using this approach (72, 151, 152). The encouragement from other subjects in the group supports the instructions and coaching from the physiotherapist (150). Furthermore, the social aspect of training should not be underestimated as it is important to achieve high attendance in the fitness training classes.

When a post-stroke subject becomes more independent, more health-related training groups supervised by qualified professionals should be considered. The objective for this training is the promotion of long term

physical fitness, comparable to training programs for the healthy elderly (153). This could be an important shift of emphasis for the planning of post-stroke intervention, moving from 'individual treatments' to more active participation in fitness training (154). However the planning of post-stroke fitness groups has to be supported by the health professionals and the health care system.

Strength training in chronic stroke

Could PRT be used as one important component for improving motor performance post-stroke? As there can be restrictions due to other medical problems than stroke, this has to be considered before the commencement of PRT. In our study the training effects from PRT appeared to be effective in chronic stroke patients, improving muscle strength regardless of the baseline level and without any adverse effect on muscle tone. Depending on the individual's baseline assessment, PRT could be targeted at various goals for chronic post-stroke subjects.

Firstly PRT can be used as a physiotherapy treatment for those with residual hemiparesis to improve strength and gait performance. In general, our results showed that improvements in strength following PRT improve gait performance, however not for all subjects. A slower walker had better gains from strength training, compared with those who could walk faster. In healthy elderly subjects it has been shown that those having a good level of physical activity, have few gains in general activities from further muscle strengthening. If muscle strength decreases, a larger proportion of the maximal capacity is used until the muscular capacity is no longer sufficient for the functional demand and the effects of muscle strength improvements might lead to a gain in activity. Therefore, both the available muscular performance, and the amount of muscle strength required for a specific activity, have to be taken into account before commencing PRT. If the level of baseline function is too low or too high the treatment effects will probably not benefit the activity even if the treatment has a positive impact on the muscle function level (Figure 10) (38, 45, 155). To improve gait performance other forms of training and treatments can be as beneficial as PRT. In our study the changes in gait performance were not significantly different between the two groups, but there were

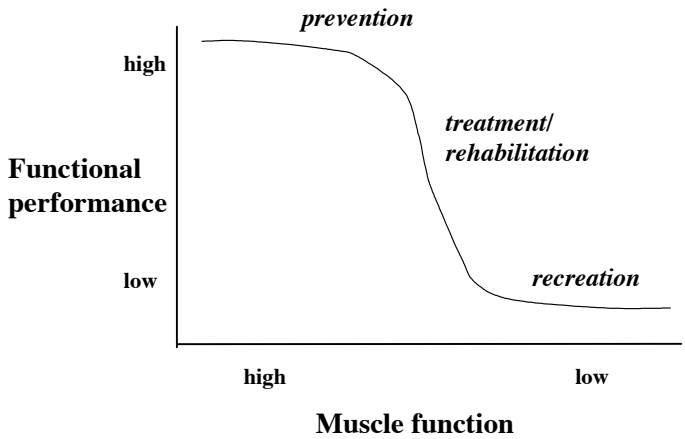

Figure 10. *The nonlinear relationship between muscle function and functional performance and the different effects of exercise.*

differences: for TUG no individual subject in the control group had a change above the limit for a real clinical improvement, even if the improvement on a group level was significant. One possible reason for this non-significant difference between the two groups might be caused by a lower power than calculated. The power analysis was based on the variation found in the two previous reliability studies and the proposed power for the study was a group size of 17 subjects in each group. As many potential subjects were too strong in the lower limb we had difficulties in recruiting enough subjects and the sample size of the control group was therefore reduced.

Another approach is to use PRT in chronic post-stroke fitness training (154). As there were significant improvements in strength for all subjects and there were no adverse effects from PRT, this training approach could be beneficial for post-stroke subject with minor weakness, to maintain and to improve muscle strength. In the long-term, to perform more demanding locomotor tasks, improvements in strength can be important for this group of post-stroke subjects. Richards et al. (23) point out that once walking ability is regained, the ability to perform more difficult mobility tasks might arise: for example jogging and walking on icy surfaces. An interesting aim for future studies would

be to evaluate the effects from strength training on more difficult mobility tasks for those post-stroke subjects who have regained a better gait performance.

Another important factor is to define the optimal practice frequency and duration for a PRT intervention: how many times per week and for how many weeks. Each improvement in strength brings the individual closer to a limiting plateau. In our study there were no signs of any plateau during the PRT, however, a longer intervention might have improved strength even more. For healthy subjects most of the strength increase takes place in the first months (39) but in elderly individuals improvements are seen over a longer period, even if the improvements are generally less in the later phase of training (46).

Could PRT also be used in the acute phase after stroke? Even if there are clear benefits from more active treatment in the acute phase (3, 4), there is no evidence that PRT positively affects post-stroke weakness in the acute phase. Furthermore, there are no accepted guidelines for determining when and how to initiate resistance training after stroke (73). Only a few studies have addressed the effects from lower limb strength training in the acute phase (70, 156, 157). As task related training regimes are important in primary rehabilitation, it would be more difficult to evaluate the single use of PRT, and improvements caused by spontaneous recovery will affect the results.

Have we used the right outcome measurements? Many subjects in the training group verbally expressed large benefits from PRT but this was not always related to measurable changes in gait performance and perceived participation. Positive outcomes regarding physical improvement were reported: feeling stronger with less stiffness, better walking ability, improved endurance and balance. Also, effects on psychological and social factors contributed to the overall positive experience from PRT: feeling better, with improved confidence and the importance of encouragement from other subjects having similar problems who attained the training sessions. In a recent study analysing the qualitative effects from PRT for people with multiple sclerosis (158) comparable results were found. When evaluating the effects from PRT qualitative assessments might have increased our knowledge of the

effects of PRT in a wider perspective of health and should therefore be included in future studies.

Future studies

We now know that PRT can be an efficient way to improve muscle strength post-stroke. In healthy young and old individuals several factors explain gains following PRT: in particular, central nervous activation and changes in muscle morphology, such as increased muscle cross sectional area, and changes in muscular architecture and metabolites (39). Studies are in progress to determine if similar factors can explain the improvements in muscle strength in subjects post-stroke.

It would be beneficial to know whether or not improvements in strength and gait performance can be maintained during the first months after completion of PRT. Improvements in strength might lead to higher activity levels and thereby better retain the improvements over time, or is the loss of strength comparable to what happens in healthy individuals. These are important questions if PRT is to be recommended as part of long-term fitness training after stroke. Such studies are also in progress.

In the present studies no subjects were above age 75 and all subjects were more than six months after stroke onset. Further studies are therefore required to determine the effects of PRT for older subjects and applying them more recently after the stroke onset.

Main conclusions of this thesis

In subjects with mild to moderate chronic post-stroke hemiparesis:

- Knee muscle strength and gait performance can be reliably measured and all tests are sensitive enough to detect a real clinical improvement following an intervention for knee muscle strength and gait performance, for a group of individuals.
- Isokinetic concentric knee muscle strength in the paretic lower limb is significantly related to gait performance, and gait performance is in turn significantly related to perceived participation.
- PRT improves knee muscles strength with no adverse effects. The increase in strength has a positive effect on gait performance, with the largest improvements for those most restricted in gait speed at baseline. Improvements in gait performance are related to positive perception of participation.
- PRT is an effective form of training in chronic stroke patients that can be used both as physiotherapy treatment for those with residual hemiparesis and as fitness training for those with a minor disability.

Populärvetenskaplig sammanfattning på svenska

Det övergripande syftet med denna avhandling var att hos individer med kvarstående muskelsvaghet efter stroke utvärdera effekterna av progressiv styrketräning (PRT) av knäledens sträck- och böjmuskler på muskelstyrka och muskelspänning, men även att analysera om en förbättrad muskelstyrka påverkar gångförmåga och upplevd delaktighet (individens egen upplevelse av hur man fungera i vardagliga situationer).

Stroke är en vanlig sjukdom. I Sverige insjuknar årligen mer än 25 000 personer och mer än 90 000 personer lever med bestående funktionshinder efter stroke. Ett vanligt symtom efter stroke är en halvsidig muskelsvaghet. Detta påverkar individens förmåga att förflytta sig och att kunna gå igen anses som ett viktigt mål efter stroke. Inom rehabiliteringen tränas ofta muskelfunktionen för att individen skall förbättra gångförmågan och därigenom lättare kunna delta i olika vardagliga aktiviteter och fritidsintressen. Efter stroke används olika behandlingsmetoder för att förbättra muskelfunktionen, men PRT har under lång tid ansetts kontraindicerat. Anledningen till detta har varit rädslan för att öka den muskelspänning (spasticitet) som förekommer efter stroke och som indirekt ansetts bidra till muskelsvagheten. Detta synsätt är nu ifrågasatt och orsaken till den nedsatta muskelstyrkan anses idag huvudsakligen vara en verklig svaghet i muskeln.

För att kunna utvärdera effekterna av PRT behövs ökad kunskap om det går att mäta muskelstyrka och gångförmåga på ett reproducerbart sätt. Det behövs även mer kunskap om vilka samband som finns mellan muskelstyrka, gångförmåga och delaktighet hos individer i en kronisk fas efter stroke. I de två första delarbetena har olika mätmetoders reproducerbarhet studerats. Dessa mätmetoder används för att bedöma muskelstyrka i knäets sträck- och böjmuskler samt gångförmåga. I det tredje delarbetet har sambanden mellan styrkan i knäledens sträck- och böjmuskler, gångförmåga och upplevd delaktighet utvärderats. Totalt 50 försökspersoner ingick i dessa delarbeten (medelålder 58 ±6.4 år, 6-46 månader efter stroke) med en kvarvarande muskelsvaghet efter den

första rehabiliteringsperioden. Samtliga individer var självständiga gångare minst 300 m, samt hade en god förståelse för muntlig och skriftlig information. Resultaten visade att mätning av styrkan i knäledens sträck- och böjmuskler samt olika tester av gångförmågan kunde utföras på ett reproducerbart sätt. För varje mätmetod har gränsvärden tagits fram som visar när en förändring är kliniskt säkerställd och dessa värden har sedan använts för att utvärdera träningseffekterna av en intervention. Det fanns även ett starkt samband mellan styrkan i det ben som var mest påverkat efter stroke och gångförmågan samt mellan gångförmågan och personens upplevda delaktighet efter stroke. Både muskelstyrka i knäets sträck- och böjmuskler samt gångförmåga går alltså att mäta på ett reproducerbart sätt och mätmetoderna är tillräckligt känsliga för att kunna utvärdera effekterna av en intervention. Dessutom skulle en förbättring av lårmuskelstyrkan kunna påverka i första hand gångförmågan positivt, men även kunna ha viss effekt på upplevd delaktighet.

I det fjärde delarbetet har effekterna av progressiv styrketräning av knäledens sträck- och böjmuskler undersökts. Studien har genomförts som en enkel-blind randomiserad, kontrollerad studie (relationen 2:1 mellan tränings- och kontrollgrupp). I studien ingick 24 försökspersoner (medelålder 61 ±4.9 år). Det hade förflutit minst 6 månader sedan det akuta sjukdomstillståndet. Alla deltagare hade en muskelsvaghet på mer än 15% (medelvärdet av isokinetisk styrka i knäledens böj- och sträckmuskler), var självständiga gångare minst 200 m och hade en god förståelse för muntlig och skriftlig information. Den progressiva styrketräningen, som var dynamisk, utfördes 2 ggr/vecka under 10 veckor med en belastning på ungefär 80 % av maximala styrka (6-8 reps i 2 set). För att utvärdera resultaten genomfördes mätningar före och efter avslutad intervention. Studien visar att 10 veckors progressiv styrketräning signifikant förbättrade styrkan i knäledens sträck- och böjmuskler utan någon ökning av muskelspänningen. Även gångförmågan förbättrades med den största förbättringen hos de individer som hade den långsammaste gånghastigheten från början. Dessutom fanns ett signifikant samband mellan denna förbättring av gångförmåga och förbättringarna i upplevelsen av delaktighet.

Slutsatsen av detta avhandlingsarbete är att PRT förbättrar muskelstyrkan i knäets sträck- och böjmuskler utan att ge någon ökad muskelspänning. Styrkeökningen påverkar i sin tur gångförmågan positivt, med de största förbättringarna för de individer som är gångare med en nedsatt gånghastighet, och för dessa individer påverkas även upplevelsen av delaktighet positivt. Sammanfattningsvis, PRT är en effektiv träningsform i en kronisk fas efter stroke, som kan användas både som en sjukgymnastisk behandlingsinsats för att öka muskulär styrka, men kan även ingå i allmän fysisk träning och friskvård för de individer som har en liten styrkenedsättning efter stroke.

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